

LEADING CHANGE TO IMPROVE
HEALTH

2012 Research DAY

22nd Annual
USF Health Research Day

Friday, February 24, 2012
8 am until 5 pm

Sponsored By: Morsani College of Medicine, College of Nursing, College of Pharmacy,
College of Public Health, School of Biomedical Sciences, School of Physical Therapy &
Rehabilitation Sciences, and the Department of Internal Medicine



A Timeless Commitment... 22 Years of Celebrating Research

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22nd Annual
RESEARCH DAY
FRIDAY, FEBRUARY 24, 2012
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22nd Annual Research Day

Friday, February 24, 2012

Marshall Student Center (MSC)

AGENDA

07:30a.m. – 08:30a.m.	<u>MSC 2nd Floor Ballroom Lobby Area</u> Registration for Oral Presenters and Posters #1 through #351 Registration for all Judges
07:30a.m. - 09:30a.m.	<u>MSC Hillsborough Room (Rm 2709)</u> Registration for Sunshine Education and Research Center and The Villages High School presenters Continental Breakfast
08:30a.m. – 10:30a.m.	<u>MSC Oval Theater</u> 3 rd Annual Joseph Krzanowski, PhD USF Health Invited Oral Presentations Session
09:00a.m. – 10:30a.m.	<u>MSC Honors Room (Rm 2703)</u> Office of Undergraduate Research Presentation Session to The Villages High School Students
07:30a.m. – 10:00a.m.	<u>MSC 2nd Floor Ballroom</u> Poster set up
10:30a.m. – 12:00p.m.	Poster Presentation Judging Session
08:30a.m. – 10:00a.m.	<u>MSC Hillsborough Room (Rm 2709)</u> Poster set up
10:30a.m. – 12:00p.m.	Sunshine Education and Research Center and The Villages High School Poster Presentation Session
12:00p.m. – 01:00p.m.	<u>MSC Hillsborough Room (Rm 2709)</u> Lunch for Presenters and Judges (attendance badge required)
01:00p.m. – 04:00p.m.	<u>MSC 2nd Floor Ballroom & Hillsborough Room</u> Posters available for viewing

MSC Oval Theater

01:00p.m. – 01:15p.m. Special Recognition: Distinguished USF Health Professorships

01:15p.m. – 02:15p.m. 16th Annual Roy H. Behnke Distinguished Lectureship

Stephen B. Liggett, MD, University of Maryland
“Personalized Medicine for Asthma: Role of Viral Genomic Variation”

02:15p.m. – 03:15p.m. Awards Ceremony

- *Best Graduate Student Oral Presentation Award*
- *The Watson Clinic Award to a Fourth Year Medical Student*
- *Dr. Christopher P. Phelps Memorial Fund Annual Morsani COM Graduate Student Travel Award*
- *Best Resident/Fellow Poster Presentation*
- *Best Postdoctoral Poster Presentation*
- *Best Pediatric Children’s Health Poster Presentation*
- *Outstanding Poster Presentation Awards by Category*

Spirit Room (Rm 2707)

02:30p.m. – 03:30p.m. Sunshine ERC Meetings
Dr. Bernard lecture

MSC 2nd Floor Ballroom Lobby Area

03:30p.m. – 04:30p.m. Reception

MSC 2nd Floor Ballroom and Hillsborough Room

04:00p.m – 04:30p.m. Remove Posters

From the Desk of:

Phillip J. Marty, PhD

Associate Vice President, USF Health
Vice Dean for Research, Morsani College of Medicine
Professor, Public Health and Medicine



Dear USF Health/University Community:

This year marks the 22nd "USF Health Research Day" Anniversary that highlights the research work of our students, trainees, staff and faculty across USF Health. This is another banner year for participation from across USF Health and the University. We have several high school students presenting this year, with 16 coming from The Villages High School. The Villages is a community near Ocala, FL in which USF Health has developed a number of health promotion initiatives. We welcome the first College of Pharmacy presenters and the Sunshine Education and Research Center Section members as well as a record number of undergraduates. With the involvement of participants from multiple units within USF Health and across campus, USF Health Research Day has been transformed into a truly USF-wide celebration. This year a total of 361 presentations will be delivered which is up from 260 last year. From this total, ten student abstracts have been selected for oral presentation to be held during the morning of Research Day.

Another important aspect of our Research Day Program is the Annual Roy H. Behnke Distinguished Lectureship. Dr. Behnke, an early faculty member of the College of Medicine and founding chair of the Department of Internal Medicine, was a nationally recognized medical educator and consummate physician. His family established this lectureship to further research at USF Health and to invite an internationally recognized Health expert to provide the Research Day keynote address on a topic of special relevance to USF Health's students, trainees, staff and faculty. This year, Stephen B. Liggett, MD, will be delivering "Personalized Medicine for Asthma: Role of Viral Genomic Variation." Dr. Liggett is Professor of Medicine and Physiology, Director of the Cardiopulmonary Genomics Program, and Associate Dean for Translational Research at the University of Maryland, School of Medicine. Dr. Liggett is an internationally recognized leader in the field of G-protein coupled receptor biology, congestive heart failure, and asthma.

In the afternoon of Research Day, we not only hold the Behnke Distinguished Lectureship, but also recognize the most noteworthy presentations of our students and trainees through an awards ceremony. Individual awards for 4th year medical student, pre-doctoral, resident/ fellow, child health, and neurosciences student awards will also be given. At this event, we will also recognize recipients who were promoted to Distinguished USF Health Professor in 2011.

With this 22nd Anniversary of Research Day, we continue to acknowledge the importance and value of research to USF Health and the University. Our goal is to continue to recognize, grow and enhance the research efforts of our students, trainees, staff and faculty. Our USF Health community has been instrumental in the continuing growth of research at the University of South Florida. We are committed to the goal of expanding the University's growth and quality of research. Research Day is but one of those special events during the year that recognizes the hard work of all our researchers and especially our students and trainees, and the great contribution they are making to the scientific advancement of their disciplines. It is an important day for this purpose and one we hope you will enjoy.



22nd Annual RESEARCH DAY

SPONSORS

- ❖ Morsani College of Medicine
- ❖ College of Nursing
- ❖ College of Pharmacy
- ❖ College of Public Health
- ❖ School of Biomedical Sciences
- ❖ School of Physical Therapy and Rehabilitation Sciences
- ❖ Department of Internal Medicine, Morsani College of Medicine



A Special Thanks to our Patron Sponsors:





**22nd Annual
RESEARCH DAY**

*16th Annual
Roy H. Behnke Distinguished Lectureship*



PLACE:

Marshall Student Center- Oval Theater

TIME:

1:00p.m.

SPEAKER:

Stephen B. Liggett, MD,
Associate Dean for Interdisciplinary Research
University of Maryland School of Medicine

TITLE:

"Personalized Medicine for Asthma: Role of Viral Genomic Variation"

Sponsored by:

Department of Internal Medicine, Morsani College of Medicine, USF

*16th Annual Roy H. Behnke Distinguished
Lectureship
Keynote Speaker*



Stephen B. Liggett, M.D.
Associate Dean for Interdisciplinary Research
Cardiopulmonary Genomics Program



Personal History

Dr. Liggett obtained a B.S. in Physics from the Georgia Institute of Technology and an M.D. from the University of Miami School of Medicine. He served an Internship, Residency (Internal Medicine) and Fellowship (Pulmonary, Critical Care Medicine) at Washington

University School of Medicine/Barnes Hospital in St. Louis. These were followed by a four year, laboratory-based post-doctoral fellowship at the Howard Hughes Medical Institute at Duke University in the laboratory of Robert Lefkowitz. He subsequently became an Assistant Professor of Medicine and Pharmacology at Duke University, and then Professor of Medicine, Pharmacology and Molecular Genetics at the University of Cincinnati College of Medicine, where he was also Director of Pulmonary and Critical Care Medicine. After 13 years as Division Director, he became the Taylor Endowed Professor of Medicine and Director of the Cardiopulmonary Research Center at UC, where he concentrated on his basic and translational research programs. In 2005 he moved to the University of Maryland School of Medicine, where he is Professor of Medicine and Physiology and Director of the Cardiopulmonary Genomics Program.

Research Interests

The laboratory has 5 major interrelated sections: 1) the study of the molecular basis of G-protein coupled receptor structure and function, 2) delineation and characterization of human genetic variants within this receptor signaling network, 3) association studies of genetic variants with heart and lung disease and their response to treatment to develop a platform for genetically-based personalized medicine, 4) creation of genetically modified mice to define the mechanisms of heart and lung disease and "humanized mice" to explore the effects of genetic variation of human genes, and 5) determination of the full genome sequences of human Rhinoviruses using high throughput next-generation sequencing technologies; analysis of the relationships between viral genomes and asthma phenotypes. These studies have led to new paradigms in our understanding of how this superfamily of receptors (the largest in the human genome) carry out signaling, how they participate in the pathophysiology of congestive heart failure and asthma, and how a patient's genetic makeup can be used to tailor drug treatment.



ADMINISTRATION

Stephen K. Klasko, MD, MBA

Senior Vice President, USF Health
Dean, Morsani College of Medicine

Phillip J. Marty, PhD

Associate Vice President,
USF Health Office of Research
Vice Dean for Research,
Morsani College of Medicine
Professor, Public Health, Internal Medicine,
Psychiatry and Neurosciences

Donna J. Petersen, MHS, ScD

Senior Associate Vice President,
USF Health Dean, College of Public Health

Dianne Morrison-Beedy, PhD, RN,
FNAP, FAANP, FAAN

Dean, College of Nursing

Kevin Sneed, PharmD

Dean, College of Pharmacy

William S. Quillen, PT, PhD, SCS,
FACSN

Associate Dean and Director,
School of Physical Therapy and
Rehabilitative Sciences



ADMINISTRATION

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President, USF

Ralph Wilcox, PhD

Provost & Executive Vice President

Karen Holbrook, PhD

Senior Vice President for Research,
Innovation and Global Affairs



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Committee on Research
2011-2012**

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Chairman Committee on Research

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Molecular Medicine

Kevin Nash, PhD

Molecular Pharmacology and Physiology

Dahui Qin, MD, PhD

Oncologic Sciences

Wenlong Bai, PhD

Pathology & Cell Biology

Jaya Padmanabhan, PhD

Molecular Medicine

DEAN'S APPOINTMENTS (AT LARGE)

Carmelina Gemma, PhD

Neurosurgery & Brain Repair

Edwin Weeber, PhD

Molecular Pharmacology & Physiology

Svitlana Garbuzova-Davis, PhD

Neurosurgery & Brain Repair

Angel Luciano, MD

Pediatrics

Branko Miladinovic, PhD

Clinical Translational Science

Andreas Seyfang, PhD

Molecular Medicine / Neurosurgery & Brain Repair

Kay-Pong Yip, PhD

Molecular Pharmacology & Physiology

CLINICAL SCIENTISTS

Alberto Chiappori, MD

Oncologic Sciences

Srinivas Nagaraj, PhD

Internal Medicine

Prasad Kulkarni, MD

Internal Medicine

Carina Rodriguez, MD

Pediatrics

LEHIGH VALLEY PARTNERSHIP:

Jeffrey Etchason, MD

LVHN / Internal Medicine

SCHOOL OF PHYSICAL THERAPY & REHABILITATION SCIENCES:

Seok H. Kim, PT, PhD

Physical Therapy & Rehabilitation Sciences

OTHER COMMITTEE MEMBERS

Phillip J. Marty, PhD

Associate VP for Research, Ex Officio



COLLEGE OF NURSING

Research Committee

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Associate Dean for Research and Innovation

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Sue Ann Girling, BSAS

Rajendra Kadel, MS

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COLLEGE OF PUBLIC HEALTH

Research Innovation & Creativity for Health (RIChes)

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Linda Detman, PhD
Anne Gallacher, MA
Ellen Kent, MPH, CPH
Russell Kirby, PhD, MS
Mihaela Madsen, BA
Wilbur Milhous, PhD
Paul Mulrenin, BA
Betty Persky
Etienne Pracht, PhD
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Judy Sommers MBA
Amy Stuart, PhD
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Arthur Williams, PhD
Jay Wolfson, DrPH, JD
Yiliang Zhu, PhD





22nd Annual **RESEARCH DAY**

STAFF ACKNOWLEDGEMENTS

USF Health Office of Research

Cheryl Lesko
Christine Tam
Carolyn Mercurio
Charmaine Disimile
Stephanie Warburton



USF Health Communications

Anne Delotto Baier
Elizabeth Peacock
Eric Younghans
Sarah Worth



Morsani College of Medicine Office of Research

Jo Ann Moore
Matt Anderson
Lindsay Guntner
Heather Clark
Erin Bhagvat
Charles Szekeres
Byeong (Jake) Cha



Morsani College of Medicine Signature Interdisciplinary Programs

Lauren Masem



STAFF ACKNOWLEDGEMENTS, CONT'D

Morsani College of Medicine Office of Clinical Research

Kimberlea Hauser
Catherine Jahrsdorfer
Liz Klingelhofer



Morsani College of Medicine Information Systems

Moayad Alzoubi
Ernest Leong
Eduardo Mendez



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Mike Masem



College of Pharmacy

Christopher Noel



College of Public Health

Ellen Kent



College of Nursing

Kelly Sullivan



USF Undergraduate Research Office

Lisa Piazza
Dr. Richard Pollenz





22nd Annual **RESEARCH DAY**

POSTERBOARDS

Location:	Marshall Student Center 2 nd floor Ballroom
<u>Set up:</u>	7:30a.m. – 10:00a.m.
<u>Judging:</u>	10:30a.m. -12:00p.m.
<u>Tear down:</u>	4:00p.m. – 4:30p.m.
Poster Size:	4 ft. by 6 ft.

JUDGING OF POSTERS

Student posters will be judged by faculty members.

Students ***must be present*** at their poster to be eligible for judging.

Posters will be judged on:

1. Presentation of poster

- Organization
- Readability
- Appearance
- Sense Appeal

2. Presentation of data

- Oral Communication

3. Knowledge of subject

- Question and answer presentation

AWARD CEREMONY

Student Winners will be announced at the Awards Ceremony
following the USF Health Keynote Lecture

Poster Presentations

10:30a.m. – 4:00p.m.



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Research Day

Listing of Presenters and Titles

Oral Presentations

Abs #	Name	Title
O-1	Naif, Athar	Polymorphisms in Folate Pathway Genes and Response to Methotrexate Treatment in Rheumatoid Arthritis
O-2	Bakour, Chighaf	Obesity and Childhood Asthma: Does Breastfeeding Make a Difference? Analysis of Data from the 2007-2008 NHANES
O-3	Michael, Ryan	Source Attribution of Atmospheric Mercury Deposition to Tampa using Positive Matrix Factorization
O-4	Bailey, Antoinette	Aberrant T-lymphocyte Development and Function in Mice Overexpressing Human Secreted Amyloid Precursor Protein Alpha: Implications for Autism
O-5	Trotter, Justin	Coordinated Regulation of Dab1 by Fyn and Cdk5
O-6	Mallela, Jaya	Natriuretic Peptide Receptor-A (NPRA) Signaling Modulates Tumor Angiogenesis
O-7	Contreras, Jessika	Screening Novel p75NTR targeted compounds that inhibit invasion for anti-angiogenic effect
O-8	Nichols, Gina	Expression of BRCA1 Protein in Human Ovaries
O-9	Alijubran, Salman	Enhancer of Zeste Homolog 2 induces Pulmonary Artery Smooth Muscle Cell Proliferation
O-10	Zhang, Xiaohui	Pathologic Features of Concurrent Clonal T-cell Large Granular Lymphocytic Expansion and Myelodysplastic Syndromes



Allergy, Immunology and Infectious Diseases Research

Abs #	Name	Poster Title
1	Alexander, Lou-Ella M.M.	PRDM1/Blimp-1 Regulates Expression of Transcriptional Elongation Factor ELL3 in B-Cell Differentiation
2	Boyapalle, Sandhya	Regulation of the Host Innate Immune Response by Respiratory Syncytial Virus (RSV) Nonstructural Protein 1
3	Cox Jr., Ruan	Resolvin Inhibits the Cryopyrin/NLRP3 Inflammasome
4	Cronin, Kevin	HDAC Inhibitor Mediated Alterations in Peptide Occupancy of HLA-DR Molecules
5	Flores-Torres, Jaime	An Unconventional Look at Microbial Dysbiosis in the Gut
6	Fukumoto, Jutaro	Deletion of NALP3 Protects Against Hyperoxia-induced Acute Lung Injury
7	Kratzer, Stella	Regulation of Mitosis in the AIDS Pathogen, <i>Toxoplasma gondii</i>
8	Lima, Amorce	Attenuated Virulence of <i>B. henselae</i> Mutants in the Zebrafish Embryo Model
9	Nelson, Allison	MHC II Retrograde Signaling in MDSC
10	Pantry, Shara	Isolation and Sequencing of an Unrelated Strain from a Patient with Inherited Human Herpesvirus-6
11	Recio, Jesus	Leukemia Inhibitory Factor Protects Oligodendrocytes from Ischemia through Akt Signaling Enhancing Antioxidant Gene Expression
12	Seifert, Hilary	A Transient Decrease in Spleen Size Following Stroke Corresponds to Splenocyte Release into Systemic Circulation
13	Teng, Michael	Inhibition of AKT Kinase Activity Decreases Replication of Human Respiratory Syncytial Virus
14	Tu, Nhan	Regulation of Gene Expression in <i>Bartonella Henselae</i> by the General Stress Response
15	Wang, Jia-Wang	miR-150 Inhibits Inflammation by Suppressing NKT Cells and Cytokine Production
16	Wong, Terianne	Respiratory syncytial virus (RSV)-Infected Elderly Mice Exhibit Impaired Expression and Activation of Pattern Recognition Receptors (PRR)
17	Venugopal, Rajan Babu	Mitochondrial Uncoupling protein-2 regulates NLRP3 Inflammasome



Cancer Biology Research

18	Barrios, Kelly	Development of Novel and Effective Therapeutic Peptide Vaccines against HPV-Induced Tumors
19	Clark, Whalen	ADAM17-Mediated Cleavage Is Required For HPP1-Associated Tumor Suppression In Colorectal Cancer
20	Cruz, Alex	Optimizing Radiation Treatment Planning for Neuroendocrine Tumors with 3D Molecular/Anatomic Imaging
21	Davis, Yvonne	Growth of Cancer cells on a Functionalized Multilayered Nanofibrous Scaffold
22	Frantz, Jean Louis	Bone Marrow-derived Mesenchymal Stem Cells Restored Tumorigenesis in Natriuretic Peptide Receptor A Knockout (NPRA-KO) Mice

- 23 Frost, Chelsea Novel Dual Inhibitors of Vascular Endothelial Growth Factor and VEGFR2 Receptor
- 24 Kasiappan, Ravi 1,25-dihydroxyvitamin D3 prevents obesity associated ovarian cancer through miR-498 induction and the suppression of estrogen induced telomerase activity
- 25 Monta, Raphael Antitumor Activity of Genetically Modified Dendritic Cells
- 26 Nelson, Nadine The Role of the Ikaros Family in Murine Pancreatic Adenocarcinoma
- 27 Pathak, Ravi Bioinformatic Analysis Correlates PTEN Loss with Oncogenic Potential of Lung Epithelial Cells
- 28 Pina, Yolanda Impact of 2-deoxy-D-glucose on Molecular Genomics Expression and as Adjuvant to Chemotherapy in the Treatment of Retinoblastoma
- 29 Schickler, Robyn Expression of Cytokeratin 19 (CK-19) in peripheral blood of women undergoing In Vitro Fertilization (IVF): a preliminary study
- 30 Woods, David Melanoma Progression is Inhibited by the Histone Deacetylase Inhibitor LBH589 by Direct Tumor Effects and Enhancement of the Immune Response
- 31 Zgheib, Nadim Bou MK2206, a Selective AKT Inhibitor, Modulates Ovarian Cancer Cell Line Sensitivity to Carboplatin Plus Paclitaxel



Cardiovascular Research

- 32 Ramanathan, Gurukumar K. Novel Role of Mir-17 in Pulmonary Arterial Hypertension
- 33 Shahaduzzaman, Md Fractalkine (CX3CL1) may be associated with human umbilical cord blood (HUCB) cell mediated neuroprotection in acute ischemic stroke
- 34 Snyder, Madeline Cardiac Dysfunction Exacerbated by Endocrinopathies in Friedreich's Ataxia



Chart Reviews and Other Case Studies

- 35 Alberdi, Taylor Subcutaneous Hizentra® (20%) is Better Tolerated and Shares Similar Efficacy Compared to Subcutaneous Vivaglobin® (16%).
- 36 Ashraf, Noman Does 18-Fluorodeoxyglucose (FDG) Uptake By Positron Emission Tomography/Computed Tomography (PET/CT) Predict Survival in Advanced Pancreatic Cancer; A Single Institution Experience
- 37 Aslam, Sadaf Diabetic Nephropathy Develops Naturally in Non Human Primates: Similarities to Humans
- 38 Baillargeon, Alicia Utility of MRI in Diagnosis and Treatment response in Eosinophilic Fasciitis (WITHDRAWN)
- 39 Baumgarten, Adam Perioperative Blood-sparing Intravascular Occlusive Balloons during Primary and Revision Total Hip Replacement
- 40 Butt, Ahmed An Unusual Reaction to Intravenous Iron Sucrose
- 41 Chacko, Sharon Group Prenatal Care at Neighborhood Health Centers of the Lehigh Valley
- 42 Chan, Isabella Vaginal Birth After Cesarean (VBAC): Provider Perspectives and Maternal Decision-Making
- 43 Chuong, Michael Definitive IMRT-based Chemoradiation for Treatment of Squamous Cell Carcinoma of the Anal Canal

- 44 Clayman, Eric Silent, Pain-free Needle Punctures – The Resealing of Surgical Gloves After Puncture May Jeopardize the Health Care Provider
- 45 Cruz, Victor Adult-Onset Henoch-Schonlein Purpura: A Case Report with Unusual Manifestations.
- 46 Culverhouse, Susan Idiopathic Isolated Orbital Angioedema
- 47 Deneve, Jeremiah Predictors of Outcome in Patients with Recurrent Gastrointestinal Stromal Tumors
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- 49 Domingo, Gelenis Two Red Herrings and a Sweet Catch
- 50 Frohman, Heather Prosthetic H-Graft Portacaval Shunts (HGPCS) Versus Transjugular Intrahepatic Portasystemic Stent Shunts (TIPS): 18-Year Follow-up of a Randomized Trial
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- 52 Henderson-Jackson, Evita Cystic Prostatic Ductal Adenocarcinoma: An Unusual Presentation and Cytological Diagnosis
- 53 Jennette, Kyle Association of Rey Auditory Verbal Learning Test (RAVLT) with Depression and Anxiety in Patients with Multiple Sclerosis
- 54 Kennedy, Alyssa Soluble Immune Activation Markers and the Early Initiation of ART in HIV –infected Adolescents
- 55 Kent, Robert Case study of five patients with severe TBI's that underwent hyperbaric oxygen treatment
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- 58 Kresak, Jesse Primary CNS-Hodgkin's Lymphoma: Case Series and Review of the Literature
- 59 Lambert, Crystal Predicting Factors that Influence Cervical Cancer Screening in HIV-Infected Women: Using the Health Belief Model
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- 68 Nyanda, Hoka Tamoxifen for the Treatment of Severe Keloids; A Case Report and Review of the Literature
- 69 Paghdal, Kapila 308 nm Excimer Laser with Concomitant Topical Calcipotriene for the Treatment of Segmental Vitiligo
- 70 Parekh, Anand Rapidly Growing Mycobacterium Infections in Cancer Patients
- 71 Parkerson, Jim A Case Of Multiple Simultaneous Urticarial Syndromes Refractory to Treatment
- 72 Patel, Midhir Paired Bilateral Internal Carotid Artery Aneurysms: An Imaging Review
- 73 Patel, Nishit Depigmentation Therapy in Vitiligo
- 74 Pepper, Andrew Outcome of Lower-Limb Preservation with an Expandable Endoprosthesis After Bone Tumor Resection in Children
- 75 Perez, Matthew Angiosarcoma of the Head and Neck: The Moffitt Cancer Center Experience
- 76 Perrone, Michael Birmingham Hip Resurfacing in the Severely Obese
- 77 Puckett, Judith Analysis of the Factors Influencing Breast Cancer Care Among Female Veterans
- 78 Rodriguez, Ariel Metabolic Surgery in Patients with End-Stage Renal Disease: A report of our case series
- 79 Sabucedo, Alberto Adult Case of Henoch-Schönlein Purpura (HSP): Possibly Secondary to Generic Lisinopril
- 80 Sajjad, Monique Bevacizumab Shows Regression of Brain Metastases and Prolonged Survival in 3 patients with Breast Cancer (WITHDRAWN)
- 81 Schilling, Eric IL-2 Induced Tachy-Brady Syndrome
- 82 Schocken, Dawn VHA Women's Health Mini Residency
- 83 Shah, Ankit Abnormal Cerebral Hemosiderin Deposits on Magnetic Resonance Imaging in a patient with pseudopapilledema
- 84 Simon, Ross Pressure Ulcer Prevalence Among the Spinal Chord Injury Population
- 85 Talreja, Neetu Diffuse Idiopathic Pulmonary Neuroendocrine Hyperplasia with Corticosteroid Dependent Asthma
- 86 Verdin, Lindsey Calvarial Metastatic Melanoma: A Case of an Enormous Exophytic Mass in an Asymptomatic Patient
- 87 Villafranca, Arnaldo Insulin-Induced Lipoatrophy in a Patient using Continuous Subcutaneous Insulin Infusion (CSII): A Case Report and Literature Review
- 88 Vyas, Nikki Mycophenolate Mofetil as a First-Line Steroid-Sparing Agent in the Treatment of Pemphigus Vulgaris
- 89 Waseem, Hena Neurological Manifestations and Human Parvovirus B19: Historical Perspective and Analysis

- 90 Weiss, Amy What Reasons do Adolescents Give for Presenting to the Emergency Department over their Primary Care Provider?



Clinical Science Research

- 91 Creelan, Ben A GM-CSF-Producing & CD40L-Expressing Cell Line Combined with Allogeneic Tumor Antigen as a Novel Vaccine for Metastatic Lung Adenocarcinoma: a Phase II Trial
- 92 Elizalde, Araceli Assessment of Repeated Measures of Fractional Exhaled Nitric Oxide in Clinically Stable Persistent Asthma
- 93 Fitzhugh, David Photoaging Attenuates Skin Test Response to Histamine More Than Natural Aging
- 94 Fluman, Sarah The Role of Glutathione in Chronic Ischemic Wounds in the Elderly
- 95 Gong, Xiaoming Regulation of Antioxidant Responses in Prostate Cancer: Effects of Lycopene
- 96 Horne, Danielle Hybrid Endovascular Exclusion of Aberrant Right Subclavian Artery Aneurysms
- 97 Hudey, Stephanie Antiretroviral Therapy (ARV) Fails To Correct B Cell Activation in Both Behaviorally-Acquired (BAH) and Perinatally-Acquired HIV-Infected (PAH) Cohorts
- 98 Lomas IV, Harry Post Chemoradiation SUV is Highly Predictive of Disease Free Survival and Overall Survival in Esophageal Cancer
- 99 Lunn, Jason Digital Holographic Adaptive Optics for Retinal Imaging
- 100 McGuire, Joseph The Role of Dysregulation in Pediatric Obsessive-Compulsive Disorder
- 101 Peir, Gene Safety and Experience of Research Lumbar Punctures in Parkinson's Disease Patients
- 102 Restrepo, Daniel Compatibility of Heparin with Ethanol for Ethanol-Lock Therapy of Central Venous Catheters
- 103 McQueen Margaret Elisa Maternal Smoking Hastens Telomere Shortening in Neonatal Umbilical Cord
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- 105 Zadikany, Ronit μ Opioid Receptors in the Enteric Nervous System



Education Research

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- 107 Graham, R. David The Business of Medicine Bootcamp – Bridge Clinic Collaboration
- 108 Greenblum, Catherine Revising Proposed Silver Alert Legislation Based on New Research Findings
- 109 Hughes, Shana Teens, Communication Technology, and New Avenues for STD Prevention
- 110 Schnaus, Michael Predicting Medical Student Surgical Career Choice: Uni- and Multi-variate Analyses of Career Choice Variables



Evidence Based Study Design and Outcomes Research

- | | | |
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| 111 | Arnold, Elysse | Cognitive-Behavioral Treatment for Anxiety Disorders in Children with Autism Spectrum Disorders |
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3rd ANNUAL

JOSEPH KRZANOWSKI, PhD

USF HEALTH

INVITED

ORAL PRESENTATIONS SESSION

Polymorphisms in Folate Pathway Genes and Response to Methotrexate Treatment in Rheumatoid Arthritis

Athar K. Naif ⁽¹⁾, Aakash R. Patel ⁽¹⁾, Xiao-Lan Mo ^(2,3), Xiao Chen ⁽²⁾, Jun Liang ⁽¹⁾ and Shufeng Zhou ⁽¹⁾ ⁽¹⁾ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa ⁽²⁾ Department of Pharmacy, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China ⁽³⁾ School of Pharmaceutical Sciences, Sun Yat-Sen University, Guangzhou, China University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Polymorphism, folate pathway, methotrexate, rheumatoid arthritis

Objective: Rheumatoid arthritis (RA) is a chronic systematic autoimmune disease that involves the inflammation of multiple joints. In this study, we aimed to study the impact of SNPs in folate pathway-related genes including RFC1, FPGS, GGH, MDR1 and MTHFR to MTX response in RA patients.

Methods: A total of 113 Chinese RA patients were recruited, and categorized into good and poor responders to MTX based on disease activity score. A patient was classified as a good responder when both the tender joint count and the swollen joint count were greater than 20% improved from baseline after at least three months therapy and at least three of the following criteria were met: visual analog scale (VAS) lesser than 20 mm, greater than 20% improvement in ESR, in physician's global assessment of disease activity, in patient's global assessment of disease activity, and in the health assessment questionnaire (HAQ). A total of 6 SNPs from the above five genes were genotyped and tested for association with MTX response using χ^2 test, logistic regression along with clinical variables, and gene-gene interaction analysis using multifactor dimensionality reduction.

Results: The probability of remission of RA symptoms was about 1.4-fold higher in carriers of the MDR1 3435TT genotype as compared to patients with the 3435CT genotype ($P = 0.020$; OR = 1.368; 95% CI = 1.160~1.614). There was a likely interaction between SNPs in the RFC1 and MTHFR genes.

Conclusion: The results from the present study suggest that the polymorphism of MDR1 3435C>T may influence the efficacy of RA therapy with MTX in Chinese RA patients.

Obesity and Childhood Asthma: Does Breastfeeding Make a Difference? Analysis of Data from the 2007-2008 NHANES

Chighaf Bakour, MD MPH; Skai W Schwartz, PHD; Tiffany Lee, BS. University of South Florida, College of Public Health, Dept. of Epidemiology & Biostatistics

Keywords: Asthma, breastfeeding, BMI, interaction

Objective: To examine whether breastfeeding or its duration modify the association between BMI and the prevalence of asthma in children six years of age or under.

Methods: This study analyzed a nationally representative sample of 994 children aged 2–6 years from the National Health and Nutrition Examination Survey 2007-2008. Logistic regression was used to examine whether BMI and breastfeeding are independently associated with asthma after controlling for covariates. We also examined the interaction between BMI and any breastfeeding and between BMI and breastfeeding duration.

Results: Being overweight (BMI \geq 85% for age) was significantly associated with the diagnosis of asthma by age six after adjusting for important covariates (OR=2.14, 95% CI 1.12, 4.11). Any breastfeeding was not significantly associated with asthma, but breastfeeding duration (as a continuous variable) had a protective effect that remained significant after adjusting for covariates (OR=0.92, 95% CI=0.87, 0.98) so was exclusive breastfeeding duration (OR=0.88, 95% CI 0.78, 1.0). The effect of overweight on asthma was significant and more prominent in children breastfed for < 6 months (OR= 3.18, 95% CI 1.13, 8.93) than for those breastfed for \geq 6 months (OR=1.62, 95% CI 0.57, 4.63). Compared with normal weight children breastfed for \geq 6 months, overweight children breastfed for < 6 months had a significantly higher risk of asthma by age six (OR=5.0, 95% CI 1.83, 13.64)

Conclusion: Results of this study suggest that while children under six who are overweight are generally at a higher risk of asthma, those who have been breastfed for \geq 6 months do not seem to be affected by this increased risk. Extended breastfeeding appears to reduce the effect of increased BMI on the risk of asthma.

Source Attribution of Atmospheric Mercury Deposition to Tampa using Positive Matrix

Factorization. Ryan Michael, Amy L. Stuart, Maya A. Trotz, and Fenda Akiwumi, University of South Florida, Tampa, Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: Positive Matrix Factorization, source apportionment, mercury deposition

Objective: Air emissions and subsequent deposition provide an important source pathway for human exposures to mercury throughout the world. However, substantial uncertainties exist in attributing deposition levels to local versus long-range emission sources. Here, we investigate the deposition and sources contributing to mercury loading in the Tampa Bay region.

Methods: Positive matrix factorization (PMF) receptor analysis was applied to one year of special precipitation event data from the Bay Regional Atmospheric Chemistry Experiment, for a site in Tampa, to apportion source influence types.

Results: An 11-factor model was found to account for maximum uncertainties in the 25-species dataset. Eleven unique source profiles were identified as contributing to the species masses observed in the dataset. Three sources were found to account for greater than 90% of mercury species mass observed in the dataset. Municipal and medical waste incineration and coal fuel combustion sources accounted for mercury mass deposition.

Conclusion: PMF receptor analysis indicates significant influences from medical and municipal waste incinerators and utility coal boilers, with a much smaller contribution from a likely traffic-related source. Taken in the context of the local emissions inventory data, these results suggest substantial contributions to area mercury wet deposition from sources in Florida and local to the Tampa Bay region.

Aberrant T-lymphocyte Development and Function in Mice Overexpressing Human Secreted Amyloid Precursor Protein Alpha: Implications for Autism.

Antoinette R. Bailey, Huayan Hou, Demian F. Obregon, Jun Tian, Yuyan Zhu, Qiang Zou, William V. Nikolic, Michael Bengston, Takashi Mori, Tanya Murphy and Jun Tan. University of South Florida, Morsani College of Medicine, Dept. of Cardiology

Keywords: T-lymphocytes, sAPP-alpha, autism, transgenic mice, cytokines

Objective: Our goal with this study was to identify any abnormalities in T-lymphocyte development and function that may be associated with over-expression of secreted amyloid precursor protein alpha (sAPP- α). Elevated levels of sAPP- α have recently been observed in autistic patient plasma and there are reports of T-lymphocyte abnormalities in autistic patients as well.

Methods: We designed and generated transgenic mice that over-express human sAPP- α in the brain, plasma, and other organs. Brain and plasma levels of sAPP- α , as well as splenocyte-secreted cytokine levels, were measured by ELISA. We used flow cytometry to investigate precursor and mature T-cell populations in the thymus and spleen. Lastly, molecular biology and immunohistochemistry techniques were used to observe apoptosis in transgenic mouse thymus and zeta-chain-associated protein kinase 70 (ZAP-70) expression in the spleen.

Results: We found that splenocytes from transgenic mice secreted increased levels of pro-inflammatory cytokines interferon gamma (IFN- γ), interleukin 2 (IL-2) and IL-4 after T-cell mitogen stimulation. The mice exhibit increased CD8⁺ T-cell populations in the spleen, and abnormal precursor cell populations in the thymus. Apoptotic signaling proteins are expressed at greater levels in sAPP- α mouse thymus. Finally, after secondary immune challenge, splenocytes from sAPP- α mice produced reduced levels of pro-inflammatory cytokines and decreased ZAP-70 expression.

Conclusion: Given our findings, we conclude that high expression of sAPP- α is associated with abnormal T-lymphocyte populations, development and function. This may explain the T-lymphocyte abnormalities seen in autism patients.

Research supported by: The Silver Foundation

Coordinated Regulation of Dab1 by Fyn and Cdk5

Justin H. Trotter, Irina Filonova, and Edwin J. Weeber USF Health Byrd Alzheimer's Center

Department of Molecular Pharmacology and Physiology University of South Florida, University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: Dab1, Cdk5, dendritic spine, phosphorylation

Objective: Binding of Reelin to the lipoprotein receptors ApoER2 and VLDLR stimulates activation of Src family kinases (SFKs) and tyrosine phosphorylation of Dab1 at several sites (Y185, Y198, Y220, and Y232). Tyrosine-phosphorylated Dab1 then activates numerous downstream effectors that are largely responsible for the modulation of synaptic function by Reelin. Dab1 is also phosphorylated by cyclin-dependent kinase 5 (cdk5) at 2 sites (S400 and S491) independent of Reelin. Understanding how Dab1 phosphorylation dynamics are regulated by fyn (an SFK member) and cdk5 will enhance our current understanding of the Reelin signaling pathway in normal and diseased brains.

Methods: Using a novel phos-tag assay, we have determined that Dab1 can exist as multiple phosphospecies in vitro and in vivo, each of which may have unique signaling capabilities. We evaluated the role of cdk5- and fyn-mediated phosphorylation of Dab1 in its sub-cellular trafficking, processing of upstream receptors (i.e. ApoER2 and APP) and formation of dendritic spines in vitro.

Results: We have found that Dab1 is constitutively-phosphorylated at S491 and that all tyrosine-phosphorylated Dab1 species are phosphorylated at this site. The neuronal activators of cdk5, p25 and p35, differentially affected Dab1 serine and tyrosine phosphorylation. In primary cortical cultures we found that Dab1 phosphorylation and trafficking could be modulated by neuronal activity. We further found that Dab1 phosphoisotypes differentially affected receptor processing (i.e. APP and ApoER2) and dendritic spine formation.

Conclusion: Collectively, our data support a model wherein normal synaptic function requires coordinated regulation of Dab1 phosphorylation by both the Reelin/SFK and cdk5 pathways.

Natriuretic Peptide Receptor-A (NPRA) Signaling Modulates Tumor Angiogenesis

Jaya Mallela^{1,2,4}, Frantz Jean Louis^{1,2,3,4}, Vignesh Chinnasamy^{1,2,4}, Ujjwalasree Garapati^{1,2,4},

Bianca Mulaney^{1,2} and Subhra Mohapatra^{1,2,3,4} Department of Molecular Medicine¹, Nanomedicine Research Center², Signature Program in Allergy and Immunology³, University of South Florida⁴, Tampa, Florida University of South Florida, Morsani College of Medicine

Keywords: Angiogenesis, Natriuretic Peptide, Tumorigenesis, Stem cells

Objective: Natriuretic peptide receptor A (NPRA), a receptor for natriuretic peptides, is expressed abundantly on cancer cells, and NPRA deficiency protects mice against development of implanted tumors; however, the mechanism underlying NPRA signaling and tumorigenesis is not known. Since, angiogenesis is critical for tumor growth, and natriuretic peptides are paracrine regulators of angiogenesis, we reasoned that NPRA signaling might regulate angiogenesis and tumor formation. This hypothesis was tested using a variety of in vitro, ex vivo and in vivo models.

Methods: 1. Cell migration assay: Endothelial cell migration was tested in a Boyden chamber. 2. Tube formation assay: Human umbilical vein endothelial cells (HUVECs) and mouse aortic endothelial cells were used to assess new capillary formation. 3. ex vivo aortic ring assay: Capillary growth from WT and NPRA knockout (NPRA-KO) aortas was analyzed and compared. 4. in vivo tumor model: Lewis lung carcinoma -1 (LLC-1) tumor angiogenesis and growth was analyzed in WT and NPRA-KO mice.

Results: Aortas from NPRA-KO mice showed significantly less angiogenesis than those from WT mice. More vascular endothelial growth factor (VEGF) was produced in WT aortic rings. Natriuretic peptide, NP73-102 inhibits NPRA signaling and reduced capillary growth. The NPRA antagonist, anantin, abrogated angiogenesis promoted by mesenchymal stem cells (MSCs) and lipopolysaccharide. MSCs rescued tumor angiogenesis and tumor growth in NPRA-KO mice.

Conclusion: These results indicate that NPRA signaling plays a significant role in promoting angiogenesis. NPRA antagonism/NPRA signaling blockade can be an effective antitumor and anti-angiogenic strategy.

Research supported by: NIH and Florida Biomedical Research Foundation.

Screening Novel p75NTR Targeted Compounds That Inhibit Invasion for Anti-Angiogenic Effect

Jessika Contreras, Susan Murphy, Marguerite Wotoczec-Obadia, Steven Brem, Department of Neuro Oncology, Moffitt Cancer Center, Morsani College of Medicine University of South Florida Morsani College of Medicine Neurosurgery & Brain Repair

Keywords: Malignant Glioma, p75NTR, Angiogenesis

Objective: Malignant Gliomas are highly invasive brain tumors that have a high degree of recurrence even after treatment. Recently the P75 Neurotrophin receptor has been identified in higher concentrations in tumor cells involved in invasion. This study explored the possible therapeutic use of in silico (SD-108 and SD-105) selected compounds that block the BDNF binding site on the p75NTR and more specifically their antiangiogenic effect.

Methods: A proliferation assay was performed to test the effects of the SD compounds on Human Brain Microvascular Endothelial Cells cells. To study antiangiogenic effects, tube formation and co-culture assays were conducted. In Tube formation, Matrigel was loaded into 24-well plates, overlaid with HBMEC, and treated with a dose range of SD compounds (1, 5, 10 μ M). In co-culture Glioma cells transfected to express p75 (U87+p75NTR) or control empty vector (U87pcDNA) were plated and allowed to grow to sub-confluency. The cells were then covered with Matrigel and HBMEC. After incubation, the capillary tube number was analyzed in both assays.

Results: In the proliferation assay SD 105 and SD 108 had inhibitory effects on HBMEC at 22 and 20 μ M. Tube formation with HBMEC demonstrated significant inhibition by SD-105 and SD-108 at 5 and 10 μ M. In the co-culture with U87+p75NTR, SD 108 significantly inhibited tube formation at 10 μ M.

Conclusion: The compounds SD-105 and SD-108 were antiangiogenic in the tube formation experiments in a dose dependent manner. In the p75NTR/HBMEC co culture SD-108 was antiangiogenic in a dose dependent manner but there was no antiangiogenic activity demonstrated in U87-. This demonstrates the effect of SD-108 on angiogenesis may be dependent on p75NTR expression.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine, Brain Tumor Association, IVY Foundation Grant

Expression of BRCA1 Protein in Human Ovaries

Gina Nichols¹; Maja Okuka²; Alvaro Monteiro, PhD³; Patricia Kruk, PhD⁴; Santo Nicosia, MD⁴; Celso Silva, MD, MS^{2,3,1}. Morsani College of Medicine ². Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of South Florida, Tampa, Florida ³. Department of Pathology and Cell Biology, University of South Florida, Tampa, Florida ⁴. Cancer Epidemiology, Moffitt Cancer Center University of South Florida Morsani College of Medicine, Dept. of Obstetrics and Gynecology

Keywords: Ovary, BRCA1, immunofluorescence, fertility

Objective: Young women who are carriers for BRCA gene mutations are also predisposed to low response to ovulation induction, raising the suspicion that the products of the BRCA genes may participate in the reproductive process. We are investigating the mechanisms by which mutations in the BRCA1 gene results in reproductive dysfunction. In this preliminary study, we determined the localization of the BRCA1 protein in different compartments of the human ovary by immunohistochemistry.

Methods: Archived formalin fixed-paraffin embedded normal human ovaries were studied. After deparaffinization, samples were permeabilized and heat-induced antigen retrieval was used. Then ovaries were incubated with anti-BRCA1 mouse monoclonal antibody at 1:200 concentration for 32 min. Incubation with anti-mouse secondary antibody for 16 min using the the Ventana ChromoMap detection system followed. Counterstaining was performed with Hematoxylin. Slides were dehydrated, coverslipped, and imaged.

Results: High levels of expression of the BRCA1 protein was present in the ovarian surface epithelial cells, and also in granulosa cells of antral follicles and corpus luteum. Conversely, the BRCA1 protein was not detected in granulosa cells of primordial follicles. Faint expression of the BRCA1 protein was found to be present in oocytes of primordial follicles.

Conclusion: The BRCA1 protein is differentially localized in compartments of the ovary. Its presence in steroidogenic competent cells raises the hypothesis that mutations in the BRCA1 gene may interfere with normal steroidogenesis. In future studies, we will investigate the impact of inactivation of the BRCA1 gene using RNA interference in immortalized culture of human granulosa cells.

Research supported by: This research was supported by the Medicine and Gender Scholarly Concentration at USF Health, Morsani College of Medicine

Enhancer of Zeste Homolog 2 induces Pulmonary Artery Smooth Muscle Cell Proliferation

Salman A. Aljubran¹, Ruan Cox Jr, Prasanna Tamarapu Parthasarathy, Gurukumar KR, Richard Lockey, and Narasaiah Kolliputi Division of Allergy and Immunology, College of Medicine, University of South Florida, 12901 Bruce B. Downs Blvd, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Methyltransferase, differentiation, EZH2, Pulmonary arterial hypertension, calponin, smooth muscle cell

Objective: Pulmonary Arterial Hypertension (PAH) is a progressively devastating disease characterized by excessive proliferation of the Pulmonary Arterial Smooth Muscle Cells (PASMCs). PAH and cancers share an apoptosis-resistant state featuring excessive cell proliferation. The proliferation of cancer cells is mediated by increased expression of Enhancer of Zeste Homolog 2 (EZH2), a mammalian histone methyltransferase that contributes to the epigenetic silencing of target genes. However, the role of EZH2 in PAH has not been studied. In this study, it is hypothesized that EZH2 could play a role in the proliferation of PASMCs

Methods: In the present study, the expression patterns of EZH2 were investigated in normal and hypertensive mouse PASMCs. The effects of EZH2 overexpression on the proliferation of human PASMCs were tested. PASMCs were transfected with EZH2 or GFP using nucleofector system. After transfection, the cells were incubated for 48 hours at 37°C. Proliferation and cell cycle analysis were performed using flow cytometry. Apoptosis was determined using annexin V staining and cell migration was tested by wound healing assay

Results: EZH2 protein expression in mouse PASMCs were correlated with an increase in right ventricular systolic pressure and Right Ventricular Hypertrophy (RVH). The overexpression of EZH2 in human PASMCs enhances proliferation, migration, and decrease in the rate of apoptosis

Conclusion: EZH2 could play a role in the development of PAH and can serve as a potential target for new therapies for PAH

Research supported by: This work was supported by the American Heart Association National Scientist Development Grant 09SDG2260957 and NIH R01 HL105932 to Narasaiah Kolliputi and the Joy McCann Culverhouse Endowment to the Division of Allergy and Immunology

Pathologic Features of Concurrent Clonal T-cell Large Granular Lymphocytic Expansion and Myelodysplastic Syndromes

Xiaohui Zhang, Lynn C. Moscinski, Reza Setoodeh, Deniz Peker, and Ling Zhang University of South Florida College of Medicine, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, University of South Florida, College of Medicine, Dept. of Oncologic Sciences

Keywords: Myelodysplastic syndromes, T-large granular cell lymphocytosis, T-large granular cell leukemia, flow cytometry

Objective: Clonal T-LGL proliferation or leukemia can coincidentally occur with myelodysplastic syndromes (MDS). However, in the setting of MDS, how clonal T-LGL cells that reside in the bone marrow interfere with hematopoiesis remains unclear. Our study is to analyze the clinicopathological features of concomitant MDS and T-LGL.

Methods: Clinical and pathologic data, including peripheral blood cell counts, bone marrow cellularity, lineage hypoplasia, flow cytometry, and T cell receptor rearrangements, from patients with MDS during 2005 and 2010 were reviewed. The features of clonal T-LGL cell proliferation in MDS were analyzed.

Results: In 76 MDS patients, clonal T-LGL cells were identified in peripheral blood of 37 patients (48.7%), including 15 high grade MDS (40.5%), and 22 low grade MDS (59.5%). The immunophenotype of the T-LGL cells was typically CD3+/CD57+/CD7 dim+/CD5 dim+/CD8+ with variable CD11b, CD11c, CD16, CD56 and HLA-DR. The TCR β or/and TCR γ gene rearrangements were positive in 35 of the 38 cases (92.1%). Comparing with MDS without T-LGL, the peripheral blood CD3+/CD57+ cell counts were significantly different, although lymphocyte counts showed no significant difference. Notably, on examination of the bone marrow, 14 of 37 (37.8%) MDS patients with clonal T-LGL cells had certain lineage hypoplasia, including erythroid hypoplasia. The difference between the two groups was statistically significant ($p=0.004$). Additionally, the T-LGL cell counts in MDS were often lower than $0.3 \times 10^9/L$.

Conclusion: Clonal T-LGL cells expansion is a fairly common finding in high grade as well as low grade MDS. LGL cells present in MDS bone marrows could be associated with lineage hypoplasia. T-LGL cell counts in low-grade MDS are lower than that in T-LGL leukemia.



USF HEALTH

ABSTRACT POSTER

SESSION

PRDM1/Blimp-1 Regulates Expression of Transcriptional Elongation Factor ELL3 in B-Cell Differentiation

Lou-Ella M.M. Alexander^{1,3}, January M. Watters¹, Michelle Maurin¹, Kenneth L. Wright^{1,2,3} ¹Department of Immunology, H. Lee Moffitt Cancer Center and Research Institute, ²Department of Oncological Sciences, University of South Florida, Tampa, FL, ³Cancer Biology Ph.D. Program, University of South Florida, College of Arts and Sciences, Dept. of Cell Biology, Microbiology & Molecular Biology

Keywords: PRDM1, ELL3, transcription elongation factor

Objective: Investigate the role of the transcriptional repressor PRDM1 in homeostasis of transcriptional elongation factor ELL3 during B-cell to plasma cell differentiation.

Methods: Global mapping of PRDM1 binding was done by chromatin immunoprecipitation (ChIP) and microarrays, ChIP-on-chip. Direct ChIP analysis was done in multiple cell lines by qPCR. ELL3 expression level was determined by qRT-PCR and immunoblotting. A 930bp ELL3 promoter was cloned into a luciferase reporter and PRDM1 sites mutated by site directed mutagenesis. Constructs were transfected by electroporation in B-cell lines.

Results: Although PRDM1 is known to be critical in B-cell differentiation, little is known about the genes that it regulates. Our previous global mapping of PRDM1 binding sites identified ELL3 as a potential target. In B-cells, ELL3 mRNA and protein levels were high, although previously only reported in testis. Consistent with PRDM1 repression, ELL3 levels decrease concomitant with PRDM1 activation during B-cell differentiation. Endogenous binding of PRDM1 to the ELL3 promoter was demonstrated by ChIP. To determine the mechanism of ELL3 repression, we mapped two potential consensus binding sites for PRDM1 within the ELL3 proximal promoter. The ELL3 promoter was highly active in B-cell lines and co-transfection with PRDM1 dramatically repressed activity. Mutation of both PRDM1 binding sites eliminated repression, while mutation of either individual site resulted in a partial loss of repression.

Conclusion: Our results indicate that ELL3 is expressed in B-cells and directly repressed by PRDM1. Silencing of ELL3 has the potential to alter gene expression and alternative splicing in B-cells and lymphomas, where PRDM1 acts as a tumor suppressor.

Research supported by: NCI R01-CA114504 (KLW)

Regulation of the Host Innate Immune Response by Respiratory Syncytial Virus (RSV) Nonstructural Protein 1 (NS1)

Sandhya Boyapalle^{1,2,3}, Terianne Wong^{2,3}, Subhra Mohapatra^{1,2,3}, Shyam Mohapatra^{1,2,3,4*} ¹James A Haley VA Hospital, ²Nanomedicine Research Center, Division of ³Translational Medicine, Department of Internal Medicine and ⁴Department of Molecular Medicine, University of South Florida Morsani College of Medicine Tampa, Florida.

Keywords: RSV, Nonstructural protein NS1, MAVS, LGP2, IFN

Objective: During RSV infection the nonstructural viral protein NS1 attenuated type-I IFN production implying that NS1 plays a direct role in the inhibition of the host's innate antiviral immune response. We previously showed that NS1 localizes to the mitochondria following RSV infection, binds to MAVS and thereby inhibits the MAVS-RIG-I interaction required for IFN production. Here we found that NS1 increases LGP2 expression and that LGP2 is required for NS1-mediated attenuation of IFN- β .

Methods: Human alveolar epithelial adenocarcinoma A549 cells were infected with wild type RSV or RSV with an NS1 deletion (Δ NS1) or transfected with plasmid expressing NS1. Interaction between MAVS and RIG-I and expression of LGP2 in the presence or absence of NS1 was determined by immunoprecipitation and western blot in both infection and transfection models. We also developed a stable HEK-293 cell line for regulated expression of NS1. The role of LGP2 in NS1-mediated inhibition of the immune response was investigated using siLGP2, qRT-PCR and immunoblot analysis.

Results: NS1 associated with MAVS in the early stages of RSV infection, disrupted MAVS binding to RIG-I and blocked the signaling necessary for the IFN antiviral response. NS1 also elevated the expression of LGP2 and down-regulating LGP2 by the expression of siLGP2 prevented NS1-induced attenuation of IFN- β .

Conclusion: NS1 subverts the host antiviral defense by interfering with RIG-I binding to MAVS and by increasing the expression of LGP2. Targeting LGP2 may be a way to develop novel therapeutics for RSV-induced lung disease.

Research supported by: VA Merit Review Award

Resolvin Inhibits the Cryopyrin/NLRP3 Inflammasome

Ruan Cox Jr, Amanda Hodgkins, Prasanna Tamarapu Parthasarathy, Michelle Kaminsky, Venugopala Rajanbabu, Fukumoto, Jutaru, Itsuko Fukumoto, Richard F. Lockey, and Narasaiah Kolliputi Division of Allergy and Immunology, Joy McCann Culverhouse Airway Disease Center Department of Internal Medicine, Morsani College of Medicine, University of South Florida, 12901 Bruce B. Downs Blvd, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: inflammasome, resolvins, IL-1 β , acute lung injury, macrophages

Objective: The cryopyrin/NLRP3 inflammasome is a protein complex that stimulates caspase-1 activation and the processing of interleukin-1 β (IL-1 β). IL-1 β is an inflammatory mediator of acute lung injury (ALI). Mutations in NLRP3 have been linked with various acute and autoimmune diseases. Therefore, inhibitors of the NALP3 inflammasome offer therapeutic promise. Resolvins, derivatives of omega-3 fatty acids, have been shown to decrease inflammation in acute injury. However, the ability of resolvins to regulate the inflammasome has not been studied. We investigated whether resolvin treatment inhibits the inflammasome and ameliorates the effects of IL-1 β secretion in vitro.

Methods: In our study, the NLRP3 inflammasome was activated by ATP and H₂O₂ in the presence and absence of resolvin D1 and D2. Inflammasome activation was assessed by analyzing IL-1 β release and caspase-1 cleavage in THP-1 cells. In another set of experiments, supernatants from these cells were added to A549 and human primary small airway epithelial cells (HPSAEC) to study inflammasome mediated functional effects.

Results: Resolvin treatment ameliorated inflammasome activation as indicated by decreased caspase-1 activity and IL-1 β release. Resolvin treatment also inhibited IL-1 β mediated epithelial cell activation as indicated by suppressed IL-8 release and ICAM expression.

Conclusion: Our findings suggest that resolvins can be used to modulate the inflammasome and blunt the effects of the IL-1 β . These results may offer a therapeutic approach to diseases such as acute lung injury, where ungoverned pro-inflammatory cytokine secretion exacerbates the disease pathology.

Research supported by: AHA 09SDG2260957, NIH R01 HL105932, and the Joy McCann Culverhouse Endowment to the Division of Allergy and Immunology

HDAC Inhibitor Mediated Alterations in Peptide Occupancy of HLA-DR Molecules

Kevin Cronin, Szekeres Karoly, George Blanck; Department of Molecular Medicine; Morsani College of Medicine, University of South Florida

Keywords: class II associated invariant peptide; HLA-DR; tumor immunology; antigenic peptides

Objective: Histone Deacetylase inhibitors (HDACi's) are used for anti-tumor therapy. HDACi's lead to increased gene transcription because HDACs, which are tethered to gene promoters, function to repress transcription. To determine whether HDACi's could affect anti-tumor immunity, we treated major histocompatibility (MHC) class II positive melanoma cells with HDACi's and assayed for potential alterations in the binding of MHC class II to antigenic peptides.

Methods: Melanoma cells were treated with 5 μ M MS-275 or 3 μ M SAHA, two HDACi's currently used to treat patients. We treated melanoma cells transformed with an expression vector for the MHC class II transactivator, CIITA, which leads to constitutive MHC class II expression. We also treated melanoma cells with naturally occurring CIITA and MHC class II expression. We assayed for surface expression of HLA-DR, the most significant MHC class II protein, by flow cytometry. We also assayed for class II associated invariant chain peptide (CLIP), the default, self-peptide occupying the antigenic peptide groove of HLA-DR when antigenic peptide is low or non-existent.

Results: HDACi's increased HLA-DR surface expression to a modest extent, at best, in cells constitutively expressing HLA-DR. CLIP occupancy was substantially reduced in the cells treated with the HDACi's.

Conclusion: A relative decrease in CLIP was seen after HDACi treatment. Further studies will assess whether this decrease in CLIP correlates with increased loading of tumor peptides in the MHC Class II cleft.

Research supported by: Departmental funds.

An Unconventional Look at Microbial Dysbiosis in the Gut

Jaime Flores-Torres, M. Gail Muller, Gary W. Litman, Larry J. Dishaw University of South Florida Morsani College of Medicine, Dept. of Pediatrics

Keywords: Gut Microbial Immune Dynamics, Dysbiosis, Homeostasis, Ciona intestinalis

Objective: We are studying gut microbial immune dynamics (GMID) in a marine invertebrate chordate, *Ciona intestinalis*. While *Ciona* is a seemingly simple organism it filters microbial-rich seawater yet its gut is inhabited by distinct microbes. It is becoming increasingly clear in medicine that gut-microbial homeostasis has prognostic value in both health and disease etiologies.

Methods: Compositional changes in gut microbiota are studied with 16s libraries, 16s RFLP, and real-time PCR. We are disrupting microbial colonization during development and monitoring the effects on gut anatomy and on innate immune sensors. Bacterial lysates and other commercial preparations (MAMPS; e.g., LPS) are used to monitor the effects of inflammation on microbial colonization and stability.

Results: Gut bacteria from several populations have been partially sampled using molecular approaches. The *Ciona* gut reveals distinct communities of bacteria that are affected by both diet and environment. Starvation induces reproducible dysbiosis and reveals conserved bacterial types. Innate immune proteins such as the secretory immunoglobulin receptor, VCBP, can be unregulated by overwhelming the gut with MAMPSs.

Conclusion: Colonization of the gut occurs almost immediately after birth and involves highly sophisticated ecological events. However, colonization is not random, and early colonizers can become long-term inhabitants resulting in life-long mutualisms. Key signals in the onset of IBD-like symptomology in mammals involves primary innate phenomena which can be more easily studied in the absence of adaptive immunity and its associated complexities. *Ciona* offers a unique opportunity to study the molecular events surrounding gut microbial homeostasis.

Deletion of NALP3 Protects against Hyperoxia-induced Acute Lung Injury

Jutaro Fukumoto, Itsuko Fukumoto, Bao Huynh, Ruan Cox, Prasanna Tamarapu Parthasarathy, Matthew Ho, Gurukumar Kollongod, Ramanathan Kollongod, Rajan Babu Venugopal, Richard F. Lockey and Narasaiah Kolliputi, Division of Allergy and Immunology, Department of Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa

Keywords: NALP3, IL-1 β , Hyperoxia, Lung, Injury

Objectives: To determine whether NALP3 deletion has the ability to ameliorate hyperoxia-induced acute lung injury.

Methods: C57BL/6 mice and age-matched NALP3 KO mice of the same genetic background were exposed to 100% oxygen. After 24, 48, and 72 hours exposure to hyperoxia, mice were sacrificed to collect bronchoalveolar lavage fluid (BAL fluid) for absolute, differential cell counts and cytokine measurement. Lung tissues were collected and were analyzed for lung pathology using H&E staining. DNA fragmentation and apoptosis was measured by using TUNEL staining and Caspase-3/7 activity assay.

Results: BAL fluid analysis revealed a significant decrease in IL-1 β levels in KO mice when compared to WT mice; while IL-6 levels showed no difference. Differential cell count showed that infiltration of macrophages and neutrophils into BAL fluid were markedly suppressed in KO mice. Semi-quantitative histological evaluation of lung tissue H&E staining revealed the lung injury score was notably less in KO mice. TUNEL staining on lung tissue sections showed that DNA fragmentation index in NALP3 KO mice was significantly less than WT mice and in fact was unchanged from the baseline. Hyperoxia induced Caspase-3/7 activity was suppressed in KO mice.

Conclusions: The deletion of NALP3 gene protects against hyperoxia-induced acute lung injury. This mechanism could be through suppressed inflammation including blunted IL-1 β production, neutrophil recruitment in the lung and decreased apoptosis in epithelial cells.

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Regulation of Mitosis in the AIDS Pathogen, *Toxoplasma gondii*

Stella Kratzer, Elena S. Suvorova, Josephine Fruehauf, and Michael White USF- College of Medicine, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Apicomplexans, *Toxoplasma gondii*, Mitosis, Cell Cycle

Objective: The intracellular parasite, *Toxoplasma gondii*, causes widespread infections in humans and animals. In the US the risk of permanent infection is 1:2 by age 50. *Toxoplasma* infections are dangerous in people with weak or compromised immune systems where tissue destruction from rounds of parasite division go unchecked. New treatments that are well tolerated are critically needed to combat toxoplasmosis in these patients.

Methods: To identify pathways required for parasite growth, we have used forward genetics to identify essential cell cycle factors. Our study was focused on a class of conditional chromosomal mis-segregation mutants that show a variety of defects in mitosis when shifted to the non-permissive temperature. We used cell biology methods to better understand the mitotic defects of specific mutants and a cosmid genomic library was used to genetically rescue the temperature restriction and identify the defective gene.

Results: The cell biology of these mutants demonstrated defects that led to irregular shapes and sizes of the parasites, the formation of zoids absent their chromosomes, unequal amount of chromosome content in the developing daughter buds, and retention of nuclear material in the mother cell. From a class of 18 mutants, we complemented 12 mutants and in 8 mutants the candidate defective gene was identified. Mutant 11-51A1 carries a defective Zn-finger protein that is weakly related to E3 ubiquitin ligases.

Conclusion: The study of conditional mutants gives us insight into the essential mechanisms required for parasite division. Novel genes found only in the parasite family were identified with one gene encoding a unique Zn-finger protein. We speculate this factor plays an important role in chromosome segregation in *Toxoplasma*.

Research supported by: NIH

Attenuated Virulence of *B. henselae* Mutants in the Zebrafish Embryo Model

Amorice Lima^{1*}, Lisa Smith¹, Byeong Cha² and Burt Anderson^{1,1} Department of Molecular Medicine, ²Department of Pathology and Cell Biology, School of Biomedical Sciences, Morsani College of Medicine, University of South Florida, Tampa, Florida

Keywords: Zebrafish; *Danio rerio*; angiogenesis; bacteria; *Bartonella henselae*; virulence factors

Objectives: *B. henselae* (*Bh*) is an emerging zoonotic pathogen and the causative agent of cat scratch disease and bacillary angiomatosis. Bacillary angiomatosis is a systemic disease that is characterized by tumor-like lesions on the skin resulting from proliferation of the small blood vessels. *VirB/VirD4 Type IV secretion system* and *Bartonella adhesin A (BadA)* are two important virulence factors shown to play a critical role in *B. henselae* infection and angiogenesis *in vitro*. Although valuable knowledge has been acquired using *in vitro* models, progress in *Bartonella* research has been hampered due to a lack of a practical *in vivo* model. The purpose of this project is to develop a model of *Bh* infection using the Tg(fli1:EGFP)^{y1} transgenic line of zebrafish (*Danio rerio*) embryos in order to test the role of *Bh* virulence factors in infection and in eliciting a pro-angiogenic host response.

Methods: The embryos are microinjected at the early stage of development with wild type and mutant strains derived from *B. henselae* Houston-1 expressing red fluorescence protein. Quantitative PCR and confocal microscopy analysis are performed to assess bacterial replication and bacterial load in the infected embryos; qRT-PCR is used to quantitatively measure host response to *Bh* infection.

Results: Data from our experiments show that zebrafish embryos microinjected with WT *Bh* become infected and display an angiogenic phenotype. Quantitative PCR results also confirm the expansion of the *Bh* in the zebrafish embryo at different time-points after microinjection. Quantitative real-time PCR data show evidence of induction of angiogenic response in the infected embryos compared to control embryos. Moreover, our data show that zebrafish infected with *Bh* mutants for the *virB* and *badA* genes display an attenuated virulence compared to those infected with WT *Bh*.

Conclusions: We conclude that the zebrafish embryo model will be invaluable in helping identify virulence factors required for *Bh* infection and their role in eliciting a proangiogenic response.

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MHC II Retrograde Signaling in MDSC

Allison Nelson, Sajitha Nair, Christina Mcmillan, Srinivas Nagaraj Division of Translational Medicine, Nanomedicine Research Center, Internal Medicine, University of South Florida, Tampa, FL, University of South Florida, Morsani College of Medicine

Keywords: MDSC, Suppression, Cox-2, ETS-1, PGE-2

Objectives: It is now evident that inadequate function of the host immune system is due to suppressive factors such as myeloid derived suppressor cells (MDSC). A number of studies demonstrated that MDSC induced antigen-specific tolerance of CD8+ T cells, but not CD4+ T cells. The objective of this study was to investigate the novel role played by retrograde major histocompatibility (MHC)-II signaling in MDSC induced CD4+ T cell suppression, and to understand the molecular events leading to this suppression.

Methods: We tested this hypothesis by using adoptive transfer of transgenic CD4+ T cells with different affinities of peptide to the TCR and MDSC and performing MHC-II cross linking experiments. We evaluated the suppression by using a standard thymidine proliferation assay and IFN-γ Elispot assay. We will analyze the expression of COX-2 using real-time PCR and by measuring PGE2 levels using ELISA. We performed crosslinking experiments to dissect retrograde signaling pathway involving Phospholipase-C(PLC) and mitogen activated protein(MAP) Kinases.

Results: We found that activated CD4+ T cells or MDSC cross linked with MHC-II were able to convert MDSC from antigen-specific suppressor cells to cells that can inhibit non-specific T-cell responses. Our studies revealed that MHC-II ligation increases the protein-binding ability of the transcription factor ETS-1, and upregulates COX-2/PGE2.

Conclusion: Our findings suggest that activated CD4+ T cells that are antigen-specific may enhance the immune suppressive activity of MDSC, a mechanism that might serve normally as a negative feedback loop to control immune responses that becomes deregulated in cancer. Ets-1 may play a major role in retrograde MHC class II signaling in MDSC that resulted in PGE2 synthesis.

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Isolation and Sequencing of an Unrelated Strain from a Patient with Inherited Human Herpesvirus-6

Shara N. Pantry¹, Janos Luka², Jesse H. Arbuckle¹, Maria M. Medveczky¹, Rolf Renne³, Dharam Ablashi⁴, Peter G. Medveczky¹, ¹USF Morsani College of Medicine, Department of Molecular Medicine, Tampa, FL, ²Bioworld Consulting Laboratories, Mt. Airy, MD, ³University of Florida, Gainesville, FL ⁴The HHV-6 Foundation, Santa Barbara, CA, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Human Herpesvirus-6, chromosomal integration, immune tolerance, chronic fatigue syndrome

Objective: Human herpesvirus-6 is the causative agent of Roseola infantum. The virus establishes latency in vitro and in vivo by integration into the telomeres of chromosomes. We previously reported germline integrated HHV-6 (gliHHV-6) in chromosomes 17, 18 of 22 of three families. Here, we aim to reactivate a latent HHV-6 strain from the cells of a patient with Inherited HHV-6, sequence the genome of this reactivated HHV-6 virus, and compare the sequence to that of the prototype HHV-6 strain and the inherited virus.

Methods: Infected cells were treated with 12-O-tetradecanoylphorbol-13-acetate (TPA) and hydrocortisone to induce reactivation. DNA from the reactivated virus was subjected to restriction enzyme digestion, Southern Blotting, and high throughput 454 Deep Sequencing. Alternately, DNA fragments were also cloned and sequenced using dye-terminator sequencing. Nucleotide and amino acid sequence alignments were performed using CLUSTALW.

Results: Treatment of patient cells with TPA and hydrocortisone resulted in the reactivation of an infectious HHV-6 virus from the cells of a patient with inherited HHV-6. Southern Blot and both nucleotide and amino acid sequence alignments indicate that the reactivated virus differs from the prototype U1102 strain. Additionally, sequencing results also indicated that the reactivated is unrelated to the inherited virus.

Conclusion: Patients with inherited HHV-6 are susceptible to infection by exogenous HHV-6 strains, and this may be due to immune tolerance involving HHV-6 antigens. Further studies are needed to understand the immune response to HHV-6 by patients with an inherited HHV-6 virus.

Research supported by: NIH and The HHV-6 Foundation

Leukemia Inhibitory Factor Protects Oligodendrocytes from Ischemia through Akt Signaling Enhancing Antioxidant Gene Expression

Jesus A. Recio, Derrick D. Rowe, Christopher C. Leonardo, Lisa A. Collier, Alison E. Willing, Keith R. Pennypacker
University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: Stroke, leukemia inhibitory factor, peroxiredoxin-4, metallothionein-3, oxidative stress

Objective: Leukemia inhibitory factor (LIF) has both anti-inflammatory and cellular protective properties that are necessary for the treatment of stroke. To test LIF, we used primary oligodendrocyte (OL) cultures since these are the most sensitive type of brain cells to oxidative stress. OL, the predominant cell types in cerebral white matter, produce myelin and are essential for proper neuronal signaling.

Methods: In this study we examined the protective signaling initiated by LIF through the Akt pathway to enhance antioxidant gene expression. Oxygen glucose deprivation (OGD) was used as an in vitro model of stroke.

Results: A concentration response study demonstrated that 200ng/ml of LIF significantly reduced cellular cytotoxicity in OLs exposed to 24 hrs OGD. Since LIF has been reported to transduce survival signaling through the Akt pathway, we discovered that LIF exposure increased Akt phosphorylation in OLs. Inhibition of Akt blocked phosphorylation of Akt and eliminated the protective effect of LIF. Treatment with LIF increased the expression of the antioxidant genes peroxiredoxin-4 (Prdx4) and metallothionein-3 (Mt3) while inhibiting Akt decreased Prdx4 expression. In the presence of Prdx4 and Mt3 antibodies, the LIF protective properties were eliminated. As a measure of oxidation, superoxide dismutase (SOD) activity was determined. Treatment with LIF significantly reduced oxidative stress. However, the addition of Akt inhibitor IV increased oxidation to levels similar to those found in OGD.

Conclusion: Consequently, LIF activity is transduced through Akt activation facilitating up regulation of antioxidant gene expression decreasing oxidative stress.

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A Transient Decrease in Spleen Size Following Stroke Corresponds to Splenocyte Release into Systemic Circulation

Hilary Seifert¹, Aaron Hall¹, Jesus Recio¹, Cortney Chapman¹, Lisa Collier¹, Alison Willing², and Keith Pennypacker¹
¹Department of Molecular Pharmacology and Physiology, School of Biomedical Sciences, Morsani College of Medicine, University of South Florida, Tampa; ²Center for Excellence in Aging and Brain Repair, Department of Neurosurgery and Brain Repair, Morsani College of Medicine, University of South Florida, Tampa, University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology and Physiology

Keywords: Immune System, Leukocytes, CFSE, MCAO

Objective: Splenectomy is protective in ischemic and hemorrhagic stroke. We investigated the cellular response of the spleen to brain ischemia.

Methods: A time course was conducted to investigate splenic size changes in rats over time following permanent middle cerebral artery occlusion (MCAO) and sham-MCAO. In a second experiment, splenocytes were labeled in situ with carboxyfluorescein diacetate, succinimidyl ester (CFSE). Splenic injections were given five days prior to MCAO or sham-MCAO. A CFSE only group was euthanized five days following injections. Spleen, brain, thymus, and blood smears were collected for all groups.

Results: The spleen was found to transiently decrease in size at 48 h following MCAO in rats compared to controls. CFSE was found to be non-toxic and five days following injection 15% of the splenocytes were labeled. In the spleen, there was a significant increase in CFSE positive cells in the 48 h sham group versus all the other groups. Blood smears showed a significant increase in total CFSE positive cells at 48 h post-MCAO. CFSE positive cells in the blood were identified by Giemsa staining. A significant increase of lymphocytes, monocytes, and neutrophils was found at 48 h post-MCAO when compared to the other groups. In the brain, CFSE positive cells were found in the blood vessels.

Conclusion: These results demonstrate that CFSE is a viable and safe way to track immune cells in situ in an animal model of stroke. The spleen transiently decreases in size post-MCAO in rats and releases splenocytes into systemic circulation at 48 h following MCAO. CFSE positive cells were found in the brain but were restricted to blood vessels. These cells are migrating to the brain or other lymphoid organs, affecting the overall immune response to ischemia.

Inhibition of AKT Kinase Activity Decreases Replication of Human Respiratory Syncytial Virus

Kim C. Tran¹, Sandra M. Fuentes², Biao He², ¹Division of Allergy and Immunology, Department of Internal Medicine, USF Health, Tampa, FL ²Department of Veterinary Sciences, University of Georgia, Athens, GA ³University of South Florida Morsani College of Medicine Internal Medicine

Keywords: RSV, antiviral, signal transduction

Objective: Human Respiratory Syncytial Virus (RSV) is a leading cause of pediatric pulmonary disease and severe RSV infection predisposes to wheezing later in life. RSV infection has also been shown to be an environmental trigger for asthma. We are investigating whether targeting host factors important for RSV infection is a viable antiviral strategy. Lowering viral burden through these therapies will result in decreased severity of infection and may also prevent the occurrence of pathologic sequelae.

Methods: Inhibition of AKT by either chemical inhibitors, siRNA, or dominant-negative mutants was tested for activity against RSV replication in cultured cells. In addition, we examined the effect of Akt on specific viral processes (entry, macromolecular synthesis, assembly) and proteins both in vitro and in RSV-infected cells.

Results: We found that AKT inhibition decreases RSV protein expression and viral titers. Expression of RSV NS2 protein activates AKT, leading to NFkB-dependent transcription. Activated AKT also phosphorylates RSV P protein. Interestingly, AKT inhibitors that target the pleckstrin homology (PH) domain of AKT showed decreased efficacy against RSV compared to those that target AKT kinase activity.

Conclusion: AKT inhibition can effectively decrease RSV replication in culture, likely by decreasing P phosphorylation and thus viral protein transcription and expression. Activation of AKT during RSV infection likely involves the NS2 protein and does not depend on the PH domain of AKT. AKT inhibitors have been found to be safe and efficacious in clinical trials for a number of different cancers; thus, AKT inhibition may be a potential therapeutic treatment for severe RSV infection.

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Regulation of Gene Expression in *Bartonella Henselae* by the General Stress Response

Nhan Tu¹, Lisa Smith¹, Stanley Stevens², Burt Anderson¹ Morsani College of Medicine¹ Department of Molecular Medicine, College of Arts and Sciences²

Objectives: The bacterial general stress response (GSR) provides broad protection. In two well-characterized GSR systems, an alternative σ factor (*rpoS* in *E. coli* and *sigB* in *Bacillus subtilis*) is the master regulator of gene expression. In α -proteobacteria, a unique GSR system has been described for some non-human pathogens. The master regulator of gene expression, an ECF σ factor, is negatively regulated by binding of the NepR anti- σ factor under non-stressed conditions. Under stress, the ECF σ factor is released when the anti-anti- σ factor PhyR binds to NepR. We identified in the human pathogen *Bartonella henselae* a putative response regulator gene divergently transcribed from a small gene encoded upstream of an ECF σ factor. We hypothesize that this gene locus encodes the GSR genes in *B. henselae*.

Methods and results: We constructed a *phyR* knockout mutant through conjugation. We performed microarray and mass spectrometry analyses on both the wild-type and mutant strains to determine the *phyR* regulon. For microarray, RNA was extracted from bacteria collected on plates and converted into cDNA. For mass spectrometry, the supernatants were collected from bacteria grown on plates and digested with trypsin. The results of the mass spectrometry and microarray analyses revealed only a few differentially regulated genes between the wild-type and mutant. However, the bacteria used were taken from agar plates and were not likely to be under stress. To address this problem we want to study sensitivity of the mutant against stress compared to the wild-type in liquid medium. We grew mutant and wild-type bacteria in Schneider's insect cell media for up to 7 days in 24-well plates. At each time point, the bacteria were cultured on agar plates to determine the number of viable bacteria. The growth curves showed that the bacteria were in exponential phase up until day 3 and entered stationary phase after day 3. We plan to use this media to expose bacteria to different stressors (list here) and repeat the gene expression analysis to define the GSR regulon.

Conclusion: We have determined that under optimal growth conditions on solid media the GSR has minimal effect on gene regulation in *B. henselae*. Further analysis under conditions of stress will allow us to further define this regulatory system.

miR-150 Inhibits Inflammation by Suppressing NKT Cells and Cytokine Production

Jia-Wang Wang*,†, PhD, Kunyu Li†, BS, Gary Hellermann*, PhD, Subhra Mohapatra*, PhD, Richard F Lockey*,†, MD and Shyam S Mohapatra*,†, PhD. *Division of Allergy and Immunology, Department of Medicine and Nanomedicine Research Center, University of South Florida Morsani College of Medicine, and †James A. Haley Veterans Hospital, Tampa, FL

Keywords: miR-150, Asthma, cytokine NKT cells, Nanoparticle

Objective: Regulatory T (Treg) cells play a pivotal role in regulating T cell response and inflammation in asthmatic lungs. A micro-RNA profile in Tregs from asthmatic mice showed a significant decrease in miR-150 expression. MiR-150 may thus be useful as an anti-inflammatory treatment for asthma. Our goal was to determine the effect of miR-150 overexpression on T cell response and lung pathology in a mouse model of asthma.

Methods: Total RNAs were isolated and subjected to miRNA profiling. Transgenic mice overexpressing miR-150 were generated. miR-150 was delivered by nanoparticles into the lungs of WT asthmatic mice. Airway hyper-responsiveness, lung histopathology and cytokines were measured.

Results: MiR-150 was significantly down-regulated during asthmatic inflammation in the lungs, in Tregs, Th1 and Th2 cells. Transgenic mice overexpressing miR-150 showed lower airway hyperreactivity, inflammatory cytokine production and NKT cells than WT. Overexpression of miR-150 delivered by chitosan nanoparticles inhibited lung inflammation and cytokines in asthmatic mice and did not cause adverse side effects. MiR-150 suppressed expression of Akt3, Cbl1 and Elk1 but up-regulated p53, inhibited cell proliferation and promoted apoptosis.

Conclusion: MiR-150 decreases inflammation probably by inhibiting cytokine production and NKT cells, inducing apoptosis and repressing cell growth by regulating critical genes such as Akt, Elk, Cbl1 and p53. Deregulation of miR-150 may be involved in the pathogenesis of asthma. Overexpressing miR-150 may be useful as a safe anti-inflammatory therapeutic strategy for attenuating lung inflammation.

Respiratory Syncytial Virus (RSV)-Infected Elderly Mice Exhibit Impaired Expression and Activation of Pattern Recognition Receptors (PRR)

T. M. Wong¹ and S. S. Mohapatra^{1,2}, ¹Dept of Molecular Medicine and Signature Program in Allergy, Immunology & Infectious Diseases and Dept of Internal Medicine-Div of Translational Medicine, Morsani College of Medicine, Tampa, FL, and ²James A. Haley VA Hospital, Tampa, FL. University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Respiratory syncytial virus, virology, immunology, aging, innate immunity

Objective: RSV-induced pneumonia causes significant morbidity and mortality in elderly; however, the molecular basis for increased susceptibility to RSV infections in elderly remains unclear. Since altered PRR signaling, particularly deficits in TLR3 and TLR7, contribute to RSV-induced inflammation and mucus overproduction, we investigated PRR gene expression and cytokine levels in young and elderly mice with or without RSV infection.

Methods: Aged (>20mo.) and young (1-3mo.) BALB/c mice were intranasally infected with RSV or mock-infected and 24hrs later, PRR gene expression was compared using qRT-PCR analysis of lung RNA. Cytokine levels in lung homogenates from RSV-treated mice were measured by bead array. Bronchoalveolar lavage was performed on another group of aged and young mice for isolation of alveolar macrophages and TLR7 activation was determined after incubating adherent cells with TLR7 ligand, R848, for 20hrs. Cytokine levels in culture supernatants were analyzed by ELISA for IL-6 to indicate TLR7 activation.

Results: RSV infection induced >2-fold upregulation of 17 PRR genes in elderly mice compared to 39 genes in the young. Of 84 genes assayed, >20 genes including TLR7, TLR9 and LGP2, were downregulated in aged mice. RSV-infected aged mice had higher levels of IL-6 and TNF- α than young. TLR7-stimulated alveolar macrophages from aged mice secreted significantly less IL-6 than cells from young mice.

Conclusion: RSV-infected elderly mice had altered expression of PRR genes, proinflammatory cytokine profile, and dysfunctional signaling of TLR7. TLR7 activation may provide an approach to reduce RSV-induced inflammation and mucus overproduction in elderly.

Research supported by: USF Signature Research Fellowship to TW; Research Career Scientist and VA Merit Review Awards to SSM

Mitochondrial Uncoupling protein-2 regulates NLRP3 Inflammasome

Venugopal Rajanbabu, Richard F. Lockey and Narasaiah Kolliputi University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Inflammasomes, NLRP3, UCP2, Genipin

Objective: Among the various types of inflammasomes, Cryopyrin/NLRP3 senses a large variety of inflammasome stimuli. Inappropriate NLRP3 inflammasome activity has been reported in ALI and other various acute and autoimmune diseases. Therefore, regulators of the NLRP3 inflammasome offer a considerable therapeutic promise. We investigate whether mitochondrial uncoupling protein (UCP)-2 regulates inflammasome activation and modulates the functional effects of inflammasome mediated IL-1 β secretion.

Methods: Differentiated human THP1 cells were pre-treated with UCP-2 inhibitor genipin followed by inflammasome activation with ATP. To mimic the infection model, THP1 cells were primed with LPS prior to genipin treatment. THP1 cells expressing UCP-2-GFP was used to check the regulation of NLRP3 by UCP2. The expression of UCP-2, NLRP3, ASC, pro-caspase-1 and pro-IL-1 β in total cell lysates was assayed by western blot. Secretion of TNF- α , IL-6 and IL-1 β were detected by ELISA.

Results: We show that when activated THP1 cells are treated with genipin, the expression of NLRP3 and UCP-2 are suppressed. Cells that were transfected with UCP2 cDNA further induced NLRP3 expression. Treatment with inflammasome stimulator ATP inhibits UCP2, but did not suppress NLRP3. In addition, the presence of ATP restores genipin mediated suppression of NLRP3. Pretreatment of genipin decreased the levels of ATP mediated secretion of mature IL-1 β .

Conclusion: Our data demonstrated that the small molecule genipin inhibits NLRP3 expression and secretion of inflammasome mediated IL-1 β . Genipin also decreased the secretion of TNF- α in ATP treated, activated THP1 cells. In addition, ATP restores the NLRP3 expression in an UCP-2 independent signaling pathway.

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Development of Novel and Effective Therapeutic Peptide Vaccines against HPV-induced Tumors

Kelly Barrios¹, Esteban Celis². ¹University of South Florida, Tampa, FL; ²H. Lee Moffitt Cancer Center, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: HPV, CD8 T cells, vaccine, peptide, immunotherapy

Objective: Our main goal is to generate effective therapeutic peptide-based vaccines against viral-induced cancers. We are first focusing on human papillomavirus (HPV) induced malignancies because of their high worldwide prevalence (e.g., cervical carcinoma and head & neck cancer).

Methods: We have used an HPV-induced mouse cancer model to test vaccines composed of a CD8 T cell peptide epitope administered with potent adjuvants designed to generate vast numbers of high avidity cytotoxic T lymphocytes specific for the HPV16-E7 antigen. One vaccination strategy (TriVax) consists of intravenous administration of synthetic peptide HPV16-E749-57 administered together with a Poly-IC (a TLR3 agonist) and anti-CD40 monoclonal antibody (α CD40 mAb) while the second more simple strategy (BiVax) comprises of peptide plus Poly-IC. We assessed both the immunogenicity and therapeutic anti-tumor effects of both vaccination strategies.

Results: While TriVax was clearly more immunogenic than BiVax, both vaccines showed remarkable anti tumor effects against the HPV16-E7 expressing tumors TC-1 and C3.43. In addition, we will present results suggesting that some peptides such as HPV16-E749-57 can be highly immunogenic in the absence of CD40 costimulation (i.e., in the BiVax format), due to their capacity to form complexes with Poly-IC. We hypothesize that peptide/Poly-IC complexes are highly immunogenic because they are targeted to professional antigen-presenting cells via some type of scavenger receptor specialized in capturing nucleic acids.

Conclusion: The results from these experiments will allow us to compare conventional vaccines with TriVax and BiVax for the induction of effective anti-tumor responses against established viral-induced tumors.

Research supported by: Moffitt Cancer Center

ADAM17-Mediated Cleavage Is Required For HPP1-Associated Tumor Suppression in Colorectal Cancer

W. Clark^{1,2}, A. Elahi¹, J. Wang¹, J. Hernandez^{1,2}, D. Shibata¹; ¹Moffitt Cancer Center And Research Institute, Tampa, FL; ²University of South Florida Morsani College of Medicine, Dept. of Surgery

Keywords: colon cancer HPP1 Epidermal Growth Factor Tumor Suppressor

Objective: HPP1 is a novel tumor suppressor gene with reduced expression in over 80% of colorectal cancers (CRC) and has emerging potential as a serum and stool-based biomarker. HPP1 has known growth suppressive effects in colon cancer but little is known about its mechanisms of action. HPP1 is an EGF-like ligand thought to undergo cleavage. We sought to determine the significance of ectodomain shedding in the tumor suppressive functions of HPP1.

Methods: Experimental cell lines included HPP1 non-expressing empty vector HCT116 controls and stable HPP1-overexpressing HCT116 transfectants (HCT-HPP1). Differential expression of candidate sheddases, ADAM (A Disintegrin And Metalloproteinase) 10, 17 and 19 were determined by RT-PCR. Western blotting measured cleaved HPP1 ectodomain in media. Selective ADAM knockdowns using siRNA were confirmed by Western blot. Cell proliferation and anchorage-independent growth were evaluated by MTT and growth in soft agar assays.

Results: Treatment of HCT-HPP1 with proinflammatory cytokines (PMA, TNF- α) augmented HPP1 ectodomain shedding, implying involvement of an ADAM family sheddase. HCT-HPP1 transfectants demonstrated increased expression of ADAM 10 and 17 but not 19. ADAM17 (but not ADAM10) knockdown resulted in attenuation of HPP1 ectodomain shedding into conditioned media. HCT-HPP1 cells treated with ADAM17 siRNA demonstrated a significant 35% increase in proliferation ($p=0.002$) and an augmentation in anchorage independent growth relative to controls ($p=0.04$).

Conclusion: Cleavage and ectodomain shedding of HPP1 are predominantly mediated by ADAM17 and are critical for HPP1's tumor suppressive functions. Investigation of the signaling effects of ADAM17 and HPP1 may help elucidate pathways amenable to therapeutic manipulation in CRC.

Optimizing Radiation Treatment Planning for Neuroendocrine Tumors with 3D Molecular/Anatomic Imaging

Cruz A, Hoffe S, Montilla-Soler, J, Shridhar R, Dilling TJ, Eikman E, Moros E, Kuykendall C, Roehnelt N, Kvols L, Cruz A - University of South Florida Morsani College of Medicine All other authors - Moffitt Cancer Center, University of South Florida, Morsani College of Medicine, Dept. of Oncologic Sciences

Keywords: Neuroendocrine tumors, gross tumor volume, SPECT/CT, PET/CT

Objective: Treatment for neuroendocrine tumors (NETs) can involve radiotherapy for localized unresectable disease or symptomatic metastases. Integration of molecular imaging improves localization of the intended tumor targets, which permits escalation of dose to the high uptake regions defining the gross tumor volume (GTV) while minimizing normal tissue toxicities. Somatostatin receptor scintigraphy using OctreoscanTM 111-IN-DTP-d-Phe {octreotide} (OS) reliably localizes over 90% of NETs using SPECT/CT. FDG-PET/CT may be employed as well in high grade tumors.

Methods: We conducted a retrospective review of NET patients treated with radiotherapy. Patients were included in the analysis if PET/CT or OS were utilized for target volume localization. Of these eight patients, five underwent simulation followed by OS in the treatment position; three scans were done using SPECT/CT. In two cases where SPECT/CT was not available, markers were placed on the patient at the time of CT and these images were fused to SPECT scans previously performed. Three of the patients underwent simulation followed by a treatment planning PET/CT.

Results: Seven patients had demonstrable uptake on molecular imaging. One patient had initial uptake on PET/CT which resolved after chemotherapy. OS and PET/CT scans were fused to the treatment planning CT to guide contouring. The two patients with OS done at our institution using SPECT followed by CT were analyzed by reviewing the position of the radio-opaque markers and using them as references to guide contouring.

Conclusion: Our initial experience suggests that available 3D molecular imaging can be fused into radiation treatment planning for NETs. This capability may enhance the delineation of the GTV, allowing potentially tighter field margins.

Growth of Cancer cells on a Functionalized Multilayered Nanofibrous Scaffold

Yvonne Davis, Chunyan Wang, Mark Howell, Ujjwalasree Garapati, Sowndharya Ravi, Shyam Mohapatra, Subhra Mohapatra University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Scaffold, nanofibers, cell culture

Objective: 3D culture systems used in cancer research are intended to increase cancer cell malignancy and retain the in vivo phenotype by mimicking the structure of the tumor micro-environment. They may come in the form of nanofiber scaffolds constructed from natural or synthetic polymers. Surface immobilized nanofiber scaffolds with bioactive molecules provide great opportunities for developing in vitro models to study tumorigenesis and therapeutic delivery of drugs. The aim of this study was to develop a functionalized multilayered nanofiber (FMN) scaffold to enhance proliferation and attachment of cancer cells in a biomimetic tumor microenvironment.

Methods: The functionalized multilayered mPEG-PLA-PLGA scaffold was first electrospun on an electrospinner, then coated with chitosan and further modified with RGD and VEGF. The morphology of the FMN scaffold were characterized by SEM. Cancer cells were cultured, then tested for viability and proliferation using calcein/EthD-1 and Ki67 assay respectively. In vivo studies of FMN scaffolds seeded with cancer cells and transplanted into mice show increased tumor size and weight compared to naked unmodified scaffolds and control.

Results: The functionalization of the scaffold allowed for increased distribution of cationic charges and made the scaffold more hydrophilic, thus allowing for better attachment and proliferation of cells compared to non-functionalized scaffolds and monolayer cultures. The addition of RGD and VEGF enhanced attachment and proliferation of cells both in vitro and in vivo.

Conclusion: These results demonstrate that functionalized multilayered nanofibrous scaffolds can be used as a promising biomaterial for in vitro culture models to screen therapeutics for cancer.

Research supported by: NIH and Florida Research Fund

Bone Marrow-derived Mesenchymal Stem Cells Restored Tumorigenesis in Natriuretic Peptide Receptor A Knockout (NPRA-KO) Mice.

Frantz Jean Louis, Jaya Mallela, Sowndharya Rajavel, Vignesh Chinnasamy, Ujjwalasree Garapati, and Subhra Mohapatra, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Stem cell, Tumorigenesis, Natriuretic peptide

Objective: The cardiac hormone atrial natriuretic peptide (ANP) receptor, natriuretic peptide receptor A (NPRA), is expressed on cancer cells and natriuretic peptides are implicated in cancers. NPRA deficiency protects against growth of implanted tumors in mice; however, a direct role of NPRA signaling in tumor angiogenesis remains unknown. Bone marrow mesenchymal stem cells (BM-MSC) are a source of various cells. Since recruitment of BM-derived cells to the tumor microenvironment promotes both angiogenesis and tumor progression, we reasoned that NPRA signaling could have a role in this process. To test this hypothesis we studied whether BM-MSCs can rescue tumorigenesis in NPRA-knockout (NPRA-KO) mice.

Methods: Immunohistochemistry: Pericyte, endothelial cell, and macrophage distribution analyzed in different tumor sections. ELISA: Angiogenic factor analyzed. in vivo tumor model: Lewis lung carcinoma-1 (LLC-1) tumor cells were injected into WT and NPRA-KO mice. Tumor growth and angiogenesis were analyzed and compared.

Results: NPRA deficiency prevented growth of implanted LLC-1 tumor cells. Tumor volumes and weights were greater in WT than in NPRA-KO mice. Tumor growth was restored in NPRA-KO mice, when tumor cells were co-injected with matrigel or mouse BM-derived MSCs. There is significant positive correlation between tumor growth and pericyte recruitment, macrophage infiltration, and new blood vessel formation.

Conclusion: These findings indicate that NPRA signaling plays an important role in tumorigenesis, likely through the angiogenesis pathway. Impaired cell recruitment due to NPRA deficiency was restored by MSCs; therefore, antagonism of NPRA signaling could be protective against tumor development.

Research supported by: NIH and Florida Biomedical Research Funds.

Novel Dual Inhibitors of Vascular Endothelial Growth Factor and VEGFR2 Receptor

Chelsea D. Frost⁽¹⁾, Jennifer P. Nguyen⁽²⁾, Meghan L. Lane⁽¹⁾, William P. Skelton IV⁽³⁾, Michelle Skelton⁽¹⁾, and David L. Vesely⁽¹⁾ ⁽¹⁾Departments of Medicine, Molecular Pharmacology and Physiology, James A. Haley VA Medical Center, and University of South Florida, Morsani College of Medicine, Tampa, Florida; ⁽²⁾Department of Biology, Wichita State University, Wichita, Kansas; ⁽³⁾University of Florida College of Medicine, Gainesville, Florida.

Keywords: vascular endothelial growth factor (VEGF); VEGFR2/KDR/Flk-1 receptor; natriuretic hormones

Objective: Vascular endothelial growth factor (VEGF) helps control tumor growth via causing new capillaries growth in tumors. Four cardiac hormones (i.e. vessel dilator, long-acting natriuretic peptide (LANP), kaliuretic peptide (KP), and atrial natriuretic peptide (ANP) which eliminate up to up to 86% of human small-cell lung cancers growing in mice were investigated for their effects on VEGF and the VEGFR2/KDR/Flk-1 receptor. The VEGFR2 receptor is the main receptor mediating VEGF's cancer enhancing effects.

Methods: Four cardiac hormones were evaluated for their ability to directly decrease VEGF/VEGFR2 levels measured by ELISAs in 3 human cancer cell lines.

Results: Vessel dilator, LANP, KP and ANP, over a concentration range of 100 pM to 10 μ M, maximally decreased the VEGFR2 receptor in human pancreatic adenocarcinoma cells by 48%, 49%, 74%, and 83%. Vessel dilator, LANP, KP, and ANP decreased the VEGFR2 receptor by 77%, 89%, 88%, and 67% in human small-cell lung cancer cells by 48%, 92%, 64%, and 71% in human prostate cancer cells. VEGF itself in human pancreatic carcinoma cells was decreased by 42%, 58%, 36%, and 40% by vessel dilator, LANP, KP, and ANP. VEGF levels were decreased 25%, 23%, 17% and 23% by vessel dilator, LANP, KP, and ANP in small-cell lung cancer cells and decreased by 24%, 20%, 23%, and 24% in human prostate cancer cells.

Conclusion: Four cardiac hormones are the first dual inhibitors of VEGF and the VEGFR2/KDR/Flk-1 receptor.

Research supported by: This work was supported in part by grants from the James and Esther King Florida Biomedical Research Program, the Florida Department of Health, and the Mama Mare Foundation.

1,25-Dihydroxyvitamin D3 Prevents Obesity Associated Ovarian Cancer Through Mir-498 Induction and the Suppression of Estrogen Induced Telomerase Activity

Ravi Kasiappan, Jinfu Tang, Panida Lungchukiet, Yuefeng Sun, Santo V. Nicosia, Xiaohong Zhang and Wenlong Bai
Department of Pathology and Cell Biology, University of South Florida, Morsani College of Medicine Tampa, Florida

Keywords: Obesity, ovarian cancer, hTERT, miR-498, 1,25-dihydroxyvitamin D3

Objective: Obesity continues to rise in the US, exceeding 30 percent in most sex and age groups. Obesity may increase cancer risks through increased levels of estrogens. Several reports indicate that estrogen signaling in cancers involves stimulation of telomerase, which we identified as a target for active 1,25-dihydroxyvitamin D3 (1,25-vitamin D3) in ovarian cancer cells. Moreover, our recent work demonstrates that 1,25-vitamin D3 suppresses telomerase activity through the induction of microRNA-498 (miR-498). Our overall hypothesis is that 1,25-vitamin D3 prevents obese-associated ovarian cancer through the up-regulation of miR-498.

Methods: In this study, we used estrogen sensitive ovarian cancer cells (BG1) to study the effect of 1,25-vitamin D3 on the regulation of hTERT through miR-498. We applied microRNA sponge technology to knockdown miR-498 to study the cell growth and hTERT mRNA expression by qRT-PCR.

Results: In the present study, we found that 1,25-vitamin D3 induced miR-498 expression in estrogen sensitive cancer cells such as ovarian, endometrial and breast cancer cell lines and that the miR-498 inhibited hTERT expression in these cells. We further demonstrated that 1,25-vitamin D3-induced miR-498 decreases leptin or estrogen induced cell growth and hTERT mRNA expression. Luciferase reporter assays revealed that leptin or estrogen induced 3'UTR of hTERT reporter gene was suppressed by 1,25-vitamin D3-induced miR-498. The ability of 1,25-vitamin D3 to decreases leptin or estrogen induced cell growth and hTERT mRNA were compromised when miR-498 was depleted using "sponge".

Conclusion: Taken together, these results indicate that induction of miR-498 by 1,25-vitamin D3 may be a mechanism that protects women from ovarian cancer associated with obesity.

Antitumor Activity of Genetically Modified Dendritic Cells

Raphael Monta, BS², Rupal Ramakrishnan, PhD¹, Dmitry I. Gabrilovich, MD, PhD¹ ¹H. Lee Moffitt Cancer Center and Research Institute, ²USF Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: DC, MDSC, CDDO-ME, IL-12

Objective: Many groups in recent years have successfully used various combination therapies for the treatment of tumors. Dendritic cell (DC) vaccines in combination with various agents have shown very promising results, but have some drawbacks in that responses are not robust and long-lasting. One factor that implicated in hindering the therapeutic efficacy of immune therapy is MDSCs. There have been many reports indicating an inverse relationship between the presence of Myeloid Derived Suppressor Cells (MDSC) and the development of a good immune response. Thus, blocking MDSC function could be pivotal in improving immune responses. One well-tolerated compound that is used for the therapeutic neutralization of MDSCs is 2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oic acid (CDDO-ME). CDDO-ME works by activating NRF2 transcription factor, which leads to reduction of intracellular ROS. Up-regulation of ROS is one of the main mechanisms of MDSC activity. Hence, CDDO-ME is highly effective in abrogation of immune-suppressive activity of MDSC in tumor-bearing hosts.

Methods: Using a Meth A sarcoma model to test our hypothesis, we treated mice with a combination of IL-12 DCs and CDDO-ME. We used DCs expressing IL-12 via the RheoSwitch Therapeutic System, which helps in controlling the gene expression of IL-12 to improve safety and efficacy. The transgene expression of IL-12 in this system is controlled by oral administration of Activator Ligand.

Results: In preliminary studies, we found that treatment of tumor-bearing mice with activated DC-IL-12 alone was effective in delaying tumor progression. We did not observe a synergistic effect of the combination of DC-IL-12 and CDDO-ME.

Conclusion: Thus, blocking MDSC function with CDDO-ME does not seem to improve immune response.

Research supported by: This research was supported by the Research Scholarly Concentration at USF Health Morsani College of Medicine

The Role of the Ikaros Family in Murine Pancreatic Adenocarcinoma

Nadine Nelson¹, Maya Jerald¹, Jemson Pierre¹, Karoly Szekeres¹, Laura Pendleton¹, Shari Pilon-Thomas² and Tomar Ghansah¹, ¹Department of Molecular Medicine, College of Medicine, University of South Florida, ²Immunology Program, Moffitt Cancer Center, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Pancreatic Cancer, Inflammation, Casein Kinase 2, Ikaros, Tregs,

Objective: Pancreatic cancer (PC) is the 4th leading cause of cancer deaths in the United States. The PC microenvironment produces inflammatory factors that negatively influence anti-tumor immune responses. Cytokine-dependent casein kinase (CK2) is over-expressed in cancers and negatively regulates Ikaros, a transcription factor that is critical for T lymphocyte development and function. The aim of this study was to determine whether PC tumor-derived cytokines increase CK2 activity, thus reducing Ikaros expression and leading to altered Regulatory T Cell (Treg) homeostasis and function

Methods: Murine Panc02 inflammatory cytokine production was measured using Cytometric Bead Array (CBA) and Flow Cytometry. We established a PC tumor-bearing (TB) model by injecting C57BL/6 mice with Panc02 cells. As a control, mice were injected with PBS. Ikaros family gene expressions were evaluated using qRT-PCR. Ikaros and Bcl-2 protein expression were detected using Western Blot (WB). Treg percentages were evaluated from TB and control splenocytes using Flow Cytometry.

Results: CBA and Flow Cytometry analyses revealed that Panc02 cells produce IL-10 and other inflammatory factors. qRT-PCR revealed no differences in Ikaros mRNA expression whereas WB analyses did not detect Ikaros protein expression in splenocytes from TB vs. control mice. WB analyses also detected increased Bcl-2 expression in splenocytes from TB vs. control mice. Flow cytometry results revealed a significant increase in Treg percentages in splenocytes from TB vs. control mice.

Conclusion: Our data suggest that in a PC microenvironment, inflammatory cytokines enhance CK2 activity that leads to Ikaros protein degradation and results in the loss of Treg homeostasis, which can suppress anti-tumor immune responses

Bioinformatic Analysis Correlates PTEN Loss with Oncogenic Potential of Lung Epithelial Cells

Ravi Ramesh Pathak (Pathology and Cell Biology), Vrushank Dave (Pathology and Cell Biology), University of South Florida, Morsani College of Medicine, Dept. of Pathology and Cell Biology

Keywords: Lung, Cancer, PTEN, Bioinformatics

Objective: To identify oncogenic pathways contributing to lung cancer after PTEN loss.

Methods: We generated triple transgenic mice SPC-rtTA/TetO-Cre/PTENdelta/delta in which Pten gene was conditionally deleted in the lung epithelium. A comprehensive analysis of in vivo gene expression profile of PTEN deleted pulmonary epithelial cells identified a number of hitherto unknown mRNA signatures that may participate in lung tumorigenesis. mRNA profiling using microarrays was performed with whole lung tissues deficient in PTEN on murine genome MOE430 chips Affymetrix. Functional clustering with the DAVID Bioinformatic resources 6.7. Pathway analysis was performed on the enriched clusters using DAVID pathway viewer, GeneGo and Ingenuity software suites.

Results: A total of 1389 genes were differentially expressed in the PTEN knockout mice. Analysis of the promoter regions of the top 20 PTEN responsive genes identified several common transcription factors that included Forkhead domain, NKX homeodomain and GATA binding factors. Comparison of the expression profile of PTEN deleted pulmonary epithelial cells with PTEN null fibroblasts revealed a number of statistically significant signatures that included DNA damage and repair, cell adhesion remodeling and myriad cancer pathways. PTEN regulated genes were also involved in pathways that regulate PPAR signaling, insulin, chemokine and JAK/STAT signaling. In addition, deletion of PTEN perturbed expression of a subset of genes participating in cell differentiation, cell-survival, invasion and polarity.

Conclusion: Our analysis demonstrates that regardless of the origin or lineage of cells, PTEN loss generates a unique oncogenic signature that can be exploited to develop targeted therapies focused to PI3K/AKT/mTOR pathway.

Impact of 2-deoxy-D-glucose on Molecular Genomics Expression and as Adjuvant to Chemotherapy in the Treatment of Retinoblastoma.

Piña Y.¹, Decatur C.² Houston S.K., MD², Murray T.G., MD², Lampidis T.J., PhD², Celdran M.¹ ¹University of South Florida, Morsani College of Medicine, Dept. of Oncologic Sciences, ²Bascom Palmer Eye Institute

Keywords: glycolytic inhibitor, genomic expression, hypoxia, retinoblastoma

Objective: To evaluate focal delivery of 2-deoxy-d-glucose (2-DG): (1) on the spatial gene expression, and (2) its effect with chemotherapy on tumor burden and hypoxia in the LH(BETA)T(AG) retinal tumors.

Methods: (1) Mice (n=24) were treated with 2 or 6 subconjunctival injections of 2-DG at 16 weeks of age. A gene expression array analysis was performed on 5 different tumor regions. (2) 17-week-old mice (n = 30) received periocular injections of saline, carboplatin, and 2-DG. Mice were divided into six groups: saline; carboplatin; 2-DG (250 mg/kg); 2-DG (500 mg/kg); carboplatin and 2-DG (250 mg/kg); and carboplatin and 2-DG (500 mg/kg). Injections were administered 2 x weekly for 3 weeks.

Results: (1) More than 100 genes were observed to be dysregulated by ≥ 2 -fold difference in expression between the three treatment groups and their dysregulation varied across the five regions assayed. (2) The difference in hypoxia after treatment with 500 mg/kg 2-DG was significant ($P < 0.015$). The difference in tumor burden was significant from the 250 mg/kg dose ($P < 0.015$) and 500 mg/kg dose ($P < 0.001$). Tumor burden became more reduced after treatment with combination therapy of carboplatin and 2-DG ($P < 0.001$).

Conclusion: 2-DG alters the gene expression in retinoblastoma cells according to their location within the tumor as well as the treatment schedule. This study demonstrates the efficacy of focal, periocular 2-DG as an adjunct to carboplatin chemotherapy to decrease both intratumoral hypoxia and tumor burden.

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Expression of Cytokeratin 19 (CK-19) in Peripheral Blood of Women Undergoing In Vitro Fertilization (IVF): A Preliminary Study

Robyn Schickler; Maria Galeano MD; Maja Okuka; Celso Silva, MD, MS University of South Florida Morsani College of Medicine Obstetrics & Gynecology

Keywords: CK-19, infertility, in-vitro fertilization

Objective: Cytokeratin 19 (CK-19) is an epithelial cell antigen, and its expression has been shown to be a reliable tumor marker in epithelial malignancies and to be present in women with endometriosis. The objective of this feasibility study was to determine the prevalence of CK-19 gene expression in women undergoing IVF and compare it with the prevalence of CK-19 expression in healthy historical controls.

Methods: IRB approval has been obtained. Peripheral blood was collected from 8 women undergoing IVF on the day of oocyte retrieval after ovarian controlled stimulation with gonadotropins. RNA was extracted, cDNA was obtained and subsequently analyzed by quantitative real-time PCR (QPCR) for the expression of the CK-19 gene using specific primer sets with target gene expression normalized to GAPDH.

Results: Expression of CK-19 was positive in 100% (8/8) of patients. Relative gene expression of CK19 ranged from 10-fold lower to 13-fold greater expression compared to GAPDH. Seven of the eight patients did not achieve pregnancy, and one achieved a twin gestation. Based on previous studies, the prevalence of CK-19 expression in women from a healthy cohort is only 0-2.2%.

Conclusion: The high prevalence of CK-19 expression in this limited cohort of patients with infertility and undergoing IVF, compared to a very low prevalence rate of CK-19 expression in healthy women, raises the possibility of using this epithelial antigen as a marker for IVF success and reproductive fitness. The differential expression levels found among our subjects may allow for the calculation of cut-off values indicative of treatment success or failure. Further studies with larger sample sizes are needed to confirm this high prevalence.

Melanoma Progression is Inhibited by the Histone Deacetylase Inhibitor LBH589 by Direct Tumor Effects and Enhancement of the Immune Response.

David M. Woods¹, Karrune V. Woan², Hongwei Wang², Fengdong Cheng², Zi Wang², Lianet Vazquez², Patricio Perez², Maritza Lienlaf², Jennifer Rock-Klotz², Eva Sahakian², John Powers², Susan Deng², Merino Oscar², Peter Atadja³, Ed Seto², Javier Pinilla-Ibarz², Jeffrey S. Weber², Eduardo M. Sotomayor², Alejandro Villagra². ¹University of South Florida, College of Medicine, Tampa, FL; ²H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; ³Novartis Institutes for BioMedical Research, Boston, MA. University of South Florida, Morsani College of Medicine, Dept. of Pathology and Cell Biology

Keywords: melanoma, histone deacetylase, HDAC, immunotherapy, cancer

Objective: The five-year survival rate for metastatic melanoma is about 16%, and few therapies exist that provide significant survival benefits. HDAC inhibitors have demonstrated promise in the treatment of various malignancies. Here we assess the mechanism and efficacy of a novel orally bioavailable HDACi, LBH589, in a murine model of melanoma.

Methods: Proliferation was measured using an MTS assay. Cell cycle distribution was determined by propidium iodide staining of DNA. ELISA was used to determine cytokine production. Cell surface marker expression was assessed by flow cytometry. LBH589 was administered in vivo by IP injections.

Results: In vitro, LBH589 treatment decreased the proliferation of both human and murine melanoma cells, inducing a cell cycle arrest in G1. Furthermore, treatment enhanced the expression of immunologically relevant receptors, MHC I and II, markers critical for immune surveillance. LBH589 also inhibited the production of the anti-inflammatory cytokine IL-10, but increased the production of the pro-inflammatory cytokine IL-12, and upregulated the surface expression of the co-stimulatory molecule B7.2 on macrophages, leading to enhanced activation of naïve and tumor-anergized T-cells evidenced by increased production of IL-2 and IFN- γ . Finally, LBH589 impaired tumor growth in vivo in mice bearing B16 murine melanoma.

Conclusion: Taken together, LBH589 demonstrates anti-melanoma effects both in vitro and in vivo, which may be mediated through both direct toxicity to tumor cells, as well as enhancing antitumor immunity. These results provide rationale for the use of LBH589 either alone or in combination with other immune enhancing therapies for the treatment of melanoma.

Research supported by: The Donald A. Adam Comprehensive Melanoma Research Center

MK2206, a Selective AKT Inhibitor, Modulates Ovarian Cancer Cell Line Sensitivity to Carboplatin Plus Paclitaxel

Nadim BOU ZGHEIB, MD¹, Yin XIONG, MS^{1,2}, Douglas C. MARCHION, PhD^{1,2}, Xiaomang Ba STICKLES, MD¹, Patricia L. JUDSON, MD^{1,4}, Ardeshtir HAKAM, MD^{3,4}, Jesus GONZALEZ-BOSQUET, MD, PhD^{1,4}, Robert M. WENHAM, MD^{1,2,4}, Sachin M. APTE, MD^{1,4}, and Johnathan M. LANCASTER, MD, PhD^{1,2,4}, Department of Women's Oncology¹, Experimental Therapeutics Program², Department of Anatomic Pathology³, Department of Oncologic Sciences⁴, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Obstetrics and Gynecology

Keywords: Akt inhibition, phospho-BAD, chemosensitivity to carboplatin and paclitaxel, ovarian cancer survival

Objective: AKT a vital regulator of diverse tumor signaling pathways has been associated with the development and progression of many human cancers, including ovarian cancer (OVCA). AKT phosphorylation of the BCL2 antagonist of cell death (BAD) protein promotes cell survival and influences OVCA response to chemotherapy. MK2206, a highly selective allosteric AKT inhibitor, prevents the phosphorylation of all three isoforms of AKT in-vitro. We investigated the effect of MK2206 on: 1) AKT and subsequent BAD phosphorylation and 2) cell proliferation in the presence and absence of carboplatin plus paclitaxel (C/T). Further, we evaluated the influence of BAD pathway expression on OVCA cell response to MK2206.

Methods: OVCA cell lines treated with MK2206 (1µM) were subjected to gene expression analysis. Principle component analysis was used to generate a numeric value that summarizes the overall level of expression of the BAD pathway. Cell viability assays were performed on a subset of OVCA cell lines using combinations of MK2206 plus C/T. Combinational index(CI) determined by the Chou-Talalay isobologram equation were used to indicate antagonistic, additive or synergistic activity

Results: Pearson's analysis identified a correlation between MK2206 sensitivity and BPGES score in OVCA cells. MK2206(0.1µM) decreased levels of phospho-AKT and phospho-BAD[ser136]. CI values indicated a synergistic induction of growth arrest with combination MK2206 plus C/T treatment at a constant molar ratio of 2.0.

Conclusion: Our findings suggest that expression of the BAD apoptosis pathway influences MK2206 response in OVCA cell lines. MK2206 inhibition of AKT and phospho-BAD sensitizes OVCA cells to C/T. MK2206, acting upon the BAD pathway, shows great promise as an OVCA therapeutic agent.

Novel Role of Mir-17 in Pulmonary Arterial Hypertension

Gurukumar KR, Prasanna Tamarapu Parthasarathy, Samuel Jalali, Asfiya Yunus, Sara Garcia, Richard F. Lockey and Narasaiah Kolliputi. Division of Allergy and Immunology, Joy McCann Culverhouse Airway Disease Center Department of Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL

Keywords: pulmonary hypertension, micro RNA, miR17-92.

Objective: Pulmonary Arterial Hypertension (PAH) is a progressively devastating disease characterized by excessive proliferation of the Pulmonary Arterial Smooth Muscle Cells (PASMCs). Recently micro-RNA (miR) have been shown to play an important role in the pathogenesis of PAH. Our previous results show that the miR17-92 cluster is over expressed in hypoxic PAH mice. In the present study we determined the effects of over expression of miR17 on human PASMC (HPASMC).

Methods: HPASMC were commercially obtained and cultured according to manufacturers instructions. Cells were transfected with plasmid encoding miR17 or control vector by electroporation. Proliferation and apoptosis of transfected HPASMCs was assessed. RNA and protein levels of important target genes in PAH were measured using Real time PCR and western blots.

Results: HPASMC transfected with miR17 show decreased proliferation and increased apoptosis. Preliminary real-time RT-PCR analysis reveal proliferation markers such as proliferating nuclear cell antigen(PCNA) and CyclinD1, SMC markers such as alpha Smooth muscle actin (SMA) myosin heavy chain(MHC) and calponin were down regulated in miR17 transfected cells. Western blots of miR17 transfected HPASMCs show reduced levels of bone morphogenic protein receptor-II (BMPRII). Further characterization of HPASMCs transfected with mir17 are being conducted and results will be presented.

Conclusion: MiR17 over expression down regulates BMPRII and SMC phenotypic markers(SMA, MHC and calponin) in hPASMCs implicating a potential role in PAH.

Research supported by: This work was supported by the American Heart Association National Scientist Development Grant 09SDG2260957 and NIH R01 HL105932 to N.K. and the Joy McCann Culverhouse Endowment to the Division of Allergy and Immunology.

Fractalkine (CX3CL1) May Be Associated With Human Umbilical Cord Blood (HUCB) Cell Mediated Neuroprotection in Acute Ischemic Stroke

Shahaduzzaman, M.^{1,2}, Glover, J.^{1,2}, Golden, J.E.^{1,3}, Mcaleer, J.^{1,2}, Gemma, C.^{1,2}, Bickford, P.C.^{1,2}, and Willing, A.E.^{1,3}. ¹Center of Excellence for Aging & Brain Repair, and Departments of ²Neurosurgery, and ³Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL 33612 University of South Florida Morsani College of Medicine, Dept. of Neurosurgery

Keywords: Fractalkine, Stroke, Inflammation, Cord Blood Cells

Objective: There is mounting evidence that inflammation plays an important role in the progression of acute ischemic stroke (AIS). Administration of HUCB cells 48 hrs. after a middle cerebral artery occlusion (MCAO) in a rat model of stroke resulted in significant improvements to behavioral and physiological outcome (Newcomb, Ajmo et al. 2006). Additionally, they showed a diminished granulocyte and monocyte infiltration in the parenchyma in animals treated with HUCB 48 hrs. post- stroke. Fractalkine (CX3CL1) and its receptor (CX3CR1) comprise a chemokine system involved in leukocyte recruitment and adhesion. The primary aim of this project was to examine the role of fractalkine in HUCB-mediated neuronal protection.

Methods: Organotypic brain slice cultures from Fractalkine knockout mice were incubated with or without HUCB under both normoxic and oxygen glucose deprivation (OGD) conditions and cell survival examined with the lactate dehydrogenase (LDH) assay. We further examined the clinical relevance of this line of investigation by determining fractalkine concentration in the serum from two AIS patients at 24, 48, 72, 96, 120, 144, 168 hours and at 30 days after onset of symptoms using human CX3CL1/Fractalkine Immunoassay.

Results: CX3CL1 concentration in the serum of both patients was significantly higher at 48 hours than at other time points examined.

Conclusion: CX3CL1-CX3CR1 is a novel inflammatory chemokine system that may play an important role in HUCB-mediated neuronal protection.

Research supported by: USF Established Investigator Award

Cardiac Dysfunction Exacerbated by Endocrinopathies in Friedreich's Ataxia

Madeline Snyder BA (a), Lauren Seyer MS CGC (b), David R. Lynch MD PhD (b), Andrew Resnick BS (a), Theresa A. Zesiewicz (a) (a)- Department of Neurology, University of South Florida, Morsani College of Medicine, Parkinson's Disease and Movement Disorders Center, Tampa, FL (b)- Department of Neurology, Children's Hospital of Philadelphia, Philadelphia, PA_University of South Florida, Morsani College of Medicine, Dept. of Neurology

Keywords: case study Friedreich's ataxia (FA) cardiomyopathy diabetes

Objective: To describe two Friedreich's ataxia (FA) patient cases in which metabolic and endocrine dysfunction triggered rapid progression of present cardiac abnormalities, to provide insight on how management of the endocrinopathies led to improvement in the patients' cardiac function, and to address the importance of screening for endocrinopathies in FA patients.

Methods: Patient #1 described is an FA teenager with previously undiagnosed diabetes that resulted in diabetic ketoacidosis, atrial fibrillation, and rapid progression to severe left ventricular dysfunction. Patient #2 described is an FA teenager whose worsening of previously undiagnosed Graves' disease led to rapid worsening of known cardiomyopathy.

Results: Patient #1 was treated with intravenous insulin, cardizem, digoxin, metoprolol, and antibiotics. Patient #2 was treated with inotropic agents, afterload reduction, and methimazole. Cardiac management and treatment for the endocrinopathies returned cardiac function to baseline in both patients.

Conclusion: The two cases illustrate the extreme degree to which cardiac function can decompensate in FA in the setting of underlying endocrinopathies. Cardiac dysfunction remains the most frequent cause of death in FA. A model relating cardiac and endocrine dysfunction with frataxin deficiency in FA was recently proposed, in which metabolic syndrome characteristics induced by frataxin deficiency arise from beta-cell death, decreased insulin levels, and skeletal muscle lipogenesis, thus promoting cardiac abnormalities. The cases we report on demonstrate the importance of aggressive screening for and awareness of underlying endocrinopathies in FA patients.

Research supported by: Friedreich's Ataxia Research Alliance (FARA)

Subcutaneous Hizentra® (20%) is Better Tolerated and Shares Similar Efficacy Compared to Subcutaneous Vivaglobin® (16%).

T. Alberdi, M.J. Dorsey, D. Nguyen, C. Duff, J. Sleasman, University of South Florida, Morsani College of Medicine, Dept. of Pediatrics

Keywords: Subcutaneous Immunoglobulin, Efficacy, Tolerability, Hizentra

Objective: Replacement Subcutaneous IgG (SCIG) therapy is effective treatment in reducing rates of infections in patients with primary immunodeficiency diseases (PIDD), but there are few comparative studies using different SCIG preparations. This study examines the tolerability and efficacy of Hizentra (20%) subcutaneous immune globulin (SCIG) product compared to Vivaglobin (16%).

Methods: A prospective, single-center, open-label cohort of 32 PIDD subjects, who received 16% Vivaglobin for at least 6 months and transitioned to 20% Hizentra for 24 weeks. Number of acute serious bacterial infections (aSBI) and overall tolerability on Vivaglobin was assessed for 8 weeks prior to switch and compared to Hizentra over 24 weeks. Average Hizentra dose was higher than Vivaglobin at 161.6 +/- 99.8 and 145.9 +/- 88.2 mg/kg/week, respectively ($p < 0.0001$).

Results: The study is ongoing and preliminary findings for all subjects through 12 weeks on Hizentra are reported. aSBI/subject/year while receiving Vivaglobin was 0.2 compared to 0.14 on Hizentra. Per-person annual rates of other infections were lower for Vivaglobin at 1.2 versus 2.63 for Hizentra ($p = 0.0167$). There were no infusion-related serious adverse events in either group. Average infusion time decreased from 108 minutes (3.2 sites) with Vivaglobin to 72 minutes (2.1 sites) with Hizentra. Mean Vivaglobin IgG were similar to Hizentra, 1096.1 (+/- 231.2) and 1105.2 (+/- 233.3) mg/dL, respectively ($p = 0.77$). Both groups had similar titers to varicella (103.1 versus 107.9 EU/mL) and tetanus (2.8 versus 2.9 IU/mL) on Vivaglobin and Hizentra, respectively.

Conclusion: Hizentra (20%) achieves better tolerability and similar efficacy to Vivaglobin (16%).

Research supported by: This is an investigator initiated study with grant from CSL Behring.

Does 18-Fluorodeoxyglucose (FDG) Uptake By Positron Emission Tomography/Computed Tomography (PET/CT) Predict Survival in Advanced Pancreatic Cancer; A Single Institution Experience

Noman Ashraf, Saqib Razzaque, Jill M. Weber, Mokenge Peter Malafa, Richard D. Kim H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL University of South Florida N/A

Keywords: Chart Review

Objective: Pancreatic cancer has a poor prognosis. Some studies suggest that 18-fluorodeoxyglucose (FDG) uptake by positron emission tomography/computed tomography (PET/CT) correlates with survival in pancreatic cancer. In this study, we aimed to determine whether standardized uptake value (SUV), a measure of FDG uptake by fusion PET/CT, had prognostic significance in patients with advanced pancreatic cancer.

Methods: Using a pancreatic cancer database at Moffitt Cancer Center, we identified patients who had PET/CT scan as initial workup for resection but were found to have advanced disease (stages III/IV) when surgery was attempted. Data from Jan 2006 to Dec 2010 was retrospectively analyzed and correlated with the maximum SUV determined by PET/CT. Other prognostic factors including stage, age, gender, CA 19-9 levels and the use of chemotherapy were also evaluated.

Results: We identified 41 patients deemed resectable by virtue of staging workup with CT, PET/CT and endoscopic ultrasound (EUS), but found to have locally advanced/metastatic disease intra-operatively. At the time of analysis, there were 30 deaths. 12 patients had metastatic disease and 29 had stage III pancreatic cancer. SUV uptake ranged from 2.9 to 16.2 with a mean of 6.4. Median overall survival for the 28 patients with $SUV \leq 6.4$ was 14 months (95% CI 10–25 months) vs. 9.1 months for the 13 patients with $SUV > 6.4$ (95% CI 4–17 months). This difference was not statistically significant ($p=0.178$). On multivariate analysis, use of chemotherapy was the only independent predictor of survival.

Conclusion: Glucose uptake by PET/CT, reflected by SUV, was not a predictor of survival in patients with advanced pancreatic cancer. The retrospective nature and limited sample size are limitations of our study.

Research supported by:

Diabetic Nephropathy Develops Naturally in Non Human Primates: Similarities to Humans

Sadaf Aslam¹, Barbara Hansen² ¹USF Clinical and Translational Sciences Institute ²USF Morsani College of Medicine, Obesity Diabetes and Aging Research Center University of South Florida Morsani College of Medicine Internal Medicine

Keywords: Diabetic nephropathy, Non human primates, Animal models,

Objective: Non-human primates (NHP) provide an exceptionally human-like model of naturally occurring spontaneous diabetic nephropathy (DN) and are unmatched in the ability to examine the earliest underlying pathophysiology and metabolic biomarkers of these pathologies. The main objective of this review is to critically analyze animal models of DN, to understand the early natural history of DN and progression to end stage renal disease and also to characterize spontaneously diabetic NHP as animal models of DN.

Methods: Presentation of DN, characterization in NHP obtained in this colony from in vivo data and from histopathology, together with review of the scientific literature concerning other NHP groups with DN and rodents with DN like pathology, with comparisons to published human data.

Results: Structural and functional aspects of DN were studied in NHP. Progression of DN from elevated GFR followed by mesangial expansion and glomerular basement membrane (GBM) thickening leading to albuminuria were studied in normal vs diabetic NHP. A recently published article together with current follow up study shows mesangial expansion in NHP similar to human DN and difference from rodent models is mainly due to the increased mesangial matrix. Trends for a positive correlation between albumin excretion rate and fractional mesangial volume were also reviewed. The limitations in rodent models to observe progressive renal changes in diabetes will be discussed.

Conclusion: While there are many animal models of DN, NHP appear to be unique among animal models in the extraordinary similarities to human DN. The level of detail and control in longitudinal study of NHP provides even greater understanding of the progressive pathophysiology than is possible in human subjects.

Research supported by: No

Utility of MRI in Diagnosis and Treatment Response in Eosinophilic Fasciitis

Alicia Baillargeon, DO John Carter, MD University of South Florida Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Case Study

Objective: In Eosinophilic Fasciitis (EF), the consensus for diagnosis has historically relied on histologic changes seen on full thickness skin biopsy. However, sufficient skin biopsy is not always available. This report describes a case of EF with a suboptimal biopsy specimen that utilizes MRI for purposes of diagnosis and monitoring of treatment response.

Methods: Case report was analyzed and reported Pathology results, laboratory results, and MRI results were reviewed

Results: The utilization of MRI is useful not only in diagnosis of EF when biopsy is inadequate but also in following the regression and resolution of the disease.

Conclusion: Currently the established diagnostic tool for EF is based on characteristic histologic changes from a full thickness skin biopsy. However, there have been reports where the use of MRI is used to provide the diagnosis when laboratory tests as well as skin biopsies do not sufficiently confirm. If biopsy is inadequate, MRI may be helpful to confirm fascial inflammation. Although data on clinical utility of MRI in the diagnosis and monitoring of EF are still limited, this case report along with others indicates that there may be some usefulness. The above case report displays the utilizing MRI not only in diagnosis when biopsy is inadequate but also in following the regression and resolution of the disease.

Research supported by: Case report References will be provided

Perioperative Blood-sparing Intravascular Occlusive Balloons During Primary and Revision Total Hip Replacement

Adam Baumgarten¹, Rita Patel MD², Steven Lyons, MD³, Thomas Bernasek, MD³, Enrico Camporesi, MD^{2,1}, and Devenand Mangar, MD², University of South Florida, Morsani College of Medicine, Dept of Orthopaedics and Sports Medicine, ²Florida Gulf to Bay Anesthesiology, ³Florida Orthopaedic Institute

Keywords: intravascular balloon occlusion, total hip replacement, revision hip replacement, Jehovah Witness

Objective: Jehovah's Witness patients provide a challenge to surgeons during high blood loss surgical procedures. Temporary arterial occlusive balloon can be used to minimize blood loss in these surgeries.

Methods: We completed a retrospective study of perioperative blood loss and fluid requirements in Jehovah's Witnesses (JW) patients using intravascular occlusive balloons. The balloon was inserted through the contralateral femoral artery with radiological guidance into the ipsilateral common iliac artery. The balloon was inflated during the exposure of the joint and disarticulation of the femoral head for 20 min alternating with reperfusion for 10 min, to avoid ischemic processes in the distal lower limb. Balloons were inflated 3 to 4 times during each surgery. Results were compared to a 4:1 control to balloon group of demographically similar patients and were statically analyzed type of surgery, gender, age, year of surgery, and preoperative diagnosis.

Results: 6 primary hip replacements and 6 hip revisions were JW. 24 controls were used for each. Blood loss for primary hip JW patients was 145 mL compared to controls with 402 mL blood loss ($p < 0.05$). Blood loss for revision hip JW patients 333 mL compared to controls with 767 mL blood loss ($p < 0.05$). Data are presented as mean. No balloon patients received blood, while the control groups received 0.6 (total hip) or 1.5 units (revision) of blood ($p < 0.05$). Total volume of crystalloids and postoperative complications showed no statistical differences. Length of surgery and length of hospitalization were also not different.

Conclusion: Although deployment of intravascular balloons adds an additional procedure by a radiologist, they are a validated blood sparing procedure in JW patients.

Research supported by: American Heart Association Medical Student Fellowship Grant

An Unusual Reaction to Intravenous Iron Sucrose

Balduzzi M, Rashid D, Butt A, Ledford D and Lockey RF. Division of Allergy & Immunology University of South Florida and James A. Haley Veterans' Hospital, Tampa, FL, University of South Florida Morsani College of Medicine, Dept. of Internal Medicine

Keywords: iron dextran, drug allergy

Objective: Identify that although the use of intravenous iron sucrose has decreased the incidence of adverse events, systemic reactions may occur in a minority of recipients.

Methods: A 62-year-old Caucasian male with multiple gastric surgeries, secondary to recurrent gastric ulcers and gastric outlet obstruction, presented with severe iron deficiency anemia (IDA) requiring IV iron therapy

Results: Chronic malnutrition and malabsorption, associated with difficulty in tolerating oral and jejunostomy tube (J-tube) feedings, resulted in a two month 30 pound weight loss. Oral iron supplementation via a J-tube did not improve the IDA. Prior administrations of IV iron dextran resulted in flushing, generalized urticaria and angioedema associated with pruritus of the face and extremities within ten minutes of infusion. The allergy/immunology service was consulted. Premedication with IV diphenhydramine, 50 mg, prednisone via J-tube, 32 mg, and IV ranitidine, 50 mg, was followed with slow administration of a test dose of IS, 25 mg, at 1.6 mg/min. Within 30 minutes of the IV IS infusion, symptoms of nausea, flushing, and generalized pruritus, and difficulty in breathing were noted. The infusion was stopped and treatment with IV methylprednisolone, 125 mg, resulted in resolution of the reaction over several hours. No eosinophilia or elevated liver transaminases occurred. Subsequently, the infusion was reattempted: pre-medications consisted of IV methylprednisolone, 60 mg, IV diphenhydramine, 50 mg, and IV ranitidine, 50 mg, 75 minutes prior to the infusion of IS, 275 mg, 1.5 mg/min. Treatment was tolerated without adverse effects.

Conclusion: Pretreatment with methylprednisolone, diphenhydramine and ranitidine 75 minutes before IS infusion was successful.

Group Prenatal Care at Neighborhood Health Centers of the Lehigh Valley

Sharon Chacko, Kristin Reihman, Abby Letcher University of South Florida Morsani College of Medicine Family Medicine

Keywords: Descriptive Case Study, Centering Pregnancy, Prenatal Care

Objective: In the Centering Pregnancy model, groups of eight to twelve women with similar gestational ages meet with their provider for about ten group prenatal visits. Kristin Reihman, M.D. facilitates Centering Pregnancy groups at NHCLV. Due to the relative newness of Centering at NHCLV, groups are typically comprised of about five women. This investigation assessed patients' feelings toward the Centering model, how their care impacted their pregnancy and postpartum, and their level of satisfaction with their care and pregnancy outcomes.

Methods: Patients were invited to participate in a descriptive case study. Nine participants spoke individually with the study investigator who asked participants both scaled and open-ended questions regarding their group prenatal care.

Results: 7/9 women said groups made them feel more empowered either via increased perception of control over their care, labor and life or increased confidence in their own abilities. 6/9 women said groups provided them with something they weren't getting elsewhere in their lives or enabled them to overcome an obstacle that would have otherwise negatively impacted their lives. 7/9 women gained valuable knowledge from the experiences of other women in their groups. 7/9 women said groups made them feel more hopeful about their pregnancy, having a baby and life in general. All patients interviewed chose to breastfeed. Seven said group experiences influenced or reaffirmed their decision and several expressed that groups influenced them to breastfeed longer.

Conclusion: The Centering Pregnancy model at NHCLV affords a majority of participants with empowerment, hope, and knowledge. A challenge this study faced was a low study sample size due to the limited number of Centering participants at NHCLV.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine and the LVHN/USF Medical Student Enrichment Summer Experience.

Vaginal Birth After Cesarean (VBAC): Provider Perspectives and Maternal Decision-Making

Allison Cantor¹, Isabella Chan^{1,2}, Emily Dunn^{1,2}, ¹Department of Anthropology, ²Department of Community and Family Health. University of South Florida, College of Arts and Sciences, Dept. of Anthropology

Keywords: VBAC, providers, maternal, decision-making

Objective: This research examines the attitudes, beliefs, and practices of women and maternal health care providers regarding vaginal birth after cesarean (VBAC). The objectives of this study were 1) explore maternal health care providers' attitudes about VBAC, 2) determine providers' motivations for these attitudes, and 3) document women's experiences with VBAC in the Tampa Area.

Methods: The data analyzed in this paper were collected from 11 in-depth, semi-structured interviews with maternal health care providers (n=6) and women who had experienced VBAC (n=5). Providers were recruited through purposive convenience and chain referral sampling from local hospitals. Women with VBAC experience were recruited through purposive convenience sampling from a local chapter of the International Cesarean Awareness Network and social networking sites. Analysis was conducted through targeted transcription and consensus coding for salient themes.

Results: Analysis identified 3 thematic areas in maternal and provider decision-making about VBAC: 1) patient-provider relationships, 2) perceptions of risk, and 3) acceptance/rejection of biomedicine. All provider participants referenced official guidelines as impacting their practice, while maternal participants challenged the same guidelines. This investigation reveals a clear distinction between providers' and women's experiences with VBAC and tensions between biomedical and alternative birthing practices.

Conclusion: This research illustrates the complex nature of decision-making regarding birth practices in the US for both providers and women and the disconnects in provider-patient communication. Future studies should seek to elaborate on the patient-provider dialogue and advance the conversation towards an integrated solution.

Definitive IMRT-based Chemoradiation for Treatment of Squamous Cell Carcinoma of the Anal Canal

MD Chuong M.D., SE Hoffe M.D., Ph.D., J Weber, M.P.H., H Lomas, PA-C, M.P.A.S., K Almhanna, M.D., C Chodkiewicz, M.D., S Dessureault, M.D., W Dinwoodie, M.D., R Kim, M.D., J Giglia, M.D., K Meredith, M.D., J Strosberg M.D., and Ravi Shridhar M.D. University of South Florida, College of Medicine, Dept. of Oncologic Sciences

Keywords: anal cancer, squamous cell carcinoma, intensity modulated radiation therapy, IMRT

Objective: Squamous cell carcinoma (SCC) of the anal canal is curable with definitive chemoradiation, significantly reducing the need for colostomy. Despite excellent long-term outcomes, chemoradiation with traditional radiation therapy techniques results in significant morbidity. More recently, data has accrued in support of intensity-modulated radiotherapy (IMRT)-based treatment. We report our institutional experience with IMRT-based definitive chemoradiation for SCC of the anal canal.

Methods: This retrospective review included patients with non-metastatic SCC of the anal canal who were received definitive concurrent chemotherapy and IMRT. Clinically node negative patients initially received 36 Gy to the elective pelvic and inguinal lymph nodes and 40 Gy to gross tumor volume (GTV) while node positive patients received 45 Gy and 50 Gy, respectively. Patients were then considered for a GTV boost, regardless of nodal status, depending on the degree of clinical response and acute treatment-related toxicity.

Results: We evaluated 52 patients with biopsy-proven T1-4N0-3M0 SCC of the anal canal. The median follow up was 18.5 months (range, 2.5-125.5 months). Two-year locoregional control, overall survival, disease-free survival, distant metastasis-free survival, and colostomy-free survival were 94.6%, 100%, 82.6%, 90%, and 94.7%, respectively. Acute grade 3+ non-hematologic and hematologic toxicities were observed in 21.1% and 59.9%, respectively. No grade 4 nonhematologic toxicity was observed. Four patients (7.7%) had a treatment break of a median 11 days (range, 6-12).

Conclusion: Our series demonstrates that definitive IMRT-based chemoradiation with standard fractionation for anal SCC results in excellent outcomes with minimal toxicity.

Silent, Pain-free Needle Punctures – The Resealing of Surgical Gloves After Puncture May Jeopardize the Health Care Provider

Eric S. Clayman (M.S. candidate at Morsani College of Medicine), Karl Muffly, Ph.D (Depts. Pathology & Cell Biology and Surgery). University of South Florida, Morsani College of Medicine Dept. of Pathology and Cell Biology

Keywords: Glove Resealing After Puncture

Objective: This study aims to determine the resealing capacity of sterile latex and non-latex surgical gloves.

Methods: Sterile Latex, Chloroprene, Nitrile, Polyisoprene, Duraprene, and Vinyl surgical gloves were perforated with 25-, 27-, and 30-gauge hollow needles. 20 fingertips and palm perforations for each type of glove were tested for leaks from these perforations using a 500ml watertight method and were observed after 10 minutes.

Results: Latex and Chloroprene fingertips resealed 100% with 25-, 27-, and 30-gauge needle punctures; Nitrile fingertips resealed 100% with both 27- and 30-gauge needle punctures and 80% with 25-gauge needle punctures; Polyisoprene fingertips resealed 100% with 30-gauge needle punctures and 60% with both 27- and 25-gauge needle punctures; Duraprene fingertips resealed 80% with 30-gauge needle punctures and 60% with both 27- and 25-gauge needle punctures; Vinyl fingertips resealed 60% with 30-gauge needle punctures, 20% with 27-gauge needle punctures, and 0% with 25-gauge needle punctures. The palm of every single glove had 0% resealing with all needle punctures.

Conclusion: The results of this study reveal that there is significant resealing of surgical gloves after needle perforation. This resealing capacity allows the health care provider to be unaware of silent, pain-free needle punctures that may result in exposure to bodily fluids. Health care providers and ancillary health care workers should have increased protection from exposure to bodily fluids when double gloving.

Research supported by: Karl Muffly, Ph.D Depts. Pathology & Cell Biology and Surgery

Adult-Onset Henoch-Schonlein Purpura: A Case Report with Unusual Manifestations.

Victor D. Cruz, MD, Internal Medicine, Morsani College of Medicine, University of South Florida, Jose Lezama, Chief of Medicine, James A. Hayley VAMC, USF Medicine

Keywords: Henoch-Schonlein Purpura, Cutaneous small-vessel vasculitis, IgA Immune Complex deposition, Acute Renal Failure, Idiopathic Pulmonary Fibrosis

Objective: Histologically, Henoch-Schonlein Purpura (HSP) is characterized by leukocytoclastic vasculitis with granular deposition of IgA in superficial blood vessels. Typically occurring in children with an incidence as high as 70.3 per 100,000, HSP is far less common in adults, with an incidence as low as 3.4 cases per million. Adults generally suffer from more severe disease as well as unusual presentations including pulmonary involvement, scrotal pain, nervous system involvement and seizures. Pulmonary involvement can manifest occasionally as interstitial pneumonia or interstitial fibrosis.

Methods: A case report of a rare adult onset leukoclastic vasculitis with unusual presenting systemic findings, as well as a review of the published literature.

Case Description: Our patient is a 67-year-old male was admitted for a routine blood transfusion after presenting with signs and symptoms of anemia in the setting of chronic kidney disease. Shortly after diffuse infiltrates were seen on X-ray imaging obtained secondary the onset of respiratory symptomatology. This was thought to be a pneumonia and placed on intravenous antibiotic therapy. As the respiratory status continued to deteriorate, CT imaging was obtained, revealing scattered bilateral areas of patchy consolidated opacity, prompting a pulmonary consult that resulted in a bronchoscopy. Further workup was warranted at this point in time therefore cardiothoracic surgery was involved for a lung biopsy. Results demonstrated an organizing inflammatory process consistent with diffuse alveolar damage superimposed on lung disease, features suggestive of an underlying interstitial pneumonia. Scrotal involvement, acute renal failure and the development a palpable purpura with lower extremity predomination ensued. A vasculitis serologic workup was remarkable for an increase in serum monoclonal light chains with a preserved ratio. After further workup, a punch biopsy revealed cutaneous small-vessel vasculitis with deposition of immune complexes containing antibody IgA, consistent with Henoch-Schonlein Purpura.

Conclusion: The diagnosis of HSP is based upon clinical manifestations of the disease, with criteria for diagnosis established in 1990 by the American College of Rheumatology. It is characterized by the clinical tetrad of non-thrombocytopenic palpable purpura, abdominal pain, arthritis and renal involvement. Of these four manifestations our patient had three along with other systemic involvement. Most cases of HSP are self-limited and may require little or no intervention, as was the case in this patient. Although rarely seen in adults, this clinical entity should be included in the differential of any patient presenting with similar symptoms in order to pursue an adequate work up as complications are generally more severe in adults and thus worsen the clinical outcomes.

Idiopathic Isolated Orbital Angioedema

Susan Culverhouse, MD Neetu Talreja, MD Richard F. Lockey, MD Department of Internal Medicine, University of South Florida and James A. Haley Veterans Hospital, Tampa, FL, University of South Florida

Keywords: proptosis, pseudotumor

Objective: Idiopathic angioedema is a term applied to recurrent episodes of angioedema of unknown etiology. The following is a casereport of idiopathic, recurrent, isolated orbital angioedema with exophthalmos, which responds to prolonged courses of oral corticosteroids.

Methods: A 67 year-old Caucasian female with aspirin exacerbated respiratory disease(AERD)sought treatment for an acute, progressive,painless left eye swelling with exophthalmos.There was no associated visual deficit or urticaria. High dose corticosteroids were initiated followed by low maintenance dose corticosteroids. The swelling subsided after one year of corticosteroid therapy. Ten years later, orbital swelling with exophthalmos reoccurred in the same eye. No medications such as aspirin or other non steroidal anti-inflammatory drugs were associated with the swelling. An MRI of the orbits revealed left eye isolated proptosis. The family history and history and physical examination was negative. High-dose systemic corticosteroid therapy was initiated. Symptoms resolved after 1 month, however, swelling of the orbit reoccurred within one week. Low dose maintenance corticosteroids were reinitiated with resolution of swelling. C1 esterase deficiency is negative.

Results: Vision normal, Motility normal. MRI of orbits:Isolated proptosis left

Conclusion: Idiopathic orbital inflammatory syndrome, also known as orbital pseudotumor,is one of the most common acute orbital processes.The pathogenesis of IOIS remains unclear. Diagnosis is mostly made on a clinical basis,often in combination with orbital imaging studies; however, in some patients biopsy is required to exclude other orbitopathies that may cause similar symptoms Treatment is with oral glucocorticoids with recurrence in 42%

Predictors of Outcome in Patients with Recurrent Gastrointestinal Stromal Tumors

Jeremiah L. Deneve, DO¹, Colin M. Parsons, MD², Sebastian G. de la Fuente, MD¹, J. Kim, BS³, Anthony P. Conley, MD¹, A. Martin, BS¹, Jonathan S. Zager, MD, FACS¹, Douglas G. Letson, MD¹, Ricardo J. Gonzalez, MD, FACS¹ Department of Sarcoma Oncology, Moffitt Cancer Center¹, Kaiser Permanente Health Systems, San Diego, CA², Department of Biostatistics, Moffitt Cancer Center³ University of South Florida, Morsani College of Medicine, Dept. of Oncologic Sciences

Keywords: GIST, recurrence, tyrosine kinase inhibitor, metastasis

Objective: Recurrence after initial resection of advanced gastrointestinal stromal tumors (GIST) is common despite tyrosine kinase inhibitor (TKI) therapy. Appropriate management of patients with recurrent GIST is not well defined. Our aim was to identify predictive factors associated with outcome in this population.

Methods: We identified patients (pts) with advanced/recurrent GIST who underwent resection from our institutional database from 1999-2009. Significant variables for recurrence and survival were analyzed.

Results: Of the 193 pts with GIST, 78 pts (46.4%) underwent treatment for recurrent/advanced GIST with a median follow up of 38 months (0.3-61). Final margin after initial primary resection was R0/R1 in 60 pts (77%) and R2 in 18 pts (23%). Thirty-eight pts (49%) received adjuvant TKI therapy. Age, gender, tumor size, mitotic rate or adjuvant TKI therapy were not associated with survival on univariate analysis, whereas stage at initial diagnosis ($p=0.0015$), initial resection margin ($p<0.0001$), presence of multifocal disease ($p=0.002$), ≥ 2 procedures for recurrence ($p=0.04$), and TKI resistance ($p<0.0001$) were significant. Resistance to TKI therapy ($p=0.04$, 95% CI 1.0-5.6) and incomplete resection at the time of initial primary GIST resection ($p=0.002$, 95% CI 1.6-9.6) were independently associated with reduced survival on multivariate analysis.

Conclusion: Incomplete initial resection and development of resistance are independent predictors of survival in patients with advanced/recurrent GIST. Selection of patients for resection versus continuing TKI therapy in the setting of recurrence requires a multidisciplinary approach. Reoperation should be reserved for TKI response and for those which complete resection of the recurrence is possible.

Patterns of Metastases and Correlation with Prognosis in Solitary Fibrous Tumor/Hemangiopericytoma at Moffitt Cancer Center

Nicholas DeVito, Ricardo Gonzalez, Marilyn Bui, Evita Henderson, Anthony Conley University of South Florida, Morsani College of Medicine, Dept. of Oncologic Sciences

Keywords: Solitary Fibrous Tumor, Hemangiopericytoma, Sarcoma, Chart Review

Objective: To describe Moffitt Cancer Center's experience with Solitary Fibrous Tumor/Hemangiopericytoma, a rare sarcoma, and to gain a better understanding of metastatic patterns, treatment (chemotherapy, surgery and radiation) and survival outcomes.

Methods: Patient charts were analyzed using the Powerchart database at Moffitt. Data from these charts was de-identified and placed in a spreadsheet for statistical analysis. This data was sent to a statistician for interpretation of the aforementioned points.

Results: Of our 87 patients, 55% were female, 45% male, the average age of disease presentation was 57 with a range of 19 to 88. Average age of pathological diagnosis was 61 years. 38% of the patients had documented deaths in the social security database. Lung/pleura was by far the most common primary site, accounting for 33% of patients, while extremity (16%) and head/neck (11%) followed. From a pathology standpoint, 39% were declared benign, 44% malignant and 17% did not have a certain dysplastic definition; 72% were CD34 positive. No patients with benign tumors had metastases at diagnosis, while 16% of those with malignant tumors did. Median overall survival was 50 months.

Conclusion: This study yields valuable information on the characteristics of patients with SFT/HPC which will hopefully be useful as a reference for future therapeutic trials.

Research Supported by: Research Scholarly Concentration at USF Health Morsani College of Medicine, University of South Florida

Two Red Herrings and a Sweet Catch

Gelenis C Domingo, MD Jennifer Coe, DO Ahsa Ramsakal, DO, MBS, FACP Lynn Moscinski, MD Lucy Guerra, MD, MPH, FACP University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Sweet Syndrome, Rash, Fever of unknown origin.

Objective: To discuss Sweet Syndrome which is a rare condition that should be included in the differential diagnosis for patients with hematological malignancies presenting with a fever of unknown origin and a rash.

Methods: A retrospective chart review of one case and a review of the literature was conducted.

Results: A 54 year old male with a history of Myelodysplastic Syndrome presented with recurrent fevers, lethargy, a twenty pound weight loss and the development of a rash on his right posterior neck and right lower extremity for one month. Initial urine analysis, urine and blood cultures, and chest radiograph were unremarkable. The patient underwent an extensive workup for fever of unknown origin including total body CT scans which revealed a pulmonary nodule and an adrenal mass. However, these incidental findings turned out to be insignificant (two red herrings). The patient's condition continued to deteriorate with persistent fevers and nearly 50 pound weight loss. Skin biopsy results were then obtained which showed a neutrophilic dermal infiltrate consistent with Sweet Syndrome. This was our Sweet Catch.

Conclusion: Sweet Syndrome is a neutrophilic dermatosis characterized by fever, leukocytosis and erythematous plaques infiltrated by neutrophils. It is often associated with multiple conditions including drugs, infections, collagen vascular diseases, leukemia and Myelodysplastic Syndrome. However, there are only ten of these cases in association with Myelodysplastic Syndrome reported in the literature. This case demonstrates an unusual diagnosis of Sweet Syndrome for a common presentation of fever of unknown origin and a rash in a patient with Myelodysplastic Syndrome.

Prosthetic H-Graft Portacaval Shunts (HGPCS) Versus Transjugular Intrahepatic Portasystemic Stent Shunts (TIPS): 18-Year Follow-up of a Randomized Trial

Heather A. Frohman¹ Alexander S.² Rosemurgy² Kenneth Lubrice² Anthony F. Teta² Sharona B. Ross¹
University of South Florida, Morsani College of Medicine, Dept of Surgery, ²Tampa General Medical Group

Keywords: Hgraft, TIPS, Randomized Controlled Trial, Portal Decompression

Objective: Widespread application of Transjugular Intrahepatic Portasystemic Shunt (TIPS) continues despite the lack of trials documenting efficacy superior to surgical shunting. Herein is 18-year follow-up of a prospective randomized trial comparing TIPS to Prosthetic H-Graft Portacaval Shunts (HGPCS) for portal decompression.

Methods: Beginning in 1993, patients were prospectively randomized to undergo TIPS or HGPCS as definitive therapy for portal hypertension due to cirrhosis. Complications of shunting and long-term outcome were noted. Failure of shunting was prospectively defined as: inability to place shunt, irreversible shunt occlusion, major variceal rehemorrhage, unanticipated liver transplantation, or death. Survival and shunt failure were compared using Kaplan-Meier curve analysis. Median data are reported.

Results: Patient presentation, circumstances of shunting, causes of cirrhosis, severity of hepatic dysfunction (e.g., Child class, Model for End-stage Liver Disease (MELD) score), and predicted survival after shunting did not differ for patients undergoing TIPS (n=66) or HGPCS (n=66). Survival was significantly longer after HGPCS for patients of Child Class A (91 vs. 19 months, p=0.009) or Class B (63 vs. 21 months, p=0.02). Shunt failure occurred later after HGPCS than TIPS (42 vs. 19 months, p=0.04).

Conclusion: Compared to TIPS, survival after HGPCS was superior for patients with better liver function (e.g., Child Class A or B). Shunt failure after HGPCS occurred later than after TIPS. Rather than TIPS, application of HGPCS is preferred for patients with complicated cirrhosis and better hepatic function.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine, Tampa General Medical Group, USFHealth Morsani College of Medicine

Proximal Tibia Reconstructions with Megaprotheses for Tumor: An Initial Investigation of Implant Survival and Complications

John Groundland¹, David Donohue¹, David Cheong, MD², G. Douglas Letson, MD² ¹University of South Florida, Morsani College of Medicine, Dept of Orthopaedics and Sports Medicine, ²Moffitt Cancer Center, Sarcoma Program

Keywords: Proximal tibial replacement, megaprosthesis, chart review

Objective: The objective of the current investigation is to describe the population of patients that received a proximal tibia megaprosthesis at a major cancer institution, and to describe the complications that led to implant failure or poor functional outcome

Methods: A retrospective chart review was performed. Patients were included if they underwent proximal tibia reconstruction with a metallic endoprosthesis, and if the indication for surgery was oncologic resection. In addition, a review of the literature was performed, summing the proximal tibia replacement surgeries and the associated complications

Results: Thirty eight (38) patients were identified as meeting inclusion criteria. Of the 38 patients who received a proximal tibia replacement, ten patients required prosthesis revision at an average of 20 months after date of surgical implant. Eight (8) patients ultimately underwent above knee amputation due to ongoing complications. Infection (12), wound dehiscence (9) and recurrent disease (3) were the most common causes of complication. Failure of the quadriceps extensor mechanism is identified as a complication of the surgery; five of the current patient cohort had a non-functioning extensor mechanism (13%). The review of literature demonstrated similar results as those herein reported

Conclusion: Proximal tibia replacement surgery provides an alternative to amputation for patients with oncologic disease of the knee. However, complications of this surgery include infection, wound dehiscence, recurrent disease and failure of the extensor mechanism. Further analysis of the data may illustrate which factors influence the success or failure of this surgical procedure

Research supported by: This research was supported by the Research Scholarly Concentration at the USF Health Morsani College of Medicine, University of South Florida

Cystic Prostatic Ductal Adenocarcinoma: An Unusual Presentation and Cytological Diagnosis

Evita Henderson-Jackson, M.D.¹, Wade Sexton, M.D.², Jingsong Zhang, M.D.², Ardesir Hakam, M.D.³, Vyacheslav S. Petrovskyy, M.D.³, Marilyn M. Bui, M.D., Ph.D.³ and Shang-Tian Chuang, D.O.³ ¹Department of Pathology and Cell Biology, University of South Florida Health, Tampa, FL ²Department of Genitourinary Oncology, Moffitt Cancer Center, Tampa, FL ³Department of Anatomic Pathology, Moffitt Cancer Center, Tampa, FL University of South Florida Morsani College of Medicine Pathology and Cell Biology

Keywords: cystic prostatic ductal adenocarcinoma, immunohistochemistry, cytology, histology, prostatic cysts

Objective: Prostatic ductal adenocarcinoma (PDA) is an uncommon histological variant of prostatic adenocarcinoma that may present clinically as a cystic mass [1-3]. Our objective is to describe the common cytological features of PDA and to analyze the differential diagnoses associated with cystic masses of the prostate.

Methods: We report a case of cystic PDA presenting as a cystic perirectal mass in a 61 year old male

Results: Fine needle aspiration cytology showed malignant cells with round-oval to focally elongated nuclei, conspicuous nucleoli and amphophilic cytoplasm with focal acinar formation. Tumor cells were positive for prostate-specific antigen, however, the cytology was non-specific for site of origin. The radical cystoprostatectomy specimen revealed the true site of origin and showed a cystic PDA adjacent to conventional prostatic acinar adenocarcinoma

Conclusion: In conclusion, important FNA findings for cystic PDA are large sheets and clusters of cells, abundant cytoplasm, bland to marked nuclear atypia with crowding and hyperchromasia, and the presence of nucleoli, all of which can be seen in conventional prostatic acinar adenocarcinoma as well as other types of adenocarcinomas. Clearly, it is significant to correlate cytological findings with clinical and radiological studies to narrow the broad differential and use immunohistochemistry as an adjunct when available to elucidate the diagnosis. FNA cytology can aid in the diagnosis of malignant cystic lesions of the prostate and promote timely intervention as well as improved management.

Research supported by:

Association of Rey Auditory Verbal Learning Test (RAVLT) with Depression and Anxiety in Patients with Multiple Sclerosis

Kyle Jennette, BA, Claire Desir, BS, and Ryan Kaufman. University of South Florida College of Medicine, Department of Psychiatry and Neurosciences

Keywords: Multiple Sclerosis, neuropsychology, memory, depression, anxiety

Objective: Multiple sclerosis (MS) is a progressive disease where axonal transmission is slowed by damage to the myelin sheath of neurons in the central nervous system. Symptom presentation is different for all individuals, but primarily entails motor and cognitive deficiencies. Of the cognitive problems in MS, most notable are deficits in executive function, attention, and memory. This study set out to analyze the relationship between performance on the Rey Auditory Verbal Learning Test (RAVLT) in relation to self-reported levels of depression and anxiety in patients diagnosed with MS.

Methods: Our hypothesis is that elevated levels of depression and/or anxiety will have a negative association with measures of memory over 5 trials of learning in the RAVLT. Data was collected from 18 MS patients that visited the USF Health Memory Disorders Clinic for diagnosis of cognitive deficiencies secondary to MS. Within the routine neuropsychological test battery, patients were administered the RAVLT, the Beck Depression Inventory II (BDI-II), and the State-Trait Anxiety Inventory (STAI).

Results: No significant association was found between depression and RAVLT scores, or anxiety and RAVLT scores. Only age and full scale IQ were found to be correlated and predictive of performance on the RAVLT; Age is negatively correlated, whereas IQ is positively correlated.

Conclusion: This result falls in line with previously published literature by McClintock, et al. (2010) that depression does not consistently, negatively associate with neurocognitive performance.

Research supported by: Eric Rinehardt, PhD, ABPP. USF Health Memory Disorders Clinic USF College of Medicine, Department of Psychiatry and Neurosciences

Soluble Immune Activation Markers and the Early Initiation of ART in HIV-Infected Adolescents.

Alyssa Kennedy, BS Susan Lukas, MPH Bret J. Rudy, MD John W. Sleasman, MD University of South Florida Morsani College of Medicine Pediatrics

Keywords: HIV, sCD14, sCD27, immune activation, ART

Objective: Clinical management of HIV-infected adolescents is dependent on reducing viral load and reducing chronic immune activation. ART decreases the viral load; however the effect of the timing of initiation of therapy on immune activation biomarkers in HIV (+) adolescents is unknown. Soluble CD27 (sCD27) and soluble CD14 (sCD14) are measurable markers of chronic inflammation that are multifactor in their effector nature. We propose to investigate effect of early initiation ART on overall immune activation in HIV (+) adolescents as measured by plasma sCD27 and sCD14 levels.

Methods: HIV (+) adolescents having CD4+ T-cell counts > 350 cells/ μ l were recruited into a study and randomized in a 3:1 manner into the experimental arm, initiating ART at entry, and a standard of care arm (SOC), initiating ART when CD4 < 350 cells/ μ l. A healthy donor cohort that was age, gender and ethnicity balanced to the study arms was recruited to serve as controls. Plasma sCD27 and sCD14 levels were measured by ELISA.

Results: sCD27 and sCD14 levels in both the experimental and the SOC arms were increased compared to the healthy control ($p < .0001$). Initiation of ART did not significantly reduce sCD27 and sCD14 levels at 48 weeks when compared to the SOC arm. sCD27 levels correlated positively with sCD14 levels. ($r = .4665$, $p = .0036$)

Conclusion: Initiation of ART did not reduce sCD27 and sCD14 levels in the experimental arm of the study. The positive correlation between sCD27 and sCD14 suggests that multiple routes of immune activation are present. These findings indicate that immune activation remains elevated despite a reduction in viral load in HIV+ patients initiating early ART with CD4+ T cell counts >350 cells/mm³.

Research supported by: This research was supported by the Research Scholarly Concentration at USF Health, Morsani College of Medicine and RFADA10014.

Case Study of Five Patients With Severe TBI's That Underwent Hyperbaric Oxygen Treatment

Robert Kent DO^{1,2}, Risa Nakase-Richardson PhD^{1,2}, Marissa McCarthy MD^{1,2}, Jill Massengale, ARNP^{1,2}, Alfred Frontera, MD^{1,2}, David Cifu MD³ ¹University of South Florida, Physical Medicine and Rehabilitation Residency Program; ²James A Haley VA Hospital, ³Virginia Commonwealth University

Keywords: TBI, hyperbaric oxygen treatment, seizure, disorder of consciousness

Objective: Identify outcomes associated with hyperbaric oxygen treatment (HBOT) in patients with severe traumatic brain injury (TBI).

Methods: A retrospective chart review of individuals who sustained severe TBI and received HBOT at an outside facility to improve functional outcome and increase level of consciousness. The families of each patient pursued off-label treatment and were transported to local clinics that offered HBOT. Review of records revealed an average number of 42 treatments with a dosing range of 1.5 to 2.0 atmospheres. Subjects were male, mean age of 28 years and were an average of 617 days post traumatic injury. Main outcome measures were Rancho Los Amigos Scale, Disorder of Consciousness Diagnosis, and medical course.

Results: No significant objective indices of improvement were noted and none of the patients advanced their level of consciousness. Family members noted minor subjective gains, not echoed by physical, occupational, speech, or neuropsychological testing. The most common and concerning side effect in this group of patients was exacerbation of their post traumatic epilepsy. New onset of seizure activity was noted in one patient and an increase in frequency after initiating HBOT in three of the remaining patients.

Conclusion: HBOT did not demonstrate efficacy in this patient group for improving level of consciousness or functional outcomes. The minimal subjective benefit was negligible, especially when compared to increase risk of adverse side effects, mainly seizures, in this patient set.

Research supported by:

A Closer Look at "Intactivism": Analyzing the Major Themes of and Attitudes towards Anti-Male-Circumcision Activism

Nolan Kline, MA¹, Loren Wilbers, MA², Becky Killik, BA³, ¹University of South Florida, College of Arts and Sciences, Department of Anthropology; College of Public Health, Department of Community of Family Health ²University of South Florida, College of Arts and Sciences, Department of Sociology ³University of South Florida, College of Arts and Sciences, Department of Women's and Gender Studies. University of South Florida, College of Arts and Sciences, Dept. of Africana Studies

Keywords: Male circumcision, biopower, resistance to public health measures

Objective: Little attention in social science and health science literature has been given to the growing anti-male circumcision movement (termed: intactivism). This exploratory research examines online intactivist rhetoric, assumptions about circumcision, the implications of intactivist messages, and suggests how social scientists and health behavior scientists should address those implications.

Methods: To examine intactivist rhetoric, we conducted a discourse analysis of anti-circumcision websites, conducted focus groups among students enrolled at the University of South Florida, and conducted key informant interviews with circumcised and uncircumcised men.

Results: The data collected in this exploratory research underscore the way in which intactivism resists circumcision as a technology of bodily governance. Through resistance, however, intactivist rhetoric reproduces technologies of otherness that target specific groups, including circumcised men, parents of circumcised men, and members of the Jewish faith. Moreover, intactivist ideals reproduce neoliberal governance rhetoric and resemble other movements that question the authority of public health measures such as vaccinating infants.

Conclusion: Circumcision has significant public health and cultural meanings, but intactivism does not always account for the deeper significance of circumcision. Anthropologists and public health practitioners have an opportunity to alter intactivist messages that sometimes ignore public health data and cultural meanings behind circumcision in an effort to promote more informed and less marginalizing anti-circumcision campaigns.

Priapism – An Unusual Presentation of Familial Adenomatous Polyposis

Kimberly Kolkhorst, DO and Patrick Brady, MD University of South Florida and Tampa General Hospital, Tampa, FL., USF College of Medicine, Dept. of Internal Medicine and Dept. of Gastroenterology.

Keywords: Priapism, familial, adenomatous, polyposis, anemia

Objective: Familial Adenomatous Polyposis (FAP) is an autosomal dominant condition that results in the development of hundreds to thousands of polyps in the gastrointestinal tract. Patients with FAP commonly present with anemia secondary to bleeding polyps and iron deficiency. Here we report the case of a previously healthy male who presented with recurrent, ischemic priapism and subsequently diagnosed with FAP.

Methods: A 26-year-old, Caucasian male with no significant medical history presented to the ER with 8 hours of painful erection requiring cavernosal aspiration. The patient denied the use of medications or recreational drugs or recent trauma. His family history was notable for a father and grandfather with colon cancer. Physical exam was unremarkable. Cavernosal blood gas analysis was consistent with ischemic priapism. Laboratory studies revealed iron-deficiency anemia with hemoglobin of 8.8. Hemoglobin electrophoresis was negative for sickle cell disease.

Results: Diagnostic colonoscopy revealed an innumerable amount of polyps carpeting the mucosa from the rectum to the cecum. The constellation of endoscopic findings and family history was most consistent with familial adenomatous polyposis. Colonic biopsies revealed extensive adenomatous polyposis with focal high grade dysplasia but no evidence of submucosal invasion. The patient underwent blood transfusion and prophylactic total proctocolectomy. One year later, the priapism has not recurred.

Conclusion: To our knowledge, this is the first documented case of priapism as the presenting feature of FAP. Our case proposes a possible link between FAP-induced iron-deficiency anemia and recurrent ischemic priapism and raises attention to a non-traditional presenting symptom of FAP.

Primary CNS-Hodgkin's Lymphoma: Case Series and Review of the Literature

Jesse Lee Kresak MD², Kondi Wong MD¹ ¹Tampa General Hospital ²University of South Florida Morsani College of Medicine Pathology and Cell Biology

Keywords: CNS-HL, CNS-Hodgkin's Lymphoma, case series

Objective: Central Nervous System – Hodgkin's Lymphoma (CNS-HL) is an exceedingly rare entity accounting for 0.02-0.5% of reported Hodgkin's Lymphoma cases. Involvement of the CNS by HL usually arises during relapsed or progressive disease. Isolated primary CNS-HL is extraordinarily rare and thus, little is noted of the disease in the literature. We compare two cases of primary CNS-HL with an exhaustive review of the literature to provide a discussion of the incidence, pathogenesis, differential diagnosis and treatment options of the disease.

Methods: We compare our experience with two cases of primary CNS-HL, one recently diagnosed and the other with a 10 year follow-up. A review of the literature lends to a discussion of incidence, pathogenesis, differential diagnosis and treatment options.

Results: CNS-HL may present with neurologic deficits, space-occupying symptoms, or seizure. The tumor does not appear to have a geographic predilection, as there have been supratentorial, dural-based, and now cerebellar cases reported. This range in intracranial locations can lend to a broad radiographic differential diagnosis. Histology most commonly reveals nodular sclerosing and mixed-cellularity subtypes. Treatment modalities include radiation and chemotherapy, with different approaches for both options. Given the rarity of CNS-HL, no standard of care has yet been established and clinical and systemic involvement should be considered.

Conclusion: Given that CNS-HL is such an infrequent diagnosis, little data is available to formulate standard clinical practices upon. CNS-HL may remain in the differential diagnosis for brain lesions regardless of clinical presentation or intracranial location. Treatment plan should be individualized within clinical context.

Research supported by:

Predicting Factors that Influence Cervical Cancer Screening in HIV-Infected Women: Using the Health Belief Model

Crystal Chapman Lambert MS, ARNP, Doctoral Candidate University of South Florida College of Nursing

Keywords: Questionnaire, chart review, cervical cancer, HIV and women.**Objective:** To evaluate the relationship of Pap test adherence in HIV-infected women with the variables in a) Champion's Health Belief Model Scale and b) Champion's Self-efficacy scale and c) HPV/cervical cancer knowledge scale.**Methods:** The research design is an exploratory, cross-sectional, quantitative correlational design. The convenience sample will consist of participants recruited from an ambulatory HIV clinic in Florida. To participate in the study, women must have a diagnosis of HIV or AIDS, be eighteen years of age or older and be able to read and understand English. Attitudes will be assessed with Champion's Health Belief Model and Champion's Self-efficacy scales. Knowledge will be measured with the HPV/Cervical Cancer Knowledge scale. Sociodemographic variables will be assessed using a Demographic Data form. Each participant will be given a unique identifier and instructed not to write any identifying information on the survey. Data will be collected in two phases. Phase 1 will be a self-survey consisting of three scales and a Demographic data form. Participants will be able to complete the survey in a private area. After the survey is completed, the participants will place it into a locked collection box and receive a gift card for participating. Phase 2 will be a chart review completed by the primary investigator. The following information will be collected during the chart review: lab values, past medical history and previous Pap history. The information will be analyzed using the latest version of SAS.***Recurrences Following Mastectomy for Ductal Carcinoma in Situ***Lewis, Jaime D. (^{1,2}); Lee, M. Catherine (^{1,2}); Chau, Alec (^{1,2}); Sun, Weihong (¹); Laronga, Christine (^{1,2})¹. H Lee Moffitt Cancer Center & Research Institute, Tampa, FL, United States. ². University of South Florida, Tampa, FL, United States, University of South Florida, Morsani College of Medicine, Dept. of Surgery**Keywords:** Ductal Carcinoma In Situ, Mastectomy, Recurrence, Chart Review**Objective:** Mastectomy reduces risk for local recurrence of breast cancer. Our goal was to evaluate recurrence following mastectomy for ductal carcinoma in situ (DCIS).**Methods:** An IRB-approved, single institution prospective database of patients treated with mastectomy for DCIS from 1997-2010 was reviewed. Clinicopathologic data, locoregional recurrences (LRR), and distant metastases were identified.**Results:** Four hundred thirty-nine patients underwent mastectomy for DCIS as primary (400 patients, 91.1%) or recurrent (39 patients, 8.9%) cancer. Thirty patients (6.8%) had prior contralateral cancer; 51 (11.6%) had synchronous bilateral cancers. Median age was 55.8 years (range 23-91); median follow-up was 28 months (range 0-195). Mastectomy was performed in 162 (36.1%) for extensive disease, 157 (35%) patient choice, 74 (16.5%) failed breast conservation, 39 (8.7%) prior radiation, and 17 (3.8%) unknown. Grade was available for 441 specimens; 46 (10.4%) were low, 154 (34.9%) intermediate, and 241 (54.6%) high grade. Hormone receptor status was available for 241 specimens; 176 (73%) were estrogen receptor positive and 135 (56%) progesterone receptor positive. Sentinel lymph node biopsy was performed in 413; 3 (0.7%) had micrometastases. After mastectomy 21 had margins <2 mm; 2 received radiation. Five of the 399 patients treated with primary mastectomy for pure DCIS developed an invasive LRR. Of the 356 patients with no history of invasive disease in either breast, 3 (0.84%) developed distant metastases. One patient developed a recurrence within 2 years, the remainder recurred 2.3 to 11.5 years after mastectomy.**Conclusion:** Recurrence after mastectomy for pure DCIS is rare, however, long-term follow up should be offered to patients treated with mastectomy for DCIS.

Perceptual Responses in Predicting Physiological Measures of Heat Stress While Wearing Three Clothing Ensembles

Rebecca M. Lopez, Jason Martuscello, Candi D. Ashley, Eric Coris. University of South Florida Morsani College of Medicine Orthopaedics and Sports Medicine

Keywords: Hyperthermia, work safety, heat strain,

Objective: To investigate the use of a modified Environmental Symptoms Questionnaire(ESQ), thirst(TST) and thermal(THM) responses in predicting body temperature(TGI) while wearing 3 ensembles.

Methods: Fifteen subjects (8 males;7 females; 24.1±4.7yr, 76.0±19.2kg, 170.9±9.3cm, BSA 1.87±.26m²) volunteered in a crossover, randomized study. Subjects completed a familiarization heat stress trial(HST) in shorts and t-shirt then in WORK(cotton shirt and pants), WATER(water-barrier, vapor-permeable coverall), and VAPOR(vapor-barrier coverall). HST consisted of treadmill walking in 35°C and 50%RH at 160w/m² for 120min, until exhaustion or TGI reached 39°C. Data were analyzed using a 2-way repeated measures (ensembles x time) ANOVA. Grouped Pearson product moment correlation was used to analyze relationships between TGI and perceptuals.

Results: TGI in VAPOR (38.57±0.12°C) was greater at finish than WORK (37.72±.09°C; p=.001), and WATER (37.64±.16°C; p=.001). Trial time for VAPOR (91.4±7.7min) was shorter than all other trials(F_{1,14}= 13.811, p=.002). Significant correlations were found between TGI and ESQ at 30-min (r=.26, n=60, p=.042), 60-min (r=.41, n=58, p=.042), 90-min (r=.26, n=55, p=.05), and finish (r=.34, n=60, p=.008). Significant correlations between TGI and TST were found at 90-min (r=.29, n=55, p=.032) and finish (r=.28, n=60, p=.031), while relationships between TGI and THM were found at 60-min (r=.56, n=58, p=.000) and finish (r=.33, n=60, p=.010).

Conclusion: Relationships were found between temperature and perceptual measures at some time points during HST with 3 ensembles. However, the ability to physiologically measure heat strain should supersede perceptual measures to ensure workplace safety and health.

Research supported by: USF Sunshine Education and Research Center

Merkel Cell Carcinoma of Unknown Primary Origin

Suroosh S. Marzban, Jeremiah L. Deneve, Jane L. Messina, Ricardo J. Gonzalez, Brooke M. Walls, Kate J. Fisher, Y. Ann Chen, C. Wayne Cruse, Vernon K. Sondak, Jonathan S. Zager University of South Florida, Morsani College of Medicine, Dept. of Pathology and Cell Biology

Keywords: merkel cell carcinoma, neuroendocrine tumor, unknown primary

Objective: Merkel cell carcinoma (MCC) is a rare neuroendocrine tumor of the skin. MCC from an unknown primary (MCCUP) can present a diagnostic and therapeutic challenge. We describe our single-institution experience with the diagnosis and management of MCCUP presenting as metastasis to lymph nodes.

Methods: After IRB approval, our institutional database spanning 1998-2010 was queried for patients with MCCUP. Clinicopathological variables and outcomes were assessed.

Results: From a database of 321 patients with MCC, 38 (12%) were identified as having nodal MCCUP. Median age was 67 years and 79% were male. Nodal basins involved at presentation were cervical (58%), axillary/epitrochlear (21%) or inguinal/iliac (21%). CK20 staining was positive in 93% of tumors tested and all were TTF-1 negative. Twenty-nine (76%) patients underwent complete regional lymph node dissection (LND): 3 had LND alone, 10 had LND and adjuvant radiation and 16 underwent LND followed by chemoradiation. Definitive chemoradiation without surgery was used in 6 (16%) while radiation alone was used in 3 (8%). Recurrence was seen in 34% of patients. Median recurrence-free survival was 35 months. Ten patients (26%) have died: 4 died of disease while 6 died of other causes. The median overall survival was 104 months.

Conclusion: Nodal MCCUP is a rare disease affecting primarily elderly white males. Recurrence is observed in approximately one-third of patients with a 104 month median OS after a multimodality treatment approach consisting of surgery along with adjuvant chemotherapy and radiation in the majority of patients

Project World Health: An International Medical Mission Trip Taking a Focus on Sustainability

Daniel Matta, Alexandra Strauss University of South Florida Morsani College of Medicine, Dept. of Family Medicine

Keywords: Sustainability

Objective: Project World Health is an annual student-run medical mission trip at USF Morsani College of Medicine that provides medical services to an under-served population in the Dominican Republic. Seeing an opportunity to provide improved care, PWH created a Sustainability Committee (SC). The goals of this committee were to improve efficiency of clinic flow, increase continuity of care, and foster relationships with selected communities.

Methods: The SC worked in collaboration with the College of Industrial Engineering and other organizations around Florida. To improve efficiency, the current clinic flow was analyzed by interviewing previous leaders of the trip and the clinical advisers. To increase continuity of care, other mission trips were contacted to establish multiple trips throughout the year. To foster relationships with selected communities, specific criteria were made to determine what type of communities would be benefited the most from our services.

Results: The projects of the SC were incorporated on the subsequent trip and proven to be beneficial to providing better care. A new clinic flow improving the interaction between triage station, medical stations, and pharmacy was utilized. Our trip followed up on the work of two previous medical mission trips by groups we had been collaborating with to establish the beginning of continuity of care. Based on the aforementioned criteria, four sites were visited and two were selected as potential continuity clinic sites.

Conclusion: The goals of improving clinic flow and initiating collaboration with multiple organizations to establish continuity were met. Further work needs to be pursued by future leaders to ensure the ongoing collaborations and continuity of care in the selected sites.

Research supported by: This research was supported the Health Disparities and Health Systems Engineering Scholarly Concentrations at USF Health, Morsani College of Medicine.

How to Effectively Reduce Costs Associated with Robotic Surgery: Is This Even Possible?

M. Martino¹, J. Shubella², W. Menard³, J. Patriarco², B. Leader², R. Morcrette², M. Allen², M. Thomas², R. Boulay² ¹Lehigh Valley Health Network, Allentown, PA, ²Lehigh Valley Hospital Cedar Crest, Allentown, PA, University of South Florida Morsani College of Medicine Obstetrics & Gynecology

Keywords: Robotic Surgery

Objective: The purpose of this study is to determine if transparency of surgeon metrics can reduce the actual costs associated with robotic surgery

Methods: This is a retrospective cohort study of all patients who had a robotic-assisted hysterectomy from July 1, 2010 to June 30, 2011. All surgeries were performed by board certified gynecologic oncologists using the da Vinci S or Si surgical systems. Studer Visibility Boards were installed in the robotic surgery rooms on January 1, 2011 and their presence was emphasized to all robotic team members. The first six month period (7/1/10-12/30/10) was identified as the pre-visibility board cohort while the latter six month period (1/1/11-6/30/11) was identified as the post-visibility board cohort. Demographic data reviewed included patient's age, BMI, uterine weight, and benign versus malignant diagnosis. Data was analyzed using Pearson's chi-squared tests and Student's t-tests in SPSS.

Results: Two hundred eighty-eight patients met the inclusion criteria (140 Pre-VB and 148 Post-VB). There were no significant differences between the groups in age, uterine weight, BMI, and benign versus malignant diagnoses. The Post-VB cohort had a significantly lower direct variable OR cost compared to the Pre-VB cohort. The Post-VB cohort also experienced a shorter total OR time and incision time compared to their Pre-VB counterparts, even though there was no statistical significance.

Conclusion: The costs associated with robotic surgery may be reduced when knowledge is provided to surgical teams of the actual costs associated with each case item by using visibility boards located near robotic operating rooms. These findings suggest that reducing operating room costs is feasible through teamwork and transparent interventions.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine and the LVHN/USF Medical Student Enrichment Summer Experience.

Maternal Arrhythmia: A Case Report and Review of the Literature

Jessica S. Moore MS, Patrick Teefey MD, Kiran Rao MD MFM, Michael S. Berlowitz MD, Sanders H. Chae MD, Jerome Yankowitz MD University of South Florida, Morsani College of Medicine, Dept. of Obstetrics and Gynecology

Keywords: maternal arrhythmia, case report

Objective: Pregnant patients with maternal arrhythmia can be challenging and difficult to treat. Medication choices may be limited in patients who are pregnant. Pregnancy carries with it a unique and complex physiology, coupled with fetal concerns. We attempt to clarify the different treatment modalities for maternal arrhythmias, their contraindications, and potential adverse fetal effects. Will also discuss antepartum monitoring and delivery planning in these patients.

Methods: We describe a pregnant patient with an arrhythmia to illustrate treatment thought process and options. We also present a comprehensive review of the literature in regard to treatment of maternal arrhythmias and their potential adverse fetal and maternal outcomes. These treatments include antiarrhythmic medications, electrical cardioversion, and radiofrequency ablation.

Results: Ultimately, almost all of the treatments described can be considered safe depending on the patient's individual clinical situation. The most important aspect in treating these patients is the use of a multidisciplinary approach.

Conclusion: The decision of what therapy to utilize must be addressed on a case-by-case basis with special attention to the patient's individual issues and concerns. However, it is essential to have the most up-to-date literature and information available to provide the best possible care to these patients.

Subcutaneous Vivaglobin® Replacement Therapy in Patients with Humoral Immunodeficiency Confers Protective Antibody Titers to Major Organisms

D. Nguyen*, M.J. Dorsey*, E. Perez*, C. Duff*, J. Sleasman* *Division of Allergy and Immunology, All Children's Hospital, University of South Florida, University of South Florida, Morsani College of Medicine, Dept. of Pediatrics

Keywords: Subcutaneous Immunoglobulin, Vivaglobin, tetanus, varicella, pneumococcal titers

Objective: Patients with humoral immune deficiency receiving subcutaneous immunoglobulin (SCIG) are presumed to receive protective passive antibody against a variety of pathogens. The goal of this study is to determine if their steady state plasma titers to tetanus, varicella and Streptococcus pneumoniae are maintained in protective range while on SCIG®.

Methods: A cohort of 34 subjects [XLA/ARAG (n=4), HIGM (n=2), SCID post BMT (n=1), CVID (n=12), SAD (n=14), THI (n=1)] receiving SCIG in the form of Vivaglobin® for at least 6 months were examined at 2 times points obtained 8 weeks apart. Plasma total IgG and specific IgG to varicella, tetanus and Streptococcus pneumoniae were measured during steady state by standard methods.

Results: Mean IgG level at diagnosis was 386.2 mg/dL (33 – 877, ±223.5). Mean IgG at steady state is 1103.3 mg/dL (490 – 1680, ± 237.8). Average Vivaglobin® dose is 153.8 mg/kg/week (37.6 – 528.4, ±94.7). All subjects have protective tetanus and varicella titers with average tetanus titer of 2.7 IU/mL (0.6 – 6.9, ± 1.2) and varicella titers of 101.9 Eu/mL (41 – 315, ± 38.85). Eight out of 14 pneumococcal serotypes (or 57%) have average protective titer defined as greater than 1.3 mcg/mL. Pneumococcal serotype 14 has an average highest titer of 8.8 mcg/mL (0.1 – 112.1, ± 15.8) with over 96.9% of subjects having protective titers. Pneumococcal serotype 12F has the lowest titer of 0.4 mcg/mL (0.3 – 1.2, ± 0.3) and none of the studied subjects have protective titers to this serotype.

Conclusion: Subjects with primary immune deficiency who receive subcutaneous Vivaglobin® and maintain average steady state IgG level above 1000 mg/dL have protective titers to tetanus, varicella and 8 out of 14 Streptococcus pneumoniae serotypes.

Research supported by: CSL Berhing Grant.

Relationship between Trunk Muscular Endurance and Anthropometric Measures in Firefighters

James L. Nuzzo, MS, CSCS, William S. Quillen, PT, DPT, PhD, FACSM, Ren Chen, MD, MPH, John M. Mayer, DC, PhD School of Physical Therapy & Rehabilitation Sciences (Nuzzo, Quillen, Mayer) and Office of Clinical Research (Chen), Morsani College of Medicine, University of South Florida University of South Florida, Morsani College of Medicine, School of Physical Therapy & Rehabilitation Sciences

Keywords: back pain, body fat, body mass index, exercise testing, ultrasonography

Objective: The purpose of this study was to assess the relationship between trunk muscular endurance and anthropometric measures in firefighters.

Methods: An observational study was conducted with 96 firefighters from Tampa Fire Rescue who were enrolled in a clinical trial. Anthropometric measures included body mass index (BMI), body fat percentage (air displacement plethysmography), and muscle thickness (ultrasonography) from four lower trunk muscles. Isometric back and core muscular endurance times were assessed by the Biering-Sorensen Test and Plank Test, respectively. Pearson product-moment correlations and univariate regression analyses were used to assess the relationships between variables.

Results: For back endurance, significant ($p < 0.05$) negative correlations were found with BMI ($r = -0.49$), body fat percentage ($r = -0.46$), and thickness of the lumbar multifidus ($r = -0.28$), transverse abdominis ($r = -0.25$), internal oblique abdominis ($r = -0.24$), and external oblique abdominis ($r = -0.41$) muscles. For core endurance, significant negative correlations were found with BMI ($r = -0.42$), body fat percentage ($r = -0.52$), and lumbar multifidus thickness ($r = -0.40$).

Conclusion: In firefighters, poor trunk muscular endurance is related to increased BMI and body fat percentage. This finding is consistent with findings from other populations. Future research is needed to assess the effect of improving body composition on trunk muscular endurance, and subsequently reducing the risk for back injury.

Research supported by: US Department of Homeland Security (grant number: EMW-2009-FP-00418, PI - Mayer)

Tamoxifen for the Treatment of Severe keloids; A Case Report and Review of the Literature

Nyanda Hoka, Hagele Thomas, Cohen George, Nicole Russell, MD, Nisht Patel, MD, University of South Florida, Morsani College of Medicine, Dept. of Dermatology

Keywords: Case Report keloids tamoxifen scars

Objective: To provide a review of the use of tamoxifen for the treatment of keloids and suggest the clinical indications for using this therapy.

Methods: The Pubmed database was searched using the search terms "management of keloids and hypertrophic scars." 109 results were obtained and relevant articles published since 2000 were reviewed. An additional search for "tamoxifen and keloids" resulted in 5 results, all of which were included in the review.

Results: The results of this report suggest that tamoxifen may be effective for the prevention and treatment of keloids.

Conclusion: Review of the literature suggests tamoxifen therapy may be beneficial for the treatment of keloids and hypertrophic scars failing to resolve with conventional management.

Research supported by: Dr. George Cohen

308 nm Excimer Laser with Concomitant Topical Calcipotriene for the Treatment of Segmental Vitiligo

Jenna Beasley, Kapila Paghdal MD, PharmD, George Cohen, MD University of South Florida, Morsani College of Medicine, Dept. of Dermatology

Keywords: excimer, vitiligo, calcipotriene, segmental, xenon-chloride

Objective: To assess whether combination therapy with 308-nm xenon chloride excimer laser and topical calcipotriene expedites response time and/or achieves a desirable degree of repigmentation in a patient with segmental vitiligo.

Methods: Our patient with segmental vitiligo of the face received a total of 96 excimer laser treatment sessions scheduled 1-2 times per week for a total of 65 weeks. Concomitantly, topical calcipotriene 0.005% cream was applied to the affected area twice daily for the duration of treatment.

Results: At completion of the above treatment regimen, the patient had achieved repigmentation of greater than 75% of the affected area. He reported no known side effects. At 3 months follow-up, degree of repigmentation remained stable.

Conclusion: This case suggests that combination therapy with excimer laser and topical calcipotriene may result in desirable treatment response in subjects with segmental vitiligo. This may represent a promising advancement for the treatment of this disorder. Segmental vitiligo is classically known to be resistant to improvement with current treatment modalities, including narrow-band UVB, which is normally associated with the greatest efficacy for treatment of generalized vitiligo. However, the 308-nm excimer laser may provide a more desirable clinical response possibly secondary to its superior ability to target T cells infiltrating the skin and to excite melanocyte proliferation and migration from hair follicles. In combination with topical immunomodulators, such as calcipotriene, optimal repigmentation rates may be achieved. Continued follow-up is needed to determine the long term efficacy and sustained success rates.

Rapidly Growing Mycobacterium Infections in Cancer Patients

John N. Greene, M.D. F.A.C.P. University of South Florida Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Mycobacterium, Mycobacterium In Cancer Patients

Objective: A limited amount of correlation has developed on the predisposing malignant condition of the patient and the specific infection that arises. This study records and analyzes these characteristics, as well as others, in order to gain better understanding of malignancies and their role in developing certain RGM infections.

Methods: This was a retrospective chart review conducted at Moffitt Cancer Center. The computerized epidemiology report provided by the microbiology lab identified cancer patients who have been diagnosed with an RGM infection from 01/01/1990- 10/07/2008. Medical records from 45 patients were obtained, and the data was recorded.

Results: Of the 45 patients, 24 were female and 21 male. The median age of these patients was 58 years. 23 of the 45 (51.1%) patients had a hematological malignancy, while 9 of the 45 (20.0%) had breast cancer. 7 cases (15.6%) were those of various forms of lung cancer. 6 cases (13.3%) were distributed through other forms of primary malignancy. Within the 45 cases analyzed, four forms of rapidly growing mycobacterium were observed. These were 25 Mycobacterium abscessus (55.6%) cases, 12 Mycobacterium fortuitum (26.7%) cases, 6 Mycobacterium chelonae (13.3%) cases, and 2 Mycobacterium mucogenicum (4.4%) cases. 14 patients (31.1%) were diagnosed with Neutropenia at the time of their infection. The average duration of treatment was 6 weeks, with the range of treatment being from as little as 1 week to over 1 year.

Conclusion: The results obtained give direction to what malignancy is most susceptible, as well as which RGM infection is more prevalent. The three most common malignancies infected, in order of prevalence, are hematological, breast, and lung.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine and Dr. John Greene.

A Case Of Multiple Simultaneous Urticarial Syndromes Refractory to Treatment

Jim Parkerson DOa, John Sleasman MD^b, Dennis Ledford MD^a a = University of South Florida Department of Internal Medicine, Division of Allergy and Immunology. b = University of South Florida Department of Pediatrics, Division of Allergy and Immunology, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: urticaria, physical urticaria

Objective: To report the case of a patient with three forms of physical urticaria and his response to treatment.

Methods: An atopic, asthmatic 11 year old male who since the age of five has experienced small, raised, red, pinpoint pruritic "bumps" over his entire body except the palms of his hands and soles of his feet. Exercise, stress, cold air, and cold water immersion trigger an outbreak of the hives. Antihistamines have not controlled his symptoms up to this time.

Results: The patient was diagnosed with cold urticaria, cholinergic urticaria, and dermatographism. The patient was instructed to double the antihistamine and return to the clinic in four weeks. Upon re-evaluation, the time to develop hives upon exposure to his known triggers increased by about 15-20% or about five minutes. The patient and his family were frustrated that he was not "cured." The patient was started on omalizumab therapy for difficult to control asthma but it was discontinued due to side effects.

Conclusion: Cases with multiple forms of urticaria are rare but are not unprecedented. Physical tests are vital to determine which forms of urticaria are present. In this case, an ice cube test confirmed the presence of cold urticaria and the negative hot test tube test eliminated a diagnosis of heat urticaria. Mixed forms of urticaria are more challenging to treat. This patient failed a combination of cyprohepatadine and hydroxyzine which has been reported to be successful in previous case reports. The patient started omalizumab therapy for difficult to control asthma but had side effects with the first two injections and the omalizumab was discontinued. Treatment with immunomodulators such as dapsone or tacrolimus are being considered for his difficult to control urticaria.

Paired Bilateral Internal Carotid Artery Aneurysms: An Imaging Review

1) Joseph R. Grajo, M.D, Midhir J. Patel, B.S. University of South Florida, Morsani College of Medicine, Dept. of Radiology

Keywords: Cerebral Aneurysms, Intracranial Aneurysms, Magnetic Resonance Angiogram (MRA), Computed Tomography Angiogram (CTA), Cerebral Angiography

Objective: 1) Understand the incidence and pathophysiology of multiple intracranial aneurysms. 2) Review an interesting case of paired bilateral internal carotid artery aneurysms with a few companion cases from our institution. 3) Review the role of various imaging techniques in diagnosis and management of intracranial aneurysms.

Methods: We will discuss the utility of computed tomography angiogram (CTA), magnetic resonance angiogram (MRA) and cerebral angiogram in diagnosis and management of intracranial aneurysms. Our case includes discussion of the patient's history and unique radiologic findings. The use of imaging for treatment will also be emphasized.

Results: Radiologic findings of bilaterally paired internal carotid artery aneurysms and other companion cases will be presented.

Conclusion: The diagnosis and management of cerebral aneurysms are critically dependent on imaging. Modalities such as CTA, MRA and cerebral angiography provide unprecedented precision in evaluation of intracranial aneurysms. This case demonstrates the importance of considering these vascular anomalies in the differential diagnosis for various clinical presentations.

Research supported by: USF Health - Department of Radiology; USF Health - Morsani College of Medicine

Depigmentation Therapy in Vitiligo

Nishit S Patel, Nicole Russel, George Cohen. University of South Florida, College of Medicine, Dept. of Dermatology & Cutaneous Surgery

Keywords: vitiligo, depigmentation therapy,

Objective: Vitiligo is a chronic, often debilitating, dyschromia affecting millions of people globally that results from the autoimmune destruction of melanocytes. Although there are a wide variety of treatments aimed, there remains a small subset of patients who fail to respond. For this group, depigmentation therapy with monobenzyl ether of hydroquinone (MBEH), which induces destruction of epidermal melanocytes, may be the only option for these patients to achieve uniform pigmentation.

Methods: We review the case of a patient with severe, treatment recalcitrant vitiligo involving great than 50% of his total body that was treated with MBEH. The patient was given MBEH to be initially applied to his face twice daily for 6 months. Special instructions were given to the patient to avoid contact with other individuals for up to an hour after application to avoid accidental depigmentation in other people.

Results: The patient tolerated topical MBEH therapy without the occurrence of significant irritant contact dermatitis (the most common side effect), pruritus or xerosis. After several months of daily therapy with topical MBEH, the patient was successfully depigmented, resulting in uniform appearance of the patient's skin.

Conclusion: In patients with treatment recalcitrant vitiligo with a large surface area of involvement, disfiguring lesions and/or psychological distress, depigmentation therapy is a useful treatment option. The optimal patient for this therapy should be capable of understanding the permanent nature of this treatment, associated societal implications with "bleaching" of skin of color, and the increased risk for photosensitivity, premature aging and skin cancer.

Outcome of Lower-Limb Preservation with an Expandable Endoprosthesis After Bone Tumor Resection in Children

Eric R. Henderson, MD*, Andrew M. Pepper, BS*, German Marulanda, MD*, Odion T. Binitie, MD*, David Cheong, MD**, and G. Douglas Letson, MD** *Department of Orthopaedic Surgery, University of South Florida, **Sarcoma Program, H. Lee Moffitt Cancer and Research Institute, 12902 Magnolia Drive, Tampa, FL University of South Florida, Morsani College of Medicine, Dept. of Orthopaedics and Sports Medicine

Keywords: limb-salvage, expandable endoprostheses, orthopaedic oncology

Objective: Optimal treatment of pediatric lower extremity bone tumors is controversial. Expandable implants allow limb preservation, but the revision rate and limited function are considered barriers to their use. This study investigated the functional/emotional/oncologic outcomes of patients treated with an expandable implant.

Methods: A retrospective chart review was performed. Surviving patients were asked to complete the MSTS outcomes instrument and the PODCI. Range of hip and knee motion, limb length discrepancy, and total lengthening were also obtained.

Results: Thirty-eight patients were treated with an expandable implant; twenty-six were alive at the time of the study. The mean global MSTS score was 26.1, and the mean global PODCI score was 85.8. The mean emotional acceptance and happiness scores were high. The mean sagittal plane hip motion in patients who had undergone replacement of the proximal aspect of the femur was 103°. The mean knee motion in patients who had undergone replacement of the proximal femur, the distal femur, or the proximal tibia was 127°, 97°, and 107°, respectively. The mean lengthening at skeletal maturity was 4.7 cm, and the mean limb length discrepancy was 0.7 cm. Forty-two percent experienced complications; eleven requiring prosthesis revision and two requiring amputation.

Conclusion: Current technology does not offer a single best reconstruction option for children. Previous studies and the present series have indicated that physical/emotional functioning in patients treated with an expandable implant are good but complication rates remain high. Amputation and rotationplasty are alternative treatments. The literature supports no single superior treatment among these three options with regard to physical or emotional health.

Research Supported by: This research was supported by the Research Scholarly Concentration at USF Health Morsani College of Medicine

Angiosarcoma of the Head and Neck: The Moffitt Cancer Center Experience

Ryan S. Jackson, MD¹; Matthew Perez, BS²; Tapan A. Padhya, MD¹ ¹Department of Otolaryngology – Head and Neck Surgery, University of South Florida, Tampa, Florida ²University of South Florida College of Medicine, Tampa, Florida University of South Florida Morsani College of Medicine Otolaryngology-Head and Neck Surgery

Keywords: angiosarcoma

Objective: The aim of this study is to review outcomes of patients treated for HNAS at Moffitt.

Methods: A retrospective review was performed on all patients with histologically confirmed HNAS, who were treated at Moffitt for HNAS between 1999 and 2011. Patient demographics, tumor characteristics, treatment and outcomes were reviewed.

Results: 43 patients were identified. Age ranged from 34 to 92 years with a mean age of 70 years. Median tumor size was 3cm overall, 1.5cm for those treated with surgery alone, and 3cm for those treated with multimodality therapy. Most patients underwent surgery + radiation (42%), surgery + radiation + chemotherapy (26%), or surgery alone (14%). Overall, 57% of patients developed recurrence, of which 40% were local. Of those who recurred, 13% had regional nodal involvement in addition to local recurrence. A total of 31% of patients developed distant metastases. Overall survival was 37% at 5 years. Tumor size was found to be a significant predictor of overall survival ($p=0.0015$). Patients with tumors $>5\text{cm}$ had a 1.3-fold increased probability of locoregional recurrence ($p=0.0199$) and a 1.4-fold increased probability of death from disease ($p=0.0106$). There was no significant difference in recurrence ($p=0.1136$) or overall survival ($p=0.4194$) when comparing patients who had surgery alone ($n=6$) to those who had surgery in combination with radiation +/- chemotherapy. Also, there was no difference in survival comparing all treatment regimens ($p=0.4194$).

Conclusion: Tumor size of $>5\text{cm}$ was a negative predictor of recurrence and survival. Similar treatment outcomes could be explained by the smaller tumor size, and thus the more favorable outcomes, of those who underwent surgery alone compared to those who underwent multimodality therapy.

Birmingham Hip Resurfacing in the Severely Obese

Matthew Stein MD Michael Perrone MPH Richard Cain MD Brian Palumbo MD Stephen Raterman MD University of South Florida Morsani College of Medicine Cardiology

Keywords: Chart Review

Objective: We assessed the correlation between severe obesity (body mass index ≥ 35), and survivorship of Birmingham Hip Resurfacing arthroplasty by comparing the clinical results of patients with a BMI ≥ 35 to those with a BMI < 35 .

Methods: We retrospectively reviewed our registry to identify all patients who had been followed for at least two years after a Birmingham Hip Resurfacing arthroplasty. Patients were divided according to BMI. The study group contained fifty-eight patients (65 hips) with a BMI ≥ 35 (average - 38.2). The control group contained 300 patients (371 hips) with a BMI < 35 (average - 27.6). We compared the clinical results (Harris Hip scores) and prosthetic survival rates of each group.

Results: There was no significant difference post-operatively ($p= 0.908$) in Harris Hip scores between the control group (97.2) and the study group (96.7). Six patients in the control group and two patients in the study group required revision surgery (control = 1.6% revision, study =3.2% revision). This difference showed no statistical significance ($p=0.333$). There were four additional complications that did not require revision surgery in the study group. This resulted in an overall complication rate of 6.3% for the study group. There were 23 additional complications that did not require revision surgery in the control group. This resulted in an overall complication rate of 6.3%, identical to that of the study group.

Conclusion: Birmingham Hip Resurfacing arthroplasty is performing well in patients with a high body mass index. Comparable function scores and survivorship rates evidence this. A reduced activity level and a greater component size in this patient population may explain the protective effect of a high body mass index on survivorship results.

Research supported by:

Analysis of the Factors Influencing Breast Cancer Care Among Female Veterans

Judith Puckett¹, Olga Zayko¹, Jessica Suber, MD², Lisa J. Gould, MD, PhD^{1,2} ¹University of South Florida College of Medicine, 12901 Bruce B. Downs Blvd., MDC 78, Tampa, FL 33612; ²Department of Veteran Affairs, James A. Haley Veterans' Hospital, 13000 Bruce B. Downs Blvd., Tampa, FL 33612, University of South Florida, Morsani College of Medicine, Dept. of Surgery

Keywords: Breast cancer, chart review, plastic surgery, veteran

Objective: The James A Haley Veterans Hospital delivers care to a number of women and is one of few institutions in the VA system that provides comprehensive care to women diagnosed with breast cancer.

Methods: A retrospective chart review of 90 female veterans who underwent breast cancer care at JAHVH between 1/2005 and 7/2010 was performed under an IRB approved protocol. 59 of 90 charts reviewed met inclusion criteria and were used in our study. Data, including diagnostic methods, breast cancer grade and stage, and treatment were abstracted into a de-identified data base.

Results: The majority of female breast cancer patients treated at JAHVH are diagnosed with with stage I disease (n=27) and 89% (n=53) opted for mastectomy. Patients who had MRI screening (n=27) or BRCA (n=11) testing frequently chose mastectomies (81% (n=22) and 100% (n=1) respectively). 25 patients underwent breast reconstruction with 2/3 of the patients being younger than age 50. Forty-eight percent (n=12) of patients who underwent breast reconstruction experienced complications. 9 of these (75%) subjects had comorbidities.

Conclusion: The rate of mastectomies performed at JAHVH is higher than in the civilian population. The use of MRI screening does not seem to influence the rate of mastectomy in our sample. The rate of mastectomy after BRCA testing was similar to the civilian population. It is possible the high rate of mastectomies among female veterans is due to the availability of on-site reconstruction. The most likely contributions to the increased rates of mastectomy at JAHVH are fear of cancer returning as well as a desire to avoid radiation. This study shows that female veterans make different decisions for their healthcare than civilians.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine and JAHVH

Metabolic Surgery in Patients with End-Stage Renal Disease: A Report Of Our Case Series.

Ariel Rodriguez, MD; Werner Andrade, MD; Tannous K. Fakhry, MD; Ovie Appresai, MD; Jason Radecke, MD; Michel M. Murr, MD. USF Morsani College of Medicine University of South Florida Morsani College of Medicine Surgery

Keywords: End-Stage Renal Disease Metabolic Surgery

Objective: To report the outcomes of bariatric surgery in obese patients with ESRD who underwent metabolic surgery.

Methods: Retrospective review of demographic and clinical data on all patients diagnosed with ESRD who underwent metabolic surgery from 2000-2010. Data included: age, sex, obesity related comorbidities, etiology of renal failure, body mass index, and excess body weight loss. Up to date follow up was obtained from electronic medical records and phone calls.

Results: Thirteen patients with ESRD underwent metabolic surgery; four patients underwent Laparoscopic Adjustable Gastric Banding, and 9 patients underwent Roux-en-Y gastric Bypass. There were 2 males and 11 females with a mean age of 54±11 years. Among the 13 patients with ESRD, 4 patients had previous kidney transplants and 9 were either on the transplant waiting list and were receiving hemodialysis. The 30-day mortality was zero. Average follow up was 6±2 years. Among the pre-transplant group one patient received a kidney transplant as weight loss ensued at 2 years after bariatric surgery. Another patient is scheduled for living related kidney transplant. Two patients died without getting a transplant. Three patients were lost to follow up. Percentage of excess body weight loss was 64±25% with an average drop in BMI of 20 points.

Conclusion: Metabolic surgery results in effective and sustainable weight loss in obese patients with ESRD. Surgically-induced weight loss eliminates obesity as a barrier for kidney transplantation.

Research supported by:

Adult Case of Henoch-Schönlein Purpura (HSP): Possibly Secondary to Generic Lisinopril

Alberto J. Sabucedo, Amr El-Husseini, Jorge Lamarche, Craig Courville, and Alfredo Peguero University of South Florida Morsani College of Medicine Internal Medicine

Keywords: HSP, Henoch-Schönlein Purpura, Lisinopril, Nephritis, IgA

Objective: Henoch-Schönlein Purpura(HSP) is characterized by small-vessel sytemic vasculitis of unknown etiology. It usually involves skin, joint, gastrointestinal manifestations as well as renal involvement in a about half of the cases. We present a rare case of adult onset refractory HSP possibly secondary to generic lisinopril ingestion

Methods: A 27 year-old white male presented to our tertiary care hospital with a recent 4 month history of refractory HSP treated at an outside hospital (OSH) with steroids, cyclophosphamide, and plasmapheresis without improvement.

Results: Patient came to our hospital because of unsatisfactory progress. Patient had an original presentation at OSH with nephrotic range proteinuria of 9 g/day, hematuria and a serum creatinine of 1 mg/dL. He presented to our hospital with a creatinine of 2 mg/dL and was still having hematuria and proteinuria. Patient was continued prednisone 60 mg daily and plasmapheresis for 18 sessions without significant improvement. Kidney biopsy was consistent with IgA deposition in mesangium. Patient was then given 3 doses of 1000 mg Rituximab infusions two weeks apart. Patient's creatinine dropped to 1.6 mg/dL and his proteinuria to 1.2 -1.5 g/day with no hematuria. Patient was discharged home with close follow up.

Conclusion: The possible use of generic drugs which are equivalent in active component, but differ in excipient formulation may present a problem in patients who develop antigenic stimuli leading to IgA deposition in the mesangium with kidney injury. The association of lisinopril and HSP has been reported in the literature. We recommend the use of Rituximab for the treatment of refractory HSP that does not respond to traditional steroids and/or plasmapheresis.

Research supported by:

Bevacizumab Shows Regression of Brain Metastases and Prolonged Survival in 3 patients with Breast Cancer

Monique Sajjad, D.O. USF Eric Schilling, D.O. USF Roohi Ismail-Khan, M.D. Moffitt Cancer Center, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Case Study, Her-2-Neu breast cancer

Objective: Her2-Neu expression portends higher probably for cerebral metastasis (CM) and indicates poor prognosis in breast cancer with limited treatment options. Survival is less than 6 months. Our goal was to discover alternative ways to control CM and improve quality of life.

Methods: In the following 3 cases, the VEGF inhibitor, bevacizumab was used to control CM. Retrospective analysis including serial imaging was performed.

Results: A 64 yo female was diagnosed with HER2Neu+ infiltrating ductal carcinoma in 2003. 6 years later she was diagnosed with CM and underwent typical treatment, however she displayed no progress and she was treated with bevacizumab. Repeat imaging showed decreasing size of CM. 9 months after initiation of bevacizumab and 27 months after diagnosis of CM, the patient continues to do well. A 38 yo female was diagnosed with HER-2Neu+ infiltrating ductal carcinoma metastatic to the liver in 2009, and developed CM in 2010. After failing typical treatment, she was begun on bevacizumab in 2011. Repeat imaging showed decreasing edema with no new lesions. 6 months since initiation of bevacizumab and 14 months after diagnosis of CM, the patient continues to do well. A 36 yo female was diagnosed with HER2-Neu + infiltrating ductal carcinoma in 2001 and CM in 2007. In 2009, the patient was begun on bevacizumab. In May 2011 however, 19 months since initiation of Bevacizumab and 45 months after diagnosis of CM, leptomeningeal involvement was evidenced and she expired shortly thereafter.

Conclusion: CM from HER 2 positive breast carcinoma may represent vascularized tumor that would respond to a VEGF regimen as seen in these patients. These cases evidence clinical improvement and radiological regression of tumor between 5-19 months.

IL-2 Induced Tachy-Brady Syndrome

Eric M. Schilling D.O., Samir Dalia M.D. University of South Florida Morsani College of Medicine

Keywords: Case Study tachy-brady Interleukin-2 cancer renal

Objective: The role of IL2 has been well established in the treatment of metastatic melanoma and renal cell carcinoma. Studies have evidenced a toxicity profile common with its use; hypotension, tachycardia and SVT being most common. Our case illustrates the first reported incidence of tachy-brady syndrome induced by IL2.

Methods: A 49yo male with history of HTN and hyperlipidemia was diagnosed with renal cell carcinoma and received care at Moffit cancer center and TGH. Clinical progression was followed during his 5month treatment course with lab data, telemetry, and vital signs documented throughout.

Results: After diagnosis of renal cell carcinoma, IL2 treatment was initiated. Preliminary treatment was tolerated well. Cycles 2-3 were terminated early secondary to dyspnea and acute renal insufficiency. On his 4th and final treatment, Pt developed acute Afib with RVR, followed by intensely symptomatic bradycardia. IL2 was discontinued, and pt returned temporarily to sinus rhythm. He then experienced multiple recurrent episodes of tachy/bradycardia ~30min apart. Transvenous pacing was required when HR trended to the low 20s. 24hours after being off IL2, tachy-brady resolved and the patient was immediately transferred to TGH for cardiac pacemaker placement.

Conclusion: Tachy-Brady syndrome is an uncommon disturbance of heart rhythm typically caused by inflammatory or infiltrative diseases and medications. IL2 acts by stimulating a proinflammatory state as is most robustly seen in septic shock. Chemotherapeutic doses have readily been associated with symptoms of systemic capillary leak syndrome, but never described to induce the cardiac affects seen above. This is a novel affect of IL2 in a patient with no other pre-disposing factors.

Research supported by:

VHA Women's Health Mini Residency

Dawn Schocken, MPH, Director, Center for Advanced Clinical Learning, USF Morsani College of Medicine, Magdalena Oxendine, MEd, Coordinator, Center for Advanced Clinical Learning, USF Morsani College of Medicine University of South Florida Morsani College of Medicine Family Medicine

Keywords: Female health, VHA, primary care, clinical skills

Objective: This project was developed with the explicit objective of improving women's health within the VA Medical system. A review of women veterans stated their care was suboptimal. A theory driven curriculum was developed explicitly to instruct current Standardized Patients (SPs) as Gynecological Teaching Associates (GTAs) to improve women's health care. This training was used for the Veterans Health Administration (VHA) Women's Health Mini Residency to address these concerns.

Methods: The GTAs were instructed in the dual role of instructor GTA and patient. Pairs of GTAs were then oriented to teach 180 VA primary care healthcare providers over two days in July 2011. A pre and post assessment from the participants was gathered to determine the provider's comfort with performing the female exam.

Results: Of the 180 healthcare providers who participated in this training, 95% (171) felt this experience provided great – excellent training (on a 1-5 likert scale) to learn and enhance their skills. Working with the GTAs, who provided instruction and guided experience, the providers were given a fresh perspective on women's health.

Conclusion: Many practicing primary care providers in the VA system lack the confidence, experience and skills related to performing adequate pelvic and breast exams. This focused holistic training helped them develop the skills and gain the knowledge necessary to provide effective care to their patients. Additionally, the providers gained a better understanding of some of the concerns that women have when they undergo this exam.

Research supported by: This research was sponsored in part by the Army through a contract, DI-MISC-80711A, Contract # W900KKCATF11064.

Abnormal Cerebral Hemosiderin Deposits on Magnetic Resonance Imaging in a Patient with Pseudopapilledema

Ankit A Shah¹, Mitchell D. Drucker M.D.¹, F. Reed Murtagh M.D.², Paul R. Winters M.D.³ ¹University of South Florida Morsani College of Medicine Ophthalmology, ²University of South Florida, Morsani College of Medicine, Dept of Radiology, ³University of South Florida, Morsani College of Medicine, Dept of Neurology

Keywords: pseudopapilledema, hemosiderin, thrombosis, shaken baby. This is a Case Report

Objective: Asymptomatic pseudopapilledema with abnormal hemosiderin deposition in the subarachnoid sulci is not presented in the literature. We describe the clinical course of such a patient, provide hypotheses for the patient's MRI findings, and outline a follow up plan.

Methods: A retrospective chart review of one case and review of the current literature was conducted.

Results: A healthy 16 year old patient with developmental delay is examined for irregular optic nerve heads. The patient denied diplopia, headaches, or vomiting. The patient's intraocular pressure, external slit lamp examination, color vision, visual acuity, extra ocular movements, and confrontational visual fields were preserved. The pupils were equally reactive to light & accommodation, brisk, and had no afferent pupillary defect. The optic discs had blurred margins, lacked a physiologic cup and were tilted inferiorly. Visual field testing illustrated an enlarged blind spot. An MRI with Gadolinium identified subarachnoid venous dilation and numerous punctuate deposits of hemosiderin in the subarachnoid sulci over the cerebral convexities bilaterally. Susceptibility weighted imaging confirmed iron deposits. Lumbar puncture illustrated a normal opening pressure

Conclusion: Pseudopapilledema is characterized by optic nerve swelling on fundoscopic examination and normal intracranial pressure, most commonly caused by optic disc drusen. The cerebral hemosiderin deposits seen on MRI are hypothesized to be from recanalization of a right sigmoid sinus thrombus. An important alternative to consider, especially with the patient's developmental delay, is potential neonatal causes such as shaken baby syndrome. This patient's management plan involved annual follow up with routine visual field testing.

Research supported by:

Pressure Ulcer Prevalence Among the Spinal Cord Injury Population

Ross Simon, MS², Lisa Gould M.D.¹, Cris Olney¹ ¹James Haley VA Hospital, Dept. of Plastic Surgery, ²University of South Florida Morsani College of Medicine Surgery

Keywords: pressure ulcer, spinal cord injury, bed sore, pressure sore

Objective: Pressure ulcer studies are common among at risk populations such as nursing home elderly and the acute spinal cord injury. This study on the veteran SCI population has focused on patients who have already developed pressure ulcers. The goal of the proposed research is to perform an epidemiological and non-invasive anthropometric investigation of spinal cord injured persons with and without a history of pressure ulcers to determine both predictive and protective variables among the population.

Methods: A chart review of 120 charts from more than 1400 patient charts of patients who completed the annual exam at the James A Haley Spinal Cord Injury Center between January 1, 2009 and December 31, 2009 was performed to determine of multitude of demographic, biological/physical and psychosocial variables among the population that are either predictive or protective of pressure ulcers.

Results: Preliminary analysis of this data set reveals that 37.8% have never had a pressure ulcer, 25% have had one, while 32% have had more than three pressure ulcers since their injury. Although 26% healed their pressure ulcers rapidly (0-3 months), 10% of the patients have never successfully healed their ulcer. They are also a population with significant co-morbidities: 29.2% currently use tobacco, 37% of those smoke at least one pack per day; 22.7% have BMI >30 and 30% have been diagnosed with depression.

Conclusion: Although this data has not been completely analyzed we expect to find a statistical correlation of pressure ulcers with well document risk factors such as elevated BMI, tobacco use, etc. Among this population however, we also expect to find a distinct population of SCI patients that have never exhibited a pressure ulcer amidst other predictive variables.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Diffuse Idiopathic Pulmonary Neuroendocrine Hyperplasia with Corticosteroid Dependent Asthma

Neetu Talreja, MD, Susan Culverhouse, MD, Mark K. Glaum, PhD, MD, Dennis K. Ledford, MD Department of Internal medicine, Division of Allergy immunology, University of South Florida_University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Case Study- Asthma, corticosteroid dependant, DIPNECH, severe asthma,

Objective: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare disorder involving generalized proliferation of pulmonary neuroendocrine cells, which leads to occlusion of the bronchial lumen and causes symptoms of obstructive lung disease. Only 40 cases have been described in the literature to date. Following is a case report of chronic corticosteroid dependant asthma (CCDA) also diagnosed with DIPNECH that responded to intramuscular octreotide therapy.

Methods: NA

Results: A 54 year-old, non-smoking, Caucasian female, with vocal cord dysfunction and gastroesophageal reflux disease, presented with 12 years of CCDA (FVC=59% and FEV1=61% of predicted; positive methacholine challenge test). Over the past year, her dyspnea became worse requiring multiple urgent care visits, hospitalizations, and high-dose, oral corticosteroids (prednisone 50 mg daily) with minimal improvement for presumed asthma exacerbations. In vitro studies revealed normal pharmacokinetics and pharmacodynamics of corticosteroid metabolism. High resolution CT scan of the chest revealed large and small airway disease suspicious for constrictive bronchiolitis with bilateral sub-centimeter nodules with mosaicism. Utilizing video assisted thoracic surgery, the largest of these nodules was biopsied. It revealed chronic bronchiolitis with evidence of neuroendocrine hyperplasia. A diagnosis of DIPNECH was made. The patient was started on intramuscular octreotide and tapering corticosteroid therapy. She is doing well after one year of therapy.

Conclusion: A case of CCDA with underlying DIPNECH is presented. A subset of patients with chronic airflow obstruction may have symptoms due to DIPNECH and this diagnosis should be in differential of poorly controlled corticosteroid-dependent asthma.

Calvarial Metastatic Melanoma: A Case of an Enormous Exophytic Mass in an Asymptomatic Patient Lindsey Verduin MS, Jesal Popat MD, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Calvarium Melanoma Metastatic

Objective: This case report demonstrates the insidiousness of melanoma and a previously unreported site of a melanoma metastasis: the calvarium. It also calls attention to the need for the development of new drugs in the treatment of stage IV melanoma.

Methods: The patient history was obtained from clinical records.

Results: 33 year old female with a history of stage IV melanoma presented following a new onset seizure. A large exophytic mass protruding from her left scalp was easily visible. The mass was first noticed over one year ago when she was diagnosed with recurrent melanoma. In addition to this skull lesion, she also had spread to lymph nodes, bone, and pleura. Over the past year, she was treated with Ipilimumab plus Temodar, followed by 3 cycles of biochemotherapy. Despite medical therapy, the mass continued to enlarge. **PHYSICAL EXAMINATION:** A large, firm, non-tender 7cm exophytic subcutaneous mass was present on the left scalp. Papilledema was noted on exam. Despite the impressive size of the mass, no neurological deficits were found. **IMAGING:** MRI showed an astonishing 8.8cm by 7.8cm solitary well-circumscribed multiloculated mass with its epicenter in the calvarium of the left parietal and occipital regions. Biopsy of the mass stained positive with S100, confirming the diagnosis of a single melanoma metastasis to the calvarium. **TREATMENT AND OUTCOME:** After failure of medical management, she underwent a craniotomy. Since the surgery, the patient has been seizure free and is undergoing IL-2 therapy.

Conclusion: • Melanoma metastasis to bone occurs in only 6.9% of patients • There are no prior case reports of a metastasis to the calvarium • Ipilimumab, a CTLA-4 inhibitor, is the new frontier of metastatic melanoma treatment

Research Supported by: This research was supported through the Research Scholarly Concentration at USF Health Morsani College of Medicine, University of South Florida

Insulin-Induced Lipoatrophy in a Patient Using Continuous Subcutaneous Insulin Infusion (CSII): A Case Report and Literature Review

Arnaldo Villafranca III, MD, USF Endocrinology Fellow Anthony Domingo, MD, USF Endocrinology Fellow, Joaquin Gomez-Daspet, MD, FACE University of South Florida Morsani College of Medicine Internal Medicine

Keywords: Lipoatrophy, Aspart, Insulin Pump, CSII

Objective: To present a case of insulin-induced lipoatrophy, a rare dermatologic complication in patients using continuous subcutaneous insulin infusion therapy with Aspart insulin.

Methods: A retrospective chart review of one patient and a related literature search was conducted.

Results: We present a case of a 31-year-old lady with type 1 Diabetes Mellitus, diagnosed about 13 years ago. Due to her busy work schedule she was started on CSII, which she had been using over the past 11 years. One day she called complaining of "large skin dimples" developing over her abdominal wall in the same areas of the insulin pump insertion site. An appointment was scheduled to evaluate the patient. During the examination, we noted that she had 1 area of subcutaneous fat atrophy, bilaterally on her abdominal wall, with a greater loss on her left side. It was determined that she had insulin-induced lipoatrophy. We discussed the management options and it was decided to discontinue CSII and restart subcutaneous insulin injections using NPH and Regular insulin. She was to avoid injecting herself in the affected areas.

Conclusion: Insulin-induced lipoatrophy is considered to be an adverse immunological side effect of insulin therapy. It is a rare complication, ever since the development of purified insulin in the 1970s, with a prevalence <1-3% in the late 1990s. Interestingly, what makes this case report even more unique is that she had been on CSII with Aspart for 11 years without any prior dermatologic complications. It is important to recognize this adverse reaction as insulin absorption can become erratic leading to ineffective glycemic control.

Mycophenolate Mofetil as a First-Line Steroid-Sparing Agent in the Treatment of Pemphigus Vulgaris

Nikki Vyas, BS; Nishit Patel, MD; George Cohen, MD Department of Dermatology and Cutaneous Surgery University of South Florida Morsani College of Medicine

Keywords: Pemphigus vulgaris, Mycophenolate Mofetil

Objective: Pemphigus vulgaris (PV) is a rare autoimmune bullous disorder that can cause significant morbidity and mortality. Prior to the widespread availability of systemic corticosteroids, mortality rates approached 75%. Although systemic corticosteroid therapy remains the initial standard of care in PV, efficient transition to a steroid-sparing immunosuppressant agent is critical. Several such agents exist, including azathioprine, cyclophosphamide and mycophenolate mofetil (MM). The use of MM in PV has only recently been implemented, and it is generally used as a second-line agent.

Methods: We review the case of a patient initially seen in consultation in the inpatient setting with PV with near-total body involvement and his subsequent management. Specifically, we review optimal immunosuppression with a combination of high-dose systemic corticosteroids and high-dose MM.

Results: Within several weeks of the above combination therapy, the patient had complete re-epithelialization without any residual activity of his PV. Subsequent rapid reduction of the dose of the patient's systemic steroids did not result in a flare of his PV. Additionally, the patient tolerated high dose MM without any significant side effects.

Conclusion: Even the most severe of PV cases can be effectively managed with an aggressive regiment of high dose systemic corticosteroids and high dose MM therapy. Serious consideration should be given to the use of MM as a first-line steroid-sparing immunosuppressive agent in PV, especially given its often-superior side effect profile.

Neurological Manifestations and Human Parvovirus B19: Historical Perspective and Analysis

Hena Waseem, B.S., Jacqueline A. Hobbs, M.D., Ph.D., USF Morsani College of Medicine, Department of Psychiatry & Neurosciences

Keywords: Cerebellum, Encephalitis, Meningitis, Ataxia, Seizure

Objective: Human parvovirus B19 (B19), discovered in 1974, is one of the smallest DNA-containing viruses known to infect and cause disease in humans, most commonly of the bone marrow. There has been an increasing awareness in the literature documenting B19 infection associated with neurological disease. The aim of this project was to identify and compile the most comprehensive review thus far of such cases.

Methods: Literature collected in this review was accessed using public databases (e.g. PubMed) and existing bibliographic material. In each of the cases, B19 infection was demonstrated by direct evidence, including anti-B19 antibodies or DNA within either serum, cerebrospinal fluid (CSF), or brain tissue. Additionally, each case had demonstrated neurological manifestations, including central nervous system (CNS) or peripheral nervous system (PNS) diseases and symptoms. Microsoft Office Excel was used for data analysis and presentation.

Results: This review identified 184 such cases and is the most extensive to date. We detail 79 cases of central nervous system disease and outline 42 peripheral nervous system disease cases. In addition, we incorporate 28 cases involving ocular abnormalities, and 33 cases of mixed neurological problems.

Conclusion: This body of evidence suggests that B19 may have an alternative pathogenic role beyond the bone marrow that presents with neurological disease. These neurological abnormalities as well as numerous others that affect the PNS, and the physical structure of the brain have led to at least 184 cases reported in the literature. Although there is an abundance of studies discussing these trends more research is required to further clarify the association between B19 and the nervous system.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine,

What Reasons do Adolescents Give for Presenting to the Emergency Department over their Primary Care Provider?

Amy L. Weiss, MD, MPH¹; Alexandra C. Rucker, MD²; Lisa K. Tuchman, MD, MPH³; Lawrence J. D'Angelo, MD, MPH⁴

¹Division of Adolescent Medicine, USF Health COM; ²Division of Emergency Medicine, Children's National Medical Center; ³Division of Adolescent and Young Adult Medicine, Children's National Medical Center; ⁴Division of Adolescent and Young Adult Medicine, Children's National Medical Center; University of South Florida Morsani College of Medicine Pediatrics

Keywords: Emergency Medicine Adolescent Medicine

Objective: Emergency departments (EDs) across the United States are burdened by over-crowding and non-urgent visits. No recent studies have examined the reasons why adolescents present to the ED rather than to their primary care provider (PCP) with a non-urgent complaint. This study aimed to characterize the population of adolescents presenting to a large, high-volume, urban children's hospital ED and to examine the reasons given for presenting to the ED rather than to the PCP's office.

Methods: ED patients aged 12-21 years were invited to participate. A 21-item, online survey was administered assessing the main reason for presentation to the ED, key characteristics of the PCP's practice, and the adolescent's relationship with the PCP.

Results: Of the 203 participants, 60% were female and 80% were African American. The median age was 15 years (S.D. 2.37 years). Sixty-six percent (n=134) had public insurance, 93% (n=189) identified a primary doctor or clinic, and 40% were triaged as non-urgent. The most common reasons for presenting to the ED instead of to the PCP were: perceived illness requiring immediate care (34%, n=70), and PCP instructions to go to the ED (21%, n=42). Adolescents with private insurance were significantly more likely (p<0.0001) to be triaged as urgent compared to those with public insurance.

Conclusion: Almost all adolescents in this study were able to identify a PCP or primary clinic. Nonetheless, they frequently perceived that they were too ill to wait to see their PCP or reported being told by their PCP's office to present to the ED. Further research is needed to evaluate how outpatient interventions in the primary care setting may impact adolescent ED use.

A GM-CSF-Producing and CD40L-Expressing Cell Line Combined with Allogeneic Tumor Antigen as a Novel Vaccine for Metastatic Lung Adenocarcinoma: a Phase II Trial.

Ben Creelan¹, Scott Antonia², Gerold Bepler³, David Noyes², Terri Hunter⁴, Alberto Chiappori^{2, 1} University of South Florida, SPOR graduate program, ²H. Lee Moffitt Cancer Center, ³Karmanos Cancer Center, ⁴University of South Florida, Division of Patents and Licensing. University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Non-small cell lung cancer, lung adenocarcinoma, GM-CSF, CD40 ligand.

Objective: A bystander cell line derived from erythroleukemia cells was transfected with hCD40L and hGM-CSF. It is designed to recruit and activate dendritic cells at a vaccine site, when primed with two antigenic human lung adenocarcinoma cell lines. To test whether vaccination induces tumor regression in metastatic lung adenocarcinoma, we initiated a single-arm phase II trial.

Methods: Participants received intradermal vaccine injections every 14 days three times, followed by monthly three times. Cyclophosphamide (300 mg/m² IV) was administered before first and fourth vaccines to deplete regulatory T-cells. All-trans retinoic acid was given (150/mg/m²/day) after first and fourth vaccines to enhance dendritic differentiation. Immune responses were tested by analysis of variance and log-rank for relationships to clinical outcomes.

Results: Characteristics of 24 participants: 12 females, median age 64, with median of 3 previous lines of chemotherapy prior to entry. Median overall survival (OS) was 7.9 months (mo) and median time-to-progression (TTP) was 2.4 mo. A total of 101 vaccines were administered. Therapy-related significant adverse events included a grade 3 hypotension and a grade 3 acute respiratory distress. The most common therapy-related toxicities were joint pain and fever. No confirmed complete or partial responses were observed. Presence of HLA-A2 correlated with reduced risk of progression at first evaluation (HR 0.41, 95% CI 0.16 - 1.03, p=0.06) and was associated with a trend towards improved TTP (p=0.07).

Conclusion: Despite absence of confirmed responses, the survival curve suggested activity in a subset of participants. A similar lung adenocarcinoma vaccine trial, incorporating a T-cell chemokine, is currently underway.

Research supported by: NIH - OBA:0608-801.

Assessment of Repeated Measures of Fractional Exhaled Nitric Oxide in Clinically Stable Persistent Asthma

A. Elizalde, R.J. Khan, S. Chinratanapisit, M.J. Dorsey. All Children's Hospital/University of South Florida, Division of Allergy and Immunology, Saint Petersburg, Florida., University of South Florida Morsani College of Medicine, Dept. of Pediatrics

Keywords: Fractional exhaled nitric oxide, asthma

Objective: The recent American Thoracic Society guidelines on interpretation of fractional exhaled nitric oxide (FENO) levels suggest monitoring changes in children with asthma. The goal of this study was to determine if changes in FENO levels are observed in children with persistent asthma during clinical stability to determine the need for repeated FENO levels once baseline values are established.

Methods: This is a prospective control cohort study of clinically stable asthmatic children (n=54) aged 4 to 18, followed in the allergy and immunology division. Patients were assessed at two visits six months apart. FENO (Aerocrine, Sweden) and spirometry (Koko Pneumotach) were conducted and clinical history was obtained at each visit. Controls (n=12) were healthy with no history of atopy or asthma. Statistical analysis was performed using Prism (Graphpad Software, California).

Results: Significant difference in FENO (p=0.02, Mann-Whitney U 57.5) was observed between the asthma (28.3 ppb+/- 4.59) and control group (9.4 ppb+/-1.42). We found no significant change in FENO values between visits (p=0.78, Mann-Whitney U 153, 22.98 ppb+/-5.24 on initial measurement and 24.66 ppb+/-5.77 on follow up). Two subgroups were identified in the asthma group, subjects with elevated FENO (54.73 ppb+/-6.38) and those with levels comparable to controls (11.66 ppb+/-1.36). There was no significant difference on follow up levels in each of these two subgroups (p>0.05).

Conclusion: FENO measurements remain unchanged in children with clinically stable persistent asthma suggesting FENO levels should be repeated based on changes in clinical symptoms.

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Photoaging Attenuates Skin Test Response to Histamine More Than Natural Aging

MJ King*, SE Phillips**, DJ Fitzhugh*, RF Lockey*. *James A. Haley Veterans' Hospital, Joy McCann-Culverhouse Airway Disease Center, Division of Allergy and Immunology, Department of Internal Medicine, University of South Florida College of Medicine, Tampa, FL; **Morton Plant Mease Health Care, Clearwater, FL, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Histamine, Skin test, Photoaging

Objective: Clinical experience suggests that skin test reactivity is often decreased in photo-exposed skin versus sun-protected skin in older individuals. The current study was designed to address whether photoaging or natural aging of skin causes a greater diminution in skin test response.

Methods: Prick-puncture skin tests to histamine were performed on sun-exposed and sun-protected areas in younger (n = 61, age 20-50) and older (n = 63, age 60-87) adult volunteers who were recruited for skin prick testing because of suspected allergic rhinitis and/or allergic asthma. The skin was scored for photoaging by physical examination and coloration was measured by a colorimeter.

Results: There was no observed difference in wheal and flare response to histamine when patients were stratified by age alone. However, photoaging was significantly correlated with decreased skin reactivity to histamine on the upper back (a sun-exposed area) as compared to the lower back (a sun-protected area). In patients with the most severely sun-damaged skin, there was a trend toward decreased skin reactivity in all areas.

Conclusion: Skin test reactivity to histamine correlates negatively to the degree of photoaging and is independent of patients' chronological age. This result has clinical implications for patients with significant photoaging, suggesting that care should be taken to perform skin testing on anatomic sites in sun-protected areas. In patients with severe photoaging, allergen-specific IgE testing should be considered to avoid possible false-negative interpretation of skin-prick testing.

Research supported by: Joy McCann Culverhouse Endowment and the Institute on Aging at the University of South Florida

The Role of Glutathione in Chronic Ischemic Wounds in the Elderly

Sarah C.², Dr. Lisa J. Gould^{2,1}, Dr. Andrea N. Moor^{2,1}, Dr. Evan K. Tummel^{2,1}, Jonathon J. Lopez^{1,2}, Dr. Jamie L. K. Prather^{2,1}, Michelle Jung^{2,1} James Haley VA Hospital, ²University of South Florida, Morsani College of Medicine, Dept. of Surgery

Keywords: aging, ischemia, wound healing

Objective: Wound healing requires a well-balanced metabolism to prevent the buildup of harmful byproducts such as reactive oxygen species [ROS]. One of the primary mechanisms involved in metabolizing ROS is the reduction of H₂O₂ to H₂O by glutathione peroxidase [GPx]. We utilized an ischemic wound model in aged Fisher 344 rats to examine the hypothesis that the glutathione metabolic pathway is dysregulated with age and ischemia.

Methods: Ischemic and non-ischemic wounds were surgically created in 8-month old (young) and 24-month old (aged) rats using a bipedicle ischemic flap model. Wounds were analyzed for the ratio of reduced to oxidized glutathione [GSH:GS-SG], glutathione levels and GPx activity during a three week post operative period.

Results: The GSH:GS-SG ratio in ischemic wounds from aged rats was lower compared to non-ischemic wounds. Total glutathione in ischemic wounds from young rats was significantly lower than from non-ischemic wounds with similar results observed in aged rats. GPx activity was up-regulated in ischemic wounds of young rats compared to aged rats. Finally, GCLM levels increased over the time course specifically in wounds from aged rats.

Conclusion: Ischemic wounds of aged rats had lower total glutathione levels, lower GSH:GS-SG ratio and less GPx activity compared to ischemic and non-ischemic wounds in young rats. Reduced glutathione provided by de novo synthesis does not overcome the deficit. These data suggest that the glutathione metabolic pathway is deficient in ischemic wounds of aged rats and that simple supplementation of glutathione may not be sufficient to restore redox balance.

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Regulation of Antioxidant Responses in Prostate Cancer: Effects of Lycopene

Xiaoming Gong, Raju Marisiddiah, Doris Wiener, Lewis P. Rubin University of South Florida Morsani College of Medicine, Dept. of Pediatrics

Keywords: Reactive oxygen species, Antioxidant, Prostate cancer, Lycopene

Objective: Objective: Reactive oxygen species (ROS) can be mutagenic and may promote cancer. Evidence from epidemiological, experimental studies and clinical trials suggests that lycopene may modify risk or delay progression of prostate cancer. However, the molecular mechanisms involved are still unclear. The aim of this study is to determine the effects of lycopene on endogenous ROS and antioxidant responses in normal prostatic epithelial cells and in prostate cancer cells.

Methods: Methods: Endogenous ROS was measured with DCFH-DA, glutathione (GSH) cycling was assayed using a luminometric technique; Nrf2 signaling was measured using PCR, western blotting, and nuclear translocation assays; Nrf2-dependent activation of the antioxidant response element (ARE) was assayed by gene reporter assays.

Results: Results: ROS levels were much higher in prostate cancer cell lines than in normal prostate cells (PrEC). Lycopene reduced ROS levels in a dose-dependent manner in androgen-dependent LNCaP, but not in androgen-independent DU145 or PC3 cells. Intracellular levels of reduced GSH differs in cancer cells with highest in DU145 and were associated with abundant Nrf2 levels. Lycopene treatment did not significantly affect cell GSH or nuclear translocation of Nrf2 in either normal or prostate cancer cell lines. Using a cell-based ARE-reporter assay, we found that lycopene treatment increased ARE transcriptional activity in LNCaP, but decreased ARE activity in DU145 cells.

Conclusion: Conclusion: These findings indicate that lycopene may impair the PC cell survival machinery through regulating intracellular ROS and the antioxidant response. Certain effects appear to be independent of Nrf2 signaling.

Research supported by: NIH, Muma Family Endowment, USF

Hybrid Endovascular Exclusion of Aberrant Right Subclavian Artery Aneurysms

Danielle C. Horne, MS, Martin R. Back, MD, Murray L. Shames, MD, Division of Vascular and Endovascular Surgery, University of South Florida, University of South Florida, Morsani College of Medicine, Dept. of Surgery

Keywords: Kommerell's Diverticulum, Hybrid Surgical Technique, Endovascular, ARSA

Objective: As an alternative to open arch reconstruction, we detail an experience with staged transcervical arch branch reconstruction and aortic endograft exclusion of symptomatic aneurysms involving the origin of an aberrant right subclavian artery (ARSA).

Methods: Since 2006, 6 patients (ages 32-84 years) presented with symptoms of chronic dysphagia (n=5) and acute type B aortic dissection (n=1) and ARSA (sizes 2.1 – 6.1cm by CTA). All patients were managed by bilateral common carotid to subclavian artery bypass (n=9) or transposition (n=3) with a right to left carotid bypass needed in one case. Left subclavian (n=6) and carotid (n=1) origin coverage was required for proximal fixation >20mm in the mid arch. Staged (1-5 days) exclusion of the ARSA origin and adjacent arch branches was done via transfemoral access (n=5) or iliac conduit (n=1) with short (10-15cm) single endografts. Open distal ligation (n=8) or retrograde embolization (n=4) with vertebral preservation completed exclusion of subclavian vessels.

Results: No mortality, spinal cord ischemia, stroke, upper limb ischemia or wound site complications occurred during follow-up. Length of stay ranged 6-21 days. Dysphagia resolved within days to weeks in each case. Surveillance ranged from 2 to 47 months (mean 29 mo) with 3 patients followed beyond 3 years. ARSA regression (-4 to -24 mm) was observed in all but 1 patient (no change) with transcervical bypasses remaining patent and no endoleaks.

Conclusion: By utilizing a hybrid endovascular technique for treating symptomatic ARSA, we have achieved durable repairs and symptom relief.

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Antiretroviral Therapy (ARV) Fails To Correct B Cell Activation in Both Behaviorally-Acquired (BAH) and Perinatally-Acquired HIV-Infected (PAH) Cohorts

S. Hudey, MS, P. Sriaroon, MD, C. Rodriguez, MD, B. Rudy, MD, J. Sleasman, MD. University of South Florida Morsani College of Medicine Pediatrics

Keywords: HIV, B cells, ART, flow cytometry, immune activation

Objective: HIV is characterized by B cell dysfunction leading to impaired antibody responses. We sought to compare B cell subpopulations among adolescents with BAH infection before and after initiation of ART, adolescents with PAH on therapy, and healthy adolescents. Increased percentages of CD21-/low and CD80/86 B cells were used as indicators of B cell activation.

Methods: Using fresh whole blood samples, multiple parameter flow cytometry analysis enumerated CD19/CD27 with extended markers including surface IgM/IgD, CD21, CD23, CD80 and CD86 in 44 healthy controls (HC), 38 BAH subjects with normal CD4 counts (>350) before and 48 weeks after initiation of ART, and 21 PAH subjects.

Results: There were no differences in total CD19+ B cell percentages among the groups. Prior to ART, CSR (class-switch recombination) in CD27+ memory B cells was lower in BAH compared to HD ($p<0.01$), but corrected with ART. In contrast, B cell activation marker CD21-/lo remained elevated in both BAH and PAH following ART ($p<0.001$ and $p<0.01$, respectively). However, activation markers CD80/86 normalized in BAH but remained elevated in treated PAH ($p<0.001$).

Conclusion: ART corrects defects in memory B cell maturation but B cell activation remains high in spite of low viral levels, suggesting ongoing immune activation independent of viral replication.

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Post Chemoradiation SUV is Highly Predictive of Disease Free Survival and Overall Survival in Esophageal Cancer

1H. Lomas, MPAS, PA-C, MSIV; 2J Weber, MPH; 3MD Chuong, MD; 3SE Hoffe, MD; 2K Almhanna, MD; 2RC Karl, MD; 2K. Meredith, MD; 3R Shridhar, MD, PhD. 1University of South Florida College of Medicine; 2Gastrointestinal Tumor Program, 3Department of Radiation Oncology; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, University of South Florida, Morsani College of Medicine

Keywords: PET SUV, Survival in Esophageal Cancer

Objective: The purpose of this study was to determine the prognostic significance of standardized uptake values (SUV) pre and post chemoradiation therapy (CRT).

Methods: Between 2006 and 2010, 77 pts underwent initial and restaging PET-CT scan prior to definitive or preoperative CRT for esophageal cancer. SUV values were measured on an AW workstation. Univariate analysis for overall survival (OS) and disease free survival (DFS) were performed with Kaplan-Meier and log-rank analysis. Median values were determined for each SUV parameter and used as a median for Kaplan-Meier analysis. Multivariate analysis for OS and DFS were performed with a Cox proportional hazard ratio for age, gender, surgery, stage, histology, tumor length, post CRT SUV mean and max, and percent change of post CRT SUV mean and max.

Results: Univariate Kaplan-Meier analysis demonstrated that post CRT mean SUV (median 2.3; $p=0.003$), post CRT max SUV (median 4.4; $p=0.0054$), percent change of SUV mean (median 61%; $p=0.0051$), and percent change of SUV max (median 57%; $p=0.0069$) were strongly predictive of OS. On multivariate analysis, age, stage, surgery, percent change of mean and max SUV, and post CRT mean and max SUV were all predictive for DFS, while gender, tumor length, and histology were not. Post CRT mean SUV (HR 1.802; 95%CI: 1.145-2.837) and post CRT max SUV (HR 1.401; 95%CI: 1.061-1.850) were predictive for OS on multivariate analysis. On multivariate analysis, age, gender, surgery, histology, tumor length, and stage, were not predictive for OS.

Conclusion: Our series demonstrates that Post CRT mean and maximum SUV were the strongest predictors for OS and DFS. This data suggests a role of post-neoadjuvant PET response for stratification of patients with esophageal cancer.

Research Supported by: This research was supported by the Research Scholarly Concentration at USF Health Morsani College of Medicine

Digital Holographic Adaptive Optics for Retinal Imaging

Dr. David Richards, Changgeng Liu, University of South Florida Morsani College of Medicine, dept. of Ophthalmology

Keywords: Digital Holography

Objective: Digital holographic adaptive optics (DHAO) is an innovative imaging technique that will revolutionize the way the retina is imaged. Currently the retina is imaged using adaptive optics (AO) which requires an expensive wavefront sensor and wavefront modulator which are used to correct for aberrations created by the human lens. DHAO uses digital holograms to correct for these aberrations, thus greatly reducing the cost of retinal imaging and improving the speed of imaging as well. It is our goal to show that DHAO can be applied to retinal imaging.

Methods: DHAO is essentially a two-step process. First a hologram of the retina is created using a pinpoint light from a laser. This hologram is used to measure the aberrations created by a broken piece glass (serving as a human lens) placed in front of the target paper (serving as a human retina). A second hologram is generated by using full field illumination of the target paper. Lastly, a mathematical algorithm is used to compare the first and second hologram and subtract out the aberrations, thus creating an unaberrated image of the retina.

Results: The results from using a test sheet paper with grading (retina) and a broken piece of glass (human lens) for imaging have been promising. Images of the target paper using DHAO show marked improvement over standard images taken without using any corrections for aberrations.

Conclusion: These results suggest that it may be possible to use DHAO to image a human retina and correct for aberrations created by the human lens. However, we will need to move our experiments onto cow eyes in order to further prove this concept.

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The Role of Dysregulation in Pediatric Obsessive-Compulsive Disorder

Joseph F. McGuire, B.A.¹ Adam B. Lewin, Ph.D.,² Tanya K. Murphy, M.D.,² and Eric A. Storch, Ph.D.^{1,2}

¹.Department of Psychology, University of South Florida, Tampa, Florida. ².Departments of Psychiatry and Behavioral Neurosciences, University of South Florida, St. Petersburg, Florida. University of South Florida, College of Arts and Sciences, Dept. of Psychology

Keywords: obsessive-compulsive disorder, dysregulation, severity, impairment

Objective: Pediatric obsessive-compulsive disorder (OCD) is complicated by comorbidity with ADHD, mood and anxiety disorders. While these disorders are associated with dysregulation, there has been no examination of dysregulation in OCD. Dysregulation is characterized by affective, behavioral and cognitive problems, and can be assessed using the Child Behavior Checklist-Dysregulation Profile (CBCL-DP). As dysregulation has been associated with impairment even in the absence of a psychiatric diagnosis, an examination of dysregulation may prove useful for impairing disorders like OCD. This study examines the relationship of dysregulation, severity and impairment in 140 youth diagnosed with OCD.

Methods: Clinicians administered measures of OCD severity (CY-BOCS), global severity (CGI-S) and a scale that assessed family accommodation. Youth completed the self-report measures of anxiety (MASC) and depression (CDI). Parents completed the CBCL, with both children and parents completing parallel versions of the Child OCD Impact Scale (COIS-C/P). T-scores ≥ 65 on all three subscales that comprise the CBCL-DP were used to indicate dysregulation.

Results: Dysregulated youth had greater symptom severity, depressive mood, and exhibited greater rates of family accommodation. Additionally, these youth had higher scores on several CBCL problem scales including both internalizing and externalizing problems. Furthermore, both children and parents rated dysregulated youth as having higher levels of impairment on the COIS-C/P total score than youth without dysregulation.

Conclusion: Findings suggest that youth with dysregulation express greater clinical severity and impairment compared to youth with more regulated functioning.

Safety and Experience of Research Lumbar Punctures in Parkinson's Disease Patients

Gene Peir BS¹, Jacqueline Rick PhD², James Minger BS², Howard Hurtig MD², Andrew Siderowf MD² ¹USF Morsani College of Medicine, Dept of Neurology, ²MCSE Morris K. Udall Center of Excellence for Parkinson's Disease Research University of Pennsylvania School of Medicine

Keywords: Parkinson's disease, lumbar puncture, safety

Objective: To assess the safety and tolerability of the lumbar puncture (LP) procedure in patients with Parkinson's disease (PD), and to explore factors associated with a positive experience as reported by PD patients.

Methods: Seventy-five PD patients had an LP and completed a brief 9 item self-report questionnaire about various aspects of the experience. A 24G x 90mm Sprotte Needle was used for the LP. Cognition and mood were assessed with the Mattis Dementia Rating Scale (DRS-2) and the Geriatric Depression Scale (GDS). Motor impairment was assessed with the Modified Hoehn and Yahr Scale.

Results: Of 90 total LPs, 7 were associated with an adverse event (AE) during or following the lumbar puncture procedure. All AEs reported were mild. Factors that were related to ratings of LP discomfort included depression and not having received enough information prior to the LP. Dementia and severe motor impairment did not affect LP tolerability.

Conclusion: Research lumbar punctures in Parkinson's disease patients are safe and the majority of patients report a satisfactory experience. Providing patients with more information ahead of time is associated with a positive experience.

Research supported by: Morris K. Udall Center of Excellence for Parkinson's Disease Research University of Pennsylvania School of Medicine

Compatibility of Heparin with Ethanol for Ethanol-Lock Therapy of Central Venous Catheters

Daniel Restrepo, BS¹, Norma Alcantar, PhD³, Mark L. Kayton, MD⁴, Saumil Patel² - ¹University of South Florida, College of Medicine, Dept of Pediatrics, ²University of South Florida, Dept of Surgery, ³University of South Florida, College of Engineering, ⁴Tampa General Hospital, Dept of Pediatrics

Keywords: Ethanol, Heparin, Ethanol-Lock Therapy, Central Venous Catheters, Central Line Infection

Objective: Central venous catheter-related bloodstream infections are the most common preventable infections in contemporary cancer care. Administration of ethanol directly into central venous catheters has shown promise for prevention of such infections, but has been associated in clinical trials with the development of thrombosis and catheter occlusion. Common anticoagulants such as heparin are not thought to be compatible with ethanol. We hypothesized that at low concentrations, heparin will be compatible in solution for co-administration with ethanol.

Methods: Heparin at concentrations from 0-100 units/mL was incubated overnight in 30%, 50%, or 70% ethanol, at temperatures ranging from 4-40 °C. Precipitate formation was assayed in nephelometric turbidity units (NTU's) using a benchtop turbidimeter. Each concentration and temperature condition was replicated 6 times, with means compared by ANOVA with post-hoc T-test (p<0.05).

Results: Precipitate formation in NTU's for heparin incubated overnight in 70% ethanol at 37 °C was 0.05 ± 0.02 for 0 units/mL heparin, 0.19 ± 0.01 for 1 unit/mL, 4.27 ± 0.01 for 10 units/mL, and 467.83 ± 11.74 for 100 units/mL (p<0.05 for 100 units/mL versus all other concentrations). There was no significant precipitation for any heparin concentration below 100 units/mL in ethanol. This held true at all ethanol concentrations tested, and at all temperature conditions.

Conclusion: Heparin at 1 unit/mL or 10 units/mL does not meaningfully precipitate with ethanol and should be evaluated in clinical trials for co-administration with ethanol. However, heparin at 100 units/mL (used by many medical centers in mediports and hemodialysis catheters) is incompatible for administration to patients with ethanol, owing to dense precipitation.

Research supported by: American Heart Association Medical Student Fellowship Grant

Maternal Smoking Hastens Telomere Shortening in Neonatal Umbilical Cord

Jael Rodriguez¹, Elisa McQueen¹, Katheryne Downes¹, Shayne Plosker¹, David Keefe² and Celso Silva¹. ¹-Obstetrics and Gynecology - Division of Reproductive Endocrinology and Infertility, University of South Florida, ² Tampa General Circle 6th floor Tampa, FL, and ²-Obstetrics and Gynecology, NYU Langone Medical Center, 660 First Avenue, 5TH floor New York, New York, University of South Florida Morsani College of Medicine Obstetrics & Gynecology

Keywords: Telomere, smoking, oxidative stress

Objective: Smoking during pregnancy is associated with adverse obstetrical outcomes. Smoking exerts its toxicity in part by generating reactive oxygen species (ROS). Telomeres preserve genomic integrity, and are susceptible to oxidative stress. Telomere length (TL) is a marker of cellular damage, and shorter telomeres are present in placentas of patients with pre-eclampsia and diabetes. We evaluated telomere attrition in leukocytes from human umbilical cord blood (UCB) in patients exposed to tobacco during pregnancy.

Methods: UCB was obtained after expulsion of the placenta from subjects with and without exposure to tobacco during pregnancy. Exposure was defined as: 1) current first hand; 2) current second hand; 3) past first hand; and 4) past second hand. Cotinine levels were assessed using ELISA, and used to confirm cigarette exposure. TL was assessed by QPCR using the Cawthon method. Linear regression analysis was used to model mean TL as a function of tobacco exposure, controlling for maternal and gestational age, obstetrical and medical conditions.

Results: Linear regression analysis showed that the adjusted mean cord blood TL was significantly different between patients with tobacco exposure and controls (beta = -705.7, p = 0.034). Differential cord blood TL was detected according to type of smoking exposure. Baseline characteristics were comparable.

Conclusion: Maternal smoking exposure negatively impacts on neonatal TL. In addition, TL was negatively impacted in neonates of past first-hand smokers, despite maternal smoking cessation during pregnancy. Further studies on the association between shorter TL in UCB and neonatal outcomes may determine if TL in these tissues could be used as marker of neonatal health.

Research supported by: USF OB/GYN Department

Occipital Nerve Stimulation for the Treatment of Chronic Headaches

Christopher R. Russo, M.D., University of South Florida Department of Neurology Pain Medicine Fellowship. Jose E. Sarria, M.D., Director- Moffitt Cancer Center Interventional Pain Clinic. Maria Carmen Wilson, M.D., Director- Tampa General Hospital Headache and Pain Center. University of South Florida, College of Medicine, Dept. of Neurology

Keywords: Occipital Nerve Stimulation Chronic Headache

Objective: A multidisciplinary approach produces the best long term result when treating chronic headaches. Occipital nerve stimulation (ONS) has shown promise as documented by multiple case reports and case series studies. Rigorous formal ONS trials are currently underway.

Methods: This data was collected from the University of South Florida College of Medicine and its affiliated medical institutions. All patients were referred from the Tampa General Hospital Headache and Pain Center to the Interventional Pain Clinic at the H. Lee Moffitt Cancer Center and Research Institute.

Results: A total of 18 patients underwent percutaneous trial ONS and 16 were implanted after completing a successful trial. The breakdown of their diagnoses included eight chronic migraine headaches, three cluster headaches, one hemicrania continua, one post-traumatic headache, one post-craniotomy headache, and one occipital neuralgia. Two trials for chronic migraine were unsuccessful. Complications included one scar revision for a painful lead site and one infection requiring system exchange. Several patients have required repeated reprogramming for shifting lead stimulation. Longest follow-up has been nine months involving two patients who continue to report successful ONS as defined by greater than 50% overall improvement in their headache symptomatology.

Conclusion: In summary, there is growing clinical evidence that ONS is beneficial in the treatment of chronic headache and should be considered in a well defined subgroup of refractory chronic headache patients.

μ Opioid Receptors in the Enteric Nervous System

Simona Patierno, Laura Anselmi, Ingrid Jaramillo, David Scott, Rachel Garcia, and Catia Sternini *CURE Digestive Diseases Research Center, Veterans Administration Greater Los Angeles Healthcare System, Los Angeles, California; Department of Medicine, Digestive Diseases Division, §Department of Physiology, and Department of Neurobiology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: G-Protein–Coupled Receptors, Opioid Peptides, Opiate Drugs, Tolerant and Naïve Animals

Objective: The μopioid receptor (μOR) undergoes endocytosis after acute stimulation with opioids and most opiates, but not with morphine. We investigated whether prolonged activation of μOR affects morphine's ability to induce receptor endocytosis in enteric neurons.

Methods: We compared the effects of morphine, a poor μOR-internalizing opiate, and enkephalin(DAMGO), a potent μOR-internalizing agonist, on μOR trafficking in enteric neurons and on the expression of dynamin and β-arrestin immunoreactivity in the ileum of guinea pigs rendered tolerant by chronic morphine administration.

Results: Morphine (100 μmol/L) strongly induced endocytosis of μOR in tolerant but not naive neurons, whereas DAMGO (10 μmol/L) strongly induced internalization of μOR in neurons from tolerant and naive animals. Morphine- or DAMGO-induced μOR endocytosis resulted from direct interactions between the ligand and the μOR because endocytosis was not affected by tetrodotoxin, a blocker of endogenous neurotransmitter release. Ligand-induced μOR internalization was inhibited by pretreatment with the dynamin inhibitor, dynasore. Chronic morphine administration resulted in a significant increase and translocation of dynamin immunoreactivity from the intracellular pool to the plasma membrane, but did not affect β-arrestin immunoreactivity.

Conclusion: Chronic activation of μORs increases the ability of morphine to induce μOR endocytosis in enteric neurons, which depends on the level and cellular localization of dynamin, a regulatory protein that has an important role in receptor-mediated signal transduction in cells.

Research supported by: National Institutes of Health grants, and pilot grant from National Institutes of Health–National Institute on Drug Abuse Center for Study of Opioid Receptors and Drugs of Abuse. This research was also supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Feasibility Study for Technology-Based Cancer Education for Latinas from an Agricultural Community

Laura E. Barnes, Ph.D., University of South Florida College of Medicine, Maria Rivera, M.P.H., University of South Florida College of Medicine, Cathy D. Meade, Ph.D., R.N., F.A.A.N., H. Lee Moffitt Cancer Center and Research Institute, Sara K. Proctor, D.W., Catholic Mobile Medical Services, Liliana Gutierrez, H. Lee Moffitt Cancer Center and Research Institute, Kristen Wells, Ph.D., M.P.H., University of South Florida College of Medicine, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: health communication, health information technology

Objective: Interactive, technology-driven health education programs improve on passive communication of health information by allowing users to interact with educational information in a highly visual manner. These interventions have not been fully explored or disseminated widely to vulnerable populations and few are available in Spanish. This study examines the feasibility of implementing a low-literacy, user friendly, interactive computer program for the delivery of cervical cancer education to primarily Spanish-speaking Latina women from an agricultural community in rural central Florida.

Methods: Study participants were recruited from the waiting room at Catholic Mobile Medical Services, a faith-based community primary care clinic in Dover, Florida. Participants were interviewed regarding their prior experience with computers. Subsequently, they were shown a video depicting a computer program delivering health information, and they were asked a series of open-end questions regarding their reactions.

Results: A total of 26 women participated in the study, all of whom spoke Spanish. One hundred percent of participants responded positively to the concept of the computer program, method of health information delivery, and stated they would trust information obtained through a similar educational program.

Conclusion: The results of this study suggest that technology-based cancer education for primarily Spanish-speaking Hispanic women from an agricultural community is feasible, and user acceptance is high. The data from this study will be used to inform the design and development of an interactive program to deliver education about cervical cancer and the human papillomavirus.

The Business of Medicine Bootcamp – Bridge Clinic Collaboration

Ronit Zadikany¹, Jason Patel¹, Joshua Shultz¹, Colin Sullivan¹, Binna Chokshi¹, Jehan Shah¹, R. David Graham¹, Chase Burns¹, Jess DeLaune¹, Joshua Kraft¹, Nerissa Moore¹, Eric Quintero¹, Jacqueline Young¹, Leon Anijar¹, Nikesh Kapadia¹, Patrick Blackburn¹, Sherry Zhao¹, Jordan Kapper¹, Vignesh Doaiswamy¹, William G. Marshall, Jr.¹ Scholalry Concentrations Program, USF Health Morsani College of Medicine, University of South Florida, Dept. of Psychiatry and Neurosciences

Keywords: BOMB, BRIDGE, Business Plan, Operations,

Objective: There is a substantial need for specialized education and training for medical students that provides skills in innovation and entrepreneurship needed to function in an evolving healthcare system. The Business of Medicine Bootcamp (BOMB) was created at the University of South Florida College of Medicine in 2010 to address this need. Each year it provides an experiential learning opportunity to apply the skills and expertise learned in the BOMB the curriculum. In 2011, the BOMB worked in collaboration with the BRIDGE Clinic, a student run and managed free health care clinic that provides healthcare services to underserved populations.

Methods: The BOMB collaborated with BRIDGE in an effort to increase the efficiency of clinical operations, improve business functions, and complete a formal Business Plan (for funding purposes).

Results: A comprehensive Business Plan was developed which included a new governance structure (a formal Board of Directors of students from participating colleges and schools). The executive leadership team and mid-level managerial teams were re-structured with development of formal Operations, Marketing, Finance, and Philanthropy teams. In addition, the BOMB graduates became the Business Operations team for the BRIDGE Clinic.

Conclusion: The BOMB/BRIDGE Clinic collaboration provides the opportunity for BOMB students, under faculty guidance, to become responsible for the leadership and management of a functioning start-up healthcare organization—a unique experience and opportunity. The students experience all aspects of the challenges of healthcare delivery from clinical, organizational, and financial standpoints. This model continues to evolve and expand and is easily transferrable to other academic institutions.

Research Supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Revising Proposed Silver Alert Legislation Based on New Research Findings

Catherine Greenblum, College of Nursing, University of South Florida, Meredith A. Rowe, College of Nursing, University of South Florida

Keywords: Dementia, Silver Alert, missing persons with dementia, caregiver, caregiver health

Objective: Understand the new research findings on missing persons with dementia and identify how legislation can be improved to better serve all missing individuals.

Methods: Reviewed 158 law enforcement reports of Silver Alerts from October 2008 to May 2010, excluding 2 reports since no dementia diagnosis. Found 154 unique drivers, 2 drivers with a second incident. Used descriptive statistics, Chi-square and t-tests to analyze the data.

Results: Almost individuals who are missing leave on foot and are found in residential areas or local businesses. Over 90% are found within 5 miles of the place last seen. Silver Alerts were instrumental in < 20% of discoveries. Over 50% of individuals will have a missing incident in a year equaling to millions of incidents. Deaths occur within a ½ mile radius of the place last seen in 50% of cases, generally from exposure. If not found in <24 hours, 50% will be found dead. Deaths almost always occur when the individuals have secluded themselves in remote areas such as woods and other natural areas. Deaths occur due to the difficulty in locating these individuals rapidly.

Conclusion: Based on these findings we propose some changes to legislation. Law enforcement education on working with and finding missing persons with dementia should be mandated. There should be intensive use of local resources such as community alert notifications systems. We also suggest formal follow-up strategies for those who have had a missing incident.

Research supported by: Departmental Funding

Teens, Communication Technology, and New Avenues for STD Prevention

Shana Hughes MPH¹, Natalie Klinkenberger MPH², Heather Blunt MPH², Eric R. Buhi, PhD, MPH³ ¹USF Department of Anthropology, ²USF COPH Department of Community and Family Health, ³USF COPH Department of Community and Family Health. University of South Florida, College of Arts and Sciences, Dept. of Anthropology

Keywords: Teens/youth; sexual health; technology; text messaging

Objective: More effective STD prevention measures are needed for U.S. teens. The Communication, Health and Teens (CH@T) Study responds to this need by examining teens' sexual practices, health outcomes, and use of communication technology. Here we report on adolescent technology ownership and preferred means of locating and receiving sexual health information.

Methods: Youth 13-19 years old, recruited at a publicly funded clinic in the Tampa Bay area, were tested for Chlamydia trachomatis and Neisseria gonorrhoeae and completed an audio computer-assisted self-interview (ACASI). The ACASI included 25 questions on demographics, device ownership, Internet access, social networking site (SNS) activities, and modalities of communication with friends. The feasibility/acceptability of several means of delivering STD prevention messages and sexual health promotion services was also assessed. The data reported here are based on the final sample of 273 participants.

Results: Virtually all teens reported owning a cell phone (93.4%), having profile on a SNS (95.2%), and accessing the Internet at least once daily (79.1%). The vast majority (84.6%) reported that social communication outside of school hours occurs through text messaging. Perhaps unsurprisingly, therefore, it is a text message service that most (50.3%) teens reported being "likely" to use to obtain answers to questions about sexual health, a finding accentuated among those with a current STD, $\chi^2(1, N = 266) = 4.21, p=.04$.

Conclusion: The next generation of STD prevention and sexual health promotion materials for teens must make use of newer communication technologies, including texting, in order to maximize effectiveness.

Research supported by: American Sexually Transmitted Disease Association (ASTDA) Developmental Award (PI: Buhi).

Predicting Medical Student Surgical Career Choice: Uni- and Multi-variate Analyses of Career Choice Variables

Michael J Schnaus BA, Steven B Goldin MD, PhD, FACS, , Greg Horn BA, James Mateka BS, Michael T Brannick PhD
University of South Florida, Morsani College of Medicine, Dept. of Surgery

Keywords: Surgical Education, prospective study, Career choice, Match

Objective: This study prospectively investigates the roles of various factors in medical student surgical career choice as indicated by their match into a surgical residency.

Methods: Students participating in the third-year 8-week surgery clerkship at the University of South Florida College of Medicine from June 2005 through May 2008 were asked to complete weekly surveys. Univariate and multivariate modeling of these factors as they related to surgical career choice was done at baseline, post surgical-clerkship, and at match.

Results: Statistically significant variables that positively influenced surgical career choice included male gender, prior experience with surgery, positive role modeling from residents and attendings, having a meaningful experience during the clerkship, and receiving an Honors grade. The strongest correlate of matching in surgery was an interest in a surgical career on the first day of the clerkship. Factors that negatively impacted student general surgery career selection included female gender, a non-surgeon physician in their family, desire for a controllable lifestyle, length of training, and debt importance. Only 3% of students not initially interested in a surgical career entered a surgical discipline.

Conclusion: The clerkship itself played almost no role in swaying those initially uninterested in a surgical career to enter a surgical career. Efforts to recruit students into a surgical career should begin prior to their surgical clerkship.

Research supported by: Dr. Steven B Goldin, MD, PhD. sgoldin@health.usf.edu

Cognitive-Behavioral Treatment for Anxiety Disorders in Children with Autism Spectrum Disorders

Elysse B. Arnold B.A., Anna M. Jones, B.S., Adam B. Lewin, Ph.D., P. Jane Mutch, Ph.D., Josh Nadeau, M.A., Lindsay Brauer, M.A., Michael Sulkowski, Ph.D., Tanya K. Murphy, M.D., Eric A. Storch, Ph.D. University of South Florida Morsani College of Medicine Pediatrics

Keywords: anxiety, autism, child, treatment, CBT

Objective: Autism spectrum disorders affect as many as 1 out of 91 children (Centers for Disease Control, 2007). Comorbid psychological disorders, especially anxiety (Bellini, 2004), are common in the ASD population (Simonoff et al., 2008). This may cause additional distress and impairment beyond the ASD diagnosis. The linguistic, cognitive, and social characteristics of ASD may render standard treatment approaches (developed for otherwise typically developing youth) for anxiety less effective for children with ASD (Volkmar & Klin, 2000). Thus, a clinical need remains for the modification of existing treatment modalities for this unique group. Accordingly, we report on a randomized controlled trial examining the efficacy of CBT relative to treatment as usual (TAU) in 44 youth ages 7-11 with ASD and comorbid anxiety disorder(s).

Methods: Forty-four children (ages 7-11) with ASD and comorbid anxiety disorder(s) were randomly assigned to 1 of 2 treatment conditions. The cognitive behavioral therapy condition (CBT) involved participants receiving immediate treatment for 16 weeks. The treatment as usual condition (TAU) delayed treatment for 16 weeks. But, during this period, participants could seek treatment outside of the study. An independent evaluator assessed primary outcome measures which included change in anxiety symptom severity; response rates; and remission rates.

Results: Those in the CBT condition experienced higher response rates to treatment than those children in the TAU condition. Relative to the TAU arm, the CBT arm was associated with significantly greater reductions in anxiety symptomology.

Conclusion: These data provide additional support for the efficacy of CBT in treating anxiety symptoms among youth with ASD.

Research supported by: All Children's Hospital Foundation.

Better Golden Hour Care Significantly Improves Outcomes for Extremely Low Birth Weight Infants

Terri L. Ashmeade, M.D.¹, Karen Fugate BSN², Sherie Collins MSN NNP-BC¹, Branko Miladinovic Ph.D.¹, Laura Haubner M.D.^{1,2} University of South Florida Morsani College of Medicine Pediatrics, ²Tampa General Hospital

Keywords: Golden Hour Low birth weight Quality Improvement

Objective: There is evidence that care provided to extremely low birth weight (ELBW) infants during the first "golden hour" of life can significantly affect outcomes. However, there are few published reports of process implementation and associated improvements in outcomes. We describe the implementation and evaluation of an evidence-based "golden hour" pathway for the care of infants born at ≤ 28 weeks gestational age or with birth weight ≤ 1000 gm.

Methods: We initiated a quality improvement project to determine if a standardized pathway for the management of ELBW infants during the first hour of life would improve the efficiency of care delivery, and improve outcomes. Data were collected prospectively for all infants delivered with an estimated gestational age < 28 wks or birth weight < 1 kg. We compared our prospective data with those from admissions that met golden hour criteria during the two years prior to implementation of the pathway.

Results: 122 ELBW infants were treated according to the "golden hour" pathway, and their data were compared with those from 173 infants treated before pathway implementation. Improvements were achieved in the time from birth to surfactant administration, body temperature on admission to NICU, and time from admission to dextrose and amino acid infusion. Infants treated under the golden hour protocol had a 64% reduction in the odds of developing chronic lung disease (OR=0.36; 95% CI 0.17, 0.74), $p=0.005$ and a 48% reduction in the odds of developing retinopathy of prematurity (OR = 0.52, 95% CI 0.28-0.98), $p=0.043$.

Conclusion: A standardized, evidence-based approach to the management of the ELBW infant during the "golden" first hour of life can result in more efficient care delivery and can significantly improve outcomes.

Research supported by:

Mathematical Pressure Modeling of Continuous Movement in Seated Individuals

Alicia R. Billington, M.Eng, MD-PhD Candidate^{1,2}, Peter J. Fabri, MD, PhD^{1,2}, Lisa Gould, MD, PhD¹, William Lee, PhD², David J. Smith Jr., MD¹, Piyush Koria, PhD², ¹Morsani College of Medicine, ²USF College of Engineering. University of South Florida, College of Engineering, Dept. of Chemical & Biomedical Engineering

Keywords: Mathematical model, pressure sores

Objective: Despite years of research on paraplegic patients, much remains unknown regarding how even normal subjects adjust themselves to relieve pressure while seated. First understanding how a normal subject alters their position is pertinent for the development of rigorous strategies for pressure relief in paraplegic patients. We have developed a quantitative, analytic method that evaluates the dynamic change in forces generated by sitting over time.

Methods: This method models each hemi-buttock as a complex of three pressures: a flat platform pressure, an eccentric hemi-ellipsoid, and a central spire. The hemi-ellipsoid principal directions and magnitudes are resolved from continuous pressure acquisition (36x36 cm pressure mat) using quadratic optimization by gradient descent using Microsoft Excel with the Solver and matrix.xla Add-ins, automated with VBA code.

Results: Data were recorded at 1 Hz for 20 minutes on an Xsensor pad. Characteristic frames were selected from the 1200 recorded time points of data for demonstration. Eigenvalues and eigenvectors were derived from the model transformation matrix and are demonstrated as a vectorgram. Platform and peak pressures and the location of the peak pressure were additionally determined.

Conclusion: We show with this method it is possible to quantify the dynamic effect of changes in movement while seated. Future work will include automating the process to allow evaluation of all 1200 timepoints per individual. Robust clinical protocols for paraplegic and insensate subjects could be created from the basis of understanding normal pressure adaptation.

Is the R.E.N.A.L Nephrometry Scoring System Predictive of the Functional Efficacy of Nephron-Sparing Surgery in the Solitary Kidney?

David D. Buethe MD¹, Sammy Moussly¹, Hui-Yi Lin PhD², Binglin Yue², Alejandro R. Rodriguez MD¹, Philippe E. Spiess MD¹ and Wade J. Sexton, MD¹ Departments of Genitourinary Oncology and Biostatistics ²H. Lee Moffitt Cancer Center and Research Institute University of South Florida Morsani College of Medicine

Keywords: nephrometry, nephron-sparing surgery, partial nephrectomy, renal cell carcinoma, solitary kidney

Objective: To evaluate the ability of a renal tumor's complexity, as assessed by the R.E.N.A.L. nephrometry scoring system, to predict the functional efficacy of nephron-sparing surgery (NSS).

Methods: We evaluated 42 patients presenting with either an anatomic (32) or functionally solitary (10) kidney who underwent partial nephrectomy (PN). Each renal unit was assigned a R.E.N.A.L. nephrometry score (RNS) utilizing pre-operative imaging. The CKD-EPI equation was utilized to calculate eGFR. The difference between the eGFR at baseline and at post-operative time points served as a measurement of renal function loss attributed to PN.

Results: Forty-two patients underwent PN with mean pre-operative eGFR of 61.5 mL/min/1.73m². The median total nephrometry score (TNS) was 8, ranging from 4 to 10. In the immediate post-operative period, the overall mean eGFR of 48.6 mL/min/1.73m² was significantly less (p=0.006) than the pre-operative value. However by 6 month follow-up, the mean value of the eGFR (54.1 mL/min/1.73m²) had recovered and was no longer significantly less than the pre-operative value (p=0.091). However, we were unable to demonstrate a relationship between the post-operative eGFR reduction and the assigned TNS or any individual component of the R.E.N.A.L. scoring system related to the targeted lesion.

Conclusion: Neither the individual components of the R.E.N.A.L. nephrometry scoring system nor the TNS was predictive of the realized functional loss as assessed by eGFR in patients with a solitary kidney undergoing NSS. However, NSS was proven quite efficacious with respect to preservation of renal function as only a durable 11.6% reduction in eGFR was noted.

Research supported by: No outside funding.

Decreasing Mortality in Young Colorectal Cancer Patients: Are We Doing Better?

M. Larone Campbell, M.D.¹, Jaime E. Sanchez, M.D.¹, Donald M. Davis, M.D.¹, Sowsan H. Rasheid, M.D.¹, Jorge E. Marcet, M.D., FACS¹, M. L. Campbell, M.D.¹, J. E. Sanchez, M.D.¹, S. H. Rasheid, M.D.¹, J. E. Marcet, M.D., FACS¹, D. M. Davis, M.D.² ¹University of South Florida, Morsani College of Medicine, Department of Surgery, Division of Colon and Rectal Surgery, ²University of South Florida, Morsani College of Medicine, Department of Surgery.

Keywords: Colorectal; colon; rectal; cancer; mortality

Objective: Recent studies have shown an increasing incidence of colorectal cancer (CRC) in patients < 50 years despite a decreasing overall trend in the United States. The most dramatic increase was in the 40-44 year age group. The aim of this study was to determine age-stratified mortality trends for CRC in order to compare these to changes in incidence.

Methods: Mortality statistics were obtained from the Cancer Query System of the SEER database. Data were obtained from 1987 to 2006 in age groups from 30 to 85+ years old in 5 year increments for CRC. Mortality and incidence trends were then compared in patients younger and older than age 50.

Results: There is an overall decreasing trend in mortality from CRC in the US over the past 20 years. This trend persists even in patients younger than age 50 despite an increasing incidence of CRC in this age group. In patients aged 40-44, the mortality rate of CRC decreased from 4.3 to 3.9 cases per 100,000 from 1987 to 2006, and from 9.7 to 7.5 cases per 100,000 in patients aged 45-49, decreases of 9.3% and 22.7% respectively. The most significant decrease was in patients ages 85 years and older, with 216.9 cases per 100,000 in 2006, down from 301.5 cases per 100,000 in 1987, a 28% decline.

Conclusion: There appears to be a decreasing trend in mortality among CRC patients younger than age 50 despite increasing incidence. Though the actual decrease in mortality rate in this age group may not appear large, it becomes more notable when the increased incidence is taken into consideration. The reasons for this improved survival may be due to improved treatment modalities and improved response to therapy in young patients with CRC. However further studies are needed to better delineate the causes of this improved survival.

Intralesional and Topical Chemotherapy of Non-Melanoma Skin Cancer: Efficacy and Cost-Analysis Compared to Excisional Treatment

Katelyn Chitwood, BS, George Cohen, MD, Jeremy Etzkorn, MD University of South Florida, Department of Dermatology and Cutaneous Surgery

Keywords: efficacy, topical chemotherapy, non-melanoma skin cancer

Objective: To compare the cost and efficacy of surgical excision with topical and intralesional therapy in the treatment of NMSC.

Methods: An extensive literature search was conducted through the Pubmed database (1970-present) to assess the efficacy of several treatment modalities (Mohs surgery, standard excision, topical chemotherapy with 5-fluorouracil (5FU), topical imiquimod, intra-lesional injection of 5FU, and intra-lesional injection of methotrexate) for NMSC. Cost comparisons for the various treatment modalities are based upon relative value unit numbers derived from the American Medical Association Current Procedural Terminology Code/Relative Value catalog. All numerical values reflect an adjustment for the "Rest of Florida" geographical region to which Tampa, Florida belongs. In order to provide the most conservative estimates for excisional therapy of NMSC, cost analysis does not reflect the cost of wound closure.

Results: The calculated cost of the average Mohs surgery is \$676.48 and the published cure rate is 97-99% for a single primary NMSC. The cost of traditional surgical excision is \$305.15 and the published cure rates range from 80-96%. The cost of topical 5FU is \$40 and published cure rates range from 80-93% for in-situ NMSC lesions, particularly. The cost of intra-lesional treatment of a single NMSC is \$300.40 for 5FU and \$120.16 for methotrexate and the published cure rates are 90-99% and 83%, respectively.

Conclusion: While there is significantly less long-term data demonstrating the efficacy of non-surgical management of NMSC, it remains a viable and relatively cost effective treatment option. It may be useful when surgery is refused by the patient, surgery is contraindicated or poses significant risk, or treatment is palliative.

Research Supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Mediators of Functional Impairment in Adult Obsessive-Compulsive Disorder

Erika A. Crawford, BA, USF; Tanya K. Murphy, MD, USF; Adam B. Lewin, PhD, USF; Anna M. Jones, BS, USF; Elysse B. Arnold, BA, USF; Eric A. Storch, PhD, USF University of South Florida Morsani College of Medicine Pediatrics

Keywords: OCD, mediators, adults, impairment,

Objective: Obsessive-compulsive disorder (OCD) is a chronic and often disabling illness with an estimated prevalence of 1-2%. OCD is associated with social, occupational, and familial impairment. To date, little research has systematically examined factors that predict OCD-related disability. The available research, however, has produced two consistent findings. First, more severe OCD symptoms and greater difficulty resisting and controlling obsessions and compulsions, appear to strongly predict higher levels of functional disability. Second, depressive and anxious symptoms, which often co-occur with OCD, were positively associated with poorer functioning. However, little research has examined the factors that contribute to OCD-related disability over and above symptom severity. The main goal of the present study is to investigate factors that mediate the relationship between illness severity and OCD-related disability. The factors examined include symptoms of depression and anxiety, sensitivity to anxiety, and ability to control symptoms.

Methods: Participants (N=47) were adults aged 18 years or older. A clinician administered two measures of obsessive-compulsive severity and participants completed several questionnaires that assessed depressive and anxiety symptoms, sensitivity to anxiety, ability to control OCD symptoms, and level of impairment.

Results: All measures were significantly correlated with functional impairment. Depressive symptoms mediated the relationship between OCD symptom severity and functional impairment.

Conclusion: These findings indicate that severity of OCD symptoms is not the only predictor of functional impairment; severity of depressive symptoms is a mediator between OCD symptom severity and OCD-related disability.

Research supported by:

Tonsillectomy/Adenoidectomy do not prevent symptom onset in Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus

Caroline De Oleo M.D., Adam B. Lewin Ph.D., Leah Jung B.A., P. Jane Mutch Ph.D., Eric Storch Ph.D., Tanya K. Murphy M.D. University of South Florida, College of Medicine, Department of Pediatrics and Psychiatry

Keywords: PANDAS, tonsillectomy, adenoidectomy, group A streptococcus

Objective: In children presenting with OCD and or tics and with temporally associated GAS pharyngitis, parents and physicians consider surgical options to mitigate the illness course. Several case reports suggest that a tonsillectomy may improve the child's neuropsychiatric symptoms (e.g., OCD/tics) yet this has not been tested in a large sample of clinical youth. Our objective is to determine if tonsillectomy/adenoidectomy impacts the GAS titers and chronicity of neuropsychiatric symptoms associated with PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus).

Methods: We recruited 112 children with tics and/or OCD having a history of infection related symptom flare-ups or history of dramatic onset. 36 had a history of tonsillectomy and/ or adenoidectomy. Assessment was made by intensive expert review and three streptococcal antibodies (ASO, DNase B, and ACHO). Chronicity of OCD and/or tic symptom-onset and surgical status were determined by medical records, and by parent and child report.

Results: 68% of our cohort had at least one of the three measured titers elevated independent of surgical status. Of the surgical group, 97.2% had a diagnosis of OCD and 91.2% had a diagnosis of tics (88.9% with both) vs 92.2% with OCD, and 85.6% with tic (77.8% with both) of the non surgical group. The average ages of OCD and TS onset were 5.92 and 6.04 respectively in the surgical group vs. 6.49 and 6.62 years for the non surgical group.

Conclusion: Streptococcal antibodies were not significantly different among groups and most developed symptoms after the surgery. Tonsillectomy/adenoidectomy does not seem to decrease the likelihood of neuropsychiatric symptoms or titer elevations in the PANDAS population.

Research supported by: The Rothman Endowment.

Gender Related Differences in Glucocorticoid Therapy and Growth Outcomes among Pubertal Children with 21-Hydroxylase Deficiency Congenital Adrenal Hyperplasia

Jessica R. Deslauriers, Anne M. Lenz, Allen W. Root, Frank I. Diamond and Barry B. Bercu Division of Pediatric Endocrinology, Diabetes and Metabolism, Department of Pediatrics, Morsani College of Medicine at the University of South Florida, Tampa, Florida 33612 and All Children's Hospital, St. Petersburg, Florida, University of South Florida, Morsani College of Medicine, Dept of Pediatrics

Keywords: CAH, gender, puberty, hydrocortisone dose, chart review

Objective: The purpose of this study is to determine if glucocorticoid dosage differences exist among pubertal males and females with 21-hydroxylase deficiency congenital adrenal hyperplasia (CAH) at various Tanner stages of puberty.

Methods: This was a retrospective chart review study at an academic Pediatric Endocrinology office in Tampa Bay, Florida. Between January 1981 and May 2011, 867 patients were evaluated for precocious puberty or CAH. Of these charts, twenty females and seventeen males were diagnosed with 21-hydroxylase deficiency simple virilizing CAH and followed through all stages of pubertal development.

Results: Males received a higher hydrocortisone dosage than females throughout all stages of pubertal development. Males received an average dose of 16.4 ± 4.8 mg/m²/day of hydrocortisone whereas females received an average dose of 13.7 ± 4.6 mg/m²/day. No significant difference in glucocorticoid dosage was found at Tanner stage 1 or 2; however, the glucocorticoid dosage in males was significantly higher than in females at Tanner stages 3-5 ($p < 0.05$). Higher doses were associated with a shorter predicted adult height. The majority of adolescents with CAH were on average 9.6 cm shorter than their mid-parental height.

Conclusion: At all Tanner stages of puberty, glucocorticoid dosage differences did exist between males and female with CAH. It is important to determine an optimal glucocorticoid dose for adolescents, as increasing dosages were negatively correlated with adult stature. A prospective study, carefully measuring compliance and ensuring appointment follow-up, would be beneficial to determine the ideal hydrocortisone dose for adolescents with CAH.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Morphometric Brain Volume Measurements in 72 Medical Cadaveric Scans with History of Cognitive Impairment and One or More Components of Metabolic Syndrome

Natasa Dragicevic MD PhD, USF Department of Radiology, Joe Grajo MD Department of Radiology, Summer Decker PhD Department of Radiology, Doug Rodriguez, MD Department of Radiology, Todd Hazelton MD Department of Radiology, University of South Florida, Morsani College of Medicine, Dept. of Radiology

Keywords: brain atrophy, morphometrics, dementia, metabolic syndrome

Objective: We have developed a fast and accurate method for quantification of subtle, subregional brain volume loss in patients who died with some form of predementia or dementia, having one or more components of metabolic syndrome. We performed volumetric measurements of frontal, parietal, temporal and occipital lobes, hippocampus, corpus callosum, septum pellucidum, ventricular dimensions and the brain stem including the cerebellum and medulla. We hypothesized that patients who had several comorbidities (diabetes, hypertension, obesity, hyperlipidemia) also suffered more prominent brain volume loss in thought and memory forming critical areas, with coexisting expansion of the ventricles due to atrophy of the gray matter

Methods: All 72 cadaveric CT and MRI scans were de-identified and the researchers making the measurements were blinded in regards to cadaver age, gender and medical background information. A morphometric measurement toolkit was written by the research team into the visualization and analysis software package, Mimics 14.1 (Materialise).

Results: Cadavers with a history of one or several risk factors had shrinkage of multiple brain regions with more prominent atrophy in those patients who had a history of several comorbid conditions such as hypercholesterolemia, hypertension, and obesity.

Conclusion: CT and MR imaging of the brain can be used as a noninvasive method to obtain accurate and reproducible quantitative measures of alterations in brain structure, including cerebral atrophy and ventricular enlargement, which can be predictive of dementia and stroke. Future goals include subregional brain volumetric measurements and comparison of atrophy in actual patients before and after treatment of comorbid conditions.

Research supported by: USF Department of Radiology

Analysis of the AJCC/ENETS Staging Classification for Midgut Neuroendocrine Tumors

Max Feldman², Jill Weber MPH¹, Larry Kvoles MD¹, Jonathan Strosberg MD¹ ¹Moffitt Cancer Center, ²University of South Florida, Morsani College of Medicine, Dept. of Oncologic Sciences

Keywords: Neuroendocrine tumor, carcinoid tumor, midgut, jejunum, ileum, staging, TNM, ENETS, AJCC

Objective: The American Joint Committee on Cancer (AJCC) and ENETS have independently introduced a novel TNM staging classification for jejunal-ileal NETs. Our objective is to assess the prognostic relevance of the AJCC/ENETS staging classification for midgut (jejunal-ileal) NETs.

Methods: Patients with jejunal-ileal NETs treated at the Moffitt Cancer Center between 2000 and 2010 were assigned stages (I-IV) based on the AJCC/ENETS TNM staging classification. Overall survival from time of initial diagnosis was measured and statistical significance was calculated using the log-rank test.

Results: Six-hundred and fifty-six patients with histologically-proven jejunal-ileal NETs were identified. The AJCC/ENETS classification in aggregate was highly prognostic for overall survival ($p < 0.00001$). 5-year overall survival rates for stages I-IV were 100%, 100%, 90% and 72% respectively. The survival difference between stages III and IV was significant ($p < 0.00001$); The difference between stages I/II versus III was borderline significant ($p = 0.1$)

Conclusion: The AJCC/ENETS staging classification for midgut NETs is statistically prognostic for overall survival. However, stages I and II are associated with a similarly favorable outcome and are unlikely to be prognostically distinct for overall survival.

Withdrawn

Designing and Developing the Database of Randomized Trials in Myeloma (DRAM)

Helen Georgiev College of Medicine Division of Evidence-Based Medicine and Health Outcomes Research, Ambuj Kumar College of Medicine Division of Evidence-Based Medicine and Health Outcomes Research, Donald Berndt College of Business, Swetha Chemudu College of Business, Benjamin Djulbegovic College of Medicine Division of Evidence-Based Medicine and Health Outcomes Research, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: myeloma, meta-analysis, RCTs, database

Objective: DRAM is a new online database whose purpose is to facilitate data storage, retrieval, and analysis of multiple myeloma (MM) health outcomes. This will allow users to access critically appraised data and to conduct meta-analysis.

Methods: A literature search of PubMed, Cochrane Central Register of Controlled Trials, and abstracts from the American Society of Hematology and the American Society of Clinical Oncology was conducted to identify all phase III randomized controlled trials (RCTs) and systematic reviews (SRs) of RCTs of MM. Data extraction forms were designed to limit the use of free text and with a logical flow to minimize errors. A web application was developed which can be used to enter, search, edit, store and analyze data.

Results: All RCTs and SRs of RCTs of MM have been found. Data extraction and entry of RCTs as of 12/2011 are complete and up to date. There are 287 records. Fifteen SRs of RCTs have been found and extracted. An online interface for RCTs has been completed where the user is able to enter, edit and view data. Trials can be searched by any entered variable. Users can create bar graphs of data such as patient characteristics, treatments and outcomes. Reports are able to be produced in which five pre-defined variables are displayed and can be exported into many document formats. Meta-analysis portion of RCT database and creation of the SR database are ongoing.

Conclusion: DRAM will be an excellent resource for clinicians, policy-makers and industry. These users will be able to evaluate the quality of existing evidence, assess the quality of researchers' innovations, guide resource allocation and target development efforts. While the focus of DRAM is MM, this new concept has implications for all areas of health.

Research supported by: Millennium

A Randomized Prospective Open-Label Comparison of Two Vitamin D3 Repletion Strategies in Vitamin D Deficient Patients

Julio Gonzalez, Vanessa C. Osting, John D. Carter, Joanne Valeriano-Marcet, University of South Florida Morsani College of Medicine, Dept. of Internal Medicine, Div. of Rheumatology

Keywords: Vitamin D deficiency oral replacement

Objective: The aim of this study was to compare two different Vitamin D oral replacement strategies in patients with low Vitamin D.

Methods: 40-day randomized prospective open-label study of two vitamin D repletion protocols aiming to determine if large intermittent dosing is more efficient at increasing 25-OH Vitamin D levels than an equivalent smaller daily dose. 25-OH Vitamin D level of less than or equal to 32 mg/dL at entry. Participants were randomized to receive 5000 IU of Vit.D3 orally daily for 40 days or 50,000 IU orally every 10 days for 40 days. The primary endpoint was a direct comparison of the change in 25-OH Vitamin D level at day 40 (+/- 3 days).

Results: 56 subjects were randomized and 48 (completers) had a 25-OH Vitamin D level at day 40. Completers randomized to the Vitamin D3 5000 IU daily arm (n=25; all females; mean age of 59.6 years) had a mean baseline 25-OH Vitamin D level of 20.6mg/dL [5.9mg/dL standard deviation] (12 with Vitamin D Deficiency and 13 in Insufficiency). Completers randomized to the Vitamin D3 50,000 IU every 10 days arm (n=23; 21 females; mean age 57.6 years) had a mean baseline 25-OH Vitamin D level of 22.3mg/dL [standard deviation of 6.8mg/dL] (7 with Vitamin D Deficiency and 16 with Insufficiency). The mean change in the 25-OH Vitamin D level at Day 40 in Group A was 11.1mg/dL [10.6mg/dL standard deviation] compared to a mean change of 14.6mg/dL [7.1mg/dL standard deviation] in Group B [p-value = 0.25].

Conclusion: It does not appear that a replacement regimen of Vitamin D3 50,000 IU every 10 days is more efficient at increasing 25-OH Vitamin D serum levels than an equivalent daily dose (5000 IU daily). However, a larger sample size might have yielded significant results.

Research supported by: USF Rheumatology Division

Meta-analysis of Clear Cell Renal Cell Carcinoma Gene Expression Defines a Variant Subgroup and Identifies Gender Influences on Tumor Biology

SM Haake, AR Brannon, KE Hacker, RS Pruthi, EM Wallen, ME Nielsen, WK Rathmell, Moffitt Cancer Center & Research Institute, Tampa, FL, U of North Carolina at Chapel Hill, Chapel Hill, NC, University of South Florida, Morsani College of Medicine, Dept. of Oncologic Sciences

Keywords: clear cell renal cell carcinoma, gene expression, gender, VHL, hypoxia

Objective: Determine whether additional subtypes of ccRCC exist and whether these subtypes are related to von Hippel-Lindau (VHL) inactivation, hypoxia-inducible factor (HIF) 1 and 2 expression, tumor histology, or gender.

Methods: Six large, publicly available ccRCC gene expression databases were identified that cumulatively provided data for 480 tumors. Meta-analysis via meta-array compilation. Unsupervised consensus clustering was performed on the meta-arrays. Tumors were examined for the relationship of multiple gene-defined consensus subtypes and expression signatures to VHL mutation and HIF status, tumor histology, and gender.

Results: Two dominant subsets of ccRCC were observed. A third, minor third subset was revealed that correlated strongly with a wild type (WT) VHL expression profile and indications of variant histologies. When variant histologies were removed, ccA tumors naturally divided by gender. This technique is limited by the potential for persistent batch effect, tumor sampling bias, and restrictions of annotated information.

Conclusion: The ccA and ccB subsets of ccRCC are robust in meta-analysis among histologically conventional ccRCC tumors. A third group of tumors was identified that may represent a new variant of ccRCC. Within definitively clear cell tumors, gender may delineate tumors in such a way that it could have implications regarding current treatments and future drug development.

Research supported by: Drs. Rathmell and Brannon received funding from the American Association for Cancer Research Landon INNOVATOR Award; Dr. Hacker received funding from the National Institutes of Health Medical Scientist Training Program, T32 GM008719; and Dr. Rathmell received funding from NCI, R01 CA121781.

Dengue Fever in Tegucigalpa, Honduras: Use of the Explanatory Model in a Sample of Urban Neighborhoods to Contextualize and Define Dengue Fever Among Community Participants.

José E. Hasemann Lara, MA, MPH^{1,2}; Heidi Castañeda, PhD, Assistant Professor¹, Boo Kwa, PhD, Professor²,

¹Department of Anthropology, ²College of Public Health. University of South Florida, College of Arts and Sciences, Dept. of Anthropology

Keywords: Folk Illness, Idiom of Distress, Arthropod-Borne Disease, Prevention and Surveillance Campaigns, Slums and Squatter Settlements

Objective: This project elucidated the explanatory model of dengue fever held by members of urban communities in Tegucigalpa, Honduras.

Methods: The study was conducted over a four-month period from May-August of 2011. The first stage of the project consisted of volunteer participation with dengue fever surveillance brigades in the three communities with the highest incidence of dengue fever during the beginning of 2011. This initial stage employed participant observation as its research method. The second stage was conducted in a different community within Tegucigalpa. The primary research methods employed during the second stage of the project were participant observation, semi-structured questionnaires (n=18), and ethnographic surveys (n=32). The semi-structured questionnaires were conducted in three different low-socioeconomic status neighborhoods within the research community, and the ethnographic surveys were administered in a higher-socioeconomic status neighborhood within the same community.

Results: The results indicated that participants had an explanatory model of dengue fever very similar to the biomedical explanatory model. Results also indicated that participants had a local-particular, etiological characterization of dengue fever that did not coincide with the biomedical explanatory model of dengue fever. Similarly, the participants in this study recognized poor communal cohesion and inadequate/inefficient governmental support or intervention as a prime promoter of dengue fever.

Conclusion: There were no differences in the explanatory model of dengue fever across socioeconomic status, and the participants were generally well informed. The results differ from previous studies suggesting improvement in prevention programs, but profiles shortcomings.

Preliminary Results of Family Based Cognitive-Behavioral Treatment for Preschoolers with Obsessive Compulsive Disorder

Anna Jones B.S., Jessie Menzel M.A., Eric Storch Ph.D., Adam Lewin Ph.D. University of South Florida Morsani College of Medicine Pediatrics

Keywords: Anxiety

Objective: Cognitive-Behavioral Therapy (CBT) with exposure and response prevention (E/RP) is efficacious for OCD and other anxiety disorders among otherwise typically developing youth. To date, the efficacy of CBT in children has been demonstrated in a number of open trials and controlled trials (Barrett et al., 2004; de Haan et al., 1998; Piacentini et al., 2011; POTS, 2004; Freeman et al., 2008). Unfortunately, there is a gap in the literature regarding the effectiveness of this approach for younger children. This study aims to evaluate the treatment efficacy of a modulated cognitive-behavioral therapy (CBT) approach for children ages 3 to 8 years of age inclusive with a principal diagnosis of OCD.

Methods: This investigation is a controlled trial of CBT in children ages 3-8 years with OCD. For inclusion, youth must meet diagnostic criteria for OCD based on a structured interview (the ADIS-IV-P) and a minimum score of 8 on the CYBOCS Compulsion Scale. Randomization occurs immediately following the pre-assessment and subjects will either receive CBT immediately or be assigned to the Treatment as Usual (TAU) arm in a 1:1 ratio. Treatment is a 12 session protocol delivered twice weekly.

Results: Preliminary findings are positive with a greater magnitude of OCD symptom reduction in the CBT group.

Conclusion: Considering the increasing awareness of OCD symptoms in young children our work provides preliminary clinically-relevant support for CBT with E/RP.

Research supported by: New Researcher Grant Awarded to Dr. Lewin by USF Research Council

Rates of Social Impairment of Youth with Tic Disorders as assessed by the Social Responsiveness Scale

Leah Jung B.A., Adam B. Lewin Ph.D., Caroline De Oleo M.D., P. Jane Mutch Ph.D., Eric Storch Ph.D., Tanya K. Murphy M.D. University of South Florida, Morsani College of Medicine, Department of Pediatrics and Psychiatry

Keywords: SRS, autism, tic disorders, Tourette Syndrome

Objective: Tic disorders, particularly Tourette Syndrome (TS), are often associated with comorbid conditions that can greatly impact psychosocial functioning. Studies have shown a higher than chance co-occurrence of tic disorders and Autism Spectrum Disorders (ASDs) in youth. Through data obtained from a CDC funded study evaluating quality of life in youth with tic disorders, we aim to assess the prevalence of symptoms associated with ASD through the use of the Social Responsiveness Scale (SRS). The SRS is a brief rating scale measuring the severity of social impairment indicative of an ASD.

Methods: 93 youth with a tic disorder (82% male, ages 6-17) were administered the Computerized Diagnostic Interview Schedule for Children (C-DISC IV), SRS parent, and Yale Global Tic Severity Scale (YGTSS).

Results: Youth with tic disorders demonstrated significantly decreased social competency on many dimensions of the SRS. Of sampled children, 46% scored within the normal range, 38% in the mild-moderate range and 16% in the severe range. As measured by the YGTSS, the tic severity mean was 22.5 (range 4-50). Subjects who tested in the mild or above range were shown to experience slightly greater tic severity (mean 24.9). 64.7% of females tested within clinically significant range on the SRS, with a mean tic severity of 26.8. Whereas 51% males tested within clinically significant range, with a mean tic severity of 21.58.

Conclusion: We found that a large portion of youth with tic disorders have SRS scores in the clinical range. Further research is needed to determine the contribution of various comorbidities including ASD to impaired social functioning in youth with tic disorders.

Research supported by: Center for Disease Control

Asset Mapping of USF Innovation Using Hub Modeling

Mohamad Kasti¹; Johnmark White^{1,2}; Michael Fountain^{2,3,4}; Eve Spengler⁵ ¹Center for Transformation and Innovation, University of South Florida; ²USF Center for Entrepreneurship, Department of Marketing, College of Business; ³Department of Industrial and Management Systems Engineering, College of Engineering; ⁴Department of Psychiatry and Behavioral Medicine, College of Medicine, University of South Florida; ⁵Alliance for Integrated Spatial Technologies, USF Center for Entrepreneurship, University of South Florida

Keywords: Innovation, Asset Map, Innovation Lifecycle, Innovation Hub, Technology Transfer

Objective: This research investigated the innovation assets at the University of South Florida. The goal was to map the innovation capacity of the university.

Methods: Thirteen organizations were selected for the study. An Innovation Lifecycle was created that consisted of five phases: Discovery; Intellectual Property Protection; Translation; Commercialization; and Diffusion. The organizations were mapped onto the Innovation Lifecycle based on their functional capabilities related to innovation. In addition, the primary target customers for each organization were analyzed to determine the support for each customer group.

Results: The coverage of the phases of the Lifecycle identified strengths in the university's ability to support the Discovery and Commercialization Phases, with focused coverage for the Intellectual Property Protection Phase by the Division of Patents and Licensing. Weaker coverage was found in the Translation and Diffusion Phases of the lifecycle. The customer groups with the strongest support were faculty, external businesses and other academic institutions. The customer groups slightly lacking in support were students and outside investors.

Conclusion: The major gap identified in the Translation and Diffusion Phases, along with the slightly lower support for students and investors, are in alignment with the university's main focus of supporting academic research, collaborating with other educational institutions, protecting and licensing university inventions, and educating students. These gaps pose an opportunity for developing partnerships with external organizations. This would allow the university to focus on its core strengths while leveraging the skill of outside partners.

Research supported by: USF Office of Research

Computer Decision Support program for Pain Management, Quality Improvement and Monitoring

Jasmin Lacevic BS, Ambuj Kumar MD MPH, Athanasios Tsalatsanis PhD, Benjamin Djulbegovic MD PhD -
Corresponding author, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: Electronic health record, Pain management, Pain measurement, Evidence base, Systematic review

Objective: At any time, about 76 million people suffer from pain in the US. Pain is inadequately treated in more than 50% of patients. This results in productivity loss, which in 2010 was estimated to exceed \$297 billion. Real world data on quality of pain management is limited by the lack of a centralized system for collection, analysis and reporting. Such a system would also aid in performing outcomes research on optimal strategies for pain management. Here we report on electronic pain management system (EPMS) for pain assessment, management, outcomes assessment and quality improvement.

Methods: The EPMS integrates the latest evidence on pain management. It also collects data on patient demographics, disease and pain characteristics, treatment and timeline of pain management. It is developed using ColdFusion and JavaScript.

Results: The EPMS has an interactive interface, and can be completed by physicians or patients. It allows a comprehensive pain assessment, computer-assisted pain management and electronic prescribing. It also allows physicians to visualize a patient's progress in real time, which can facilitate shared decision making between physicians and their patients. The graphical tool also enables "benchmarking" individual patient's pain scores against those of a cohort of patients with similar characteristics (Fig). This option is critical for quality monitoring and outcome research. Data is secured, and multiple users can access the data at same time.

Conclusion: EPMS promotes evidence based pain management and facilitates real time tracking which is key to patient centered care. EPMS will provide long term outcomes data related to effectiveness of currently available treatments for pain management.

Research supported by: DoD

Kidney Transplantation: A Regulated, Market-Based Model to Eliminate Shortages of Organs

Margaret Elisa McQueen, BS¹, Binna M Chokshi, BS¹, Leon Anijar, BS¹, Jehan Shah, BS¹, Eric Quintero, BS¹, Chris Thomas, PhD¹, William G. Marshall, Jr., MD, MBA^{2,1} University of South Florida Morsani College of Medicine Psychiatry and Neurosciences, ²University of South Florida, College of Business & Administration

Keywords: Organ Transplant, kidney, ethics, economics

Objective: Technologic advances in surgery and immunosuppressive pharmaceuticals have expanded dramatically over the past three decades, resulting in kidney transplantation being the preferred treatment for end stage renal disease (ESRD). Transplantation confers significantly longer survival, as well as much greater quality of life, compared to the alternative, dialysis. Despite a variety of attempts to narrow the gap between organ supply and demand, there continues to be an ever increasing shortage. In an era of limited financial resources, without a dramatic change to the structure of organ procurement in the United States, the wait-list and mortality rate due to ESRD will only continue to grow. Therefore, we propose a re-evaluation of the current model and initiation of discussions for "real" solutions.

Conclusion: Of the topics to be thoroughly reviewed and evaluated, the most fundamental is if a regulated, market-based system can be economically, clinically (for recipients and donors), legally, and ethically supported in the current socio-political milieu; and if so, how would this system be organized and managed? The critical issues and success factors will be addressed from an interdisciplinary standpoint in a succinct, focused manner identifying mechanisms for the implementation of effective strategies to provide optimal transplant care for more ESRD patients.

Research supported by: Scholarly Concentrations Program at USF Health Morsani College of Medicine, and USF College of Business

True Methodological Quality of Trials Are Not Reflected in Their Reporting

Rahul Mhaskar, PhD, MPH,¹ Benjamin Djulbegovic, MD, PhD^{1,2}, Anja Magazini², Heloisa P. Soares², Ambuj Kumar, MD, MPH^{1,2} ¹University of South Florida Morsani College of Medicine, Center for Evidence-Based Medicine and Health Outcomes Research ²Moffitt Cancer Center, Tampa, Florida University of South Florida Morsani College of Medicine Internal Medicine

Keywords: Methodological quality, Protocol, Systematic review, Bias, Randomized controlled trial

Objective: To compare the reported methodological quality of a randomized controlled trial (RCT) as reflected in publications with actual methodological quality as depicted in the protocols, and assess association of RCT sample size with published versus actual methodological quality.

Methods: All consecutive published phase III RCTs conducted by 8 National Cancer Institute sponsored Cooperative Groups (NCICOG) until year 2006 were eligible for inclusion. Data on methodological quality domains relevant to minimizing bias and random error were extracted from protocols and publications for each study.

Results: A total of 429 RCTs met the inclusion criteria. Overall reporting of elements of methodological quality domains relevant to minimizing bias and random error was poor and did not reflect the actual high methodological quality of RCTs. Similarly, the results showed a positive correlation between RCT sample size and reported methodological quality domains of adequacy of blinding procedures, ITT analysis and the choice of the comparator (p value < 0.001). However, this correlation disappeared when actual methodological quality was considered.

Conclusion: This largest study to-date comparing published versus actual methodological quality of RCTs shows that poor quality of reporting by NCICOGs does not reflect the actual high methodological quality. We found no association between RCT sample size and its actual methodological quality. The positive correlation between methodological quality of reporting and RCT sample size is misleading. Our findings underline the need for adherence to the CONSORT statement and highlight the importance of publication of RCT protocols in public domain.

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Distractions and Diversions: Preliminary Results from a Study Examining the Academic Impact of Pediatric Obsessive-Compulsive Disorder

Joshua Nadeau, M.A.², Anna M. Jones, B.S.¹, Elysse Arnold, B.A.¹, Jennifer Parks, B.S.¹, Erika Crawford, B.S.¹, Cary Jordan, Ph.D.¹, Eric A. Storch, Ph.D.¹, Kathy Bradley-Klug, Ph.D.², Shannon M. Suldo, Ph.D.², Robert F. Dedrick, Ph.D.² ¹Department of Pediatrics, University of South Florida College of Medicine, St. Petersburg, FL, ²Department of Psychological & Social Foundations, University of South Florida College of Education, Tampa, FL. University of South Florida, College of Education, Dept. of Psychological & Social Foundations

Keywords: Subjective Well Being, Obsessive-Compulsive Disorder, Academic Impact

Objective: This presentation offers preliminary results from a study exploring the relationship between pediatric obsessive-compulsive disorder (OCD) and student subjective well-being (SWB). Investigation has the potential to explain why the disorder impacts some youth more strongly than others, which could inform systemic efforts at prevention and early intervention for pediatric OCD.

Methods: A non-experimental correlational addressed the research questions for this study via collection and analysis of rating scale and clinical interview data. Participants (preliminary n=34) were recruited from families seeking treatment from the Rothman Pediatric Neuropsychiatry Clinic at the University of South Florida. In addition to basic descriptive analyses, Pearson Product-Moment Correlation Coefficients (PPMCC) were calculated between measures of symptom severity and participant SWB ratings.

Results: Participants' ages ranged from 7-16 years (M=11.6). The primary measure of OCD symptom severity (CY-BOCS Total Score) ranged from 5-29 (M=24.2) on a 30-point scale. SWB ratings ranged from -32 to 51 (M=20.84) on a 120-point scale. Correlation coefficients between SWB and symptom severity (CY-BOCS Obsessive and Compulsive sub-scores, and Total score) ranged from low (r=-.02, SWB:Compulsive) to moderate (r=-.13, SWB:Total; r=-.20, SWB:Obsessive).

Conclusion: Results are consistent with previous findings of increased OCD prevalence among males in school-aged populations. A moderate relationship was found between obsession severity and SWB. This finding supports the hypothesis that as the severity endorsed by participants with respect to obsessive thoughts increased, corresponding SWB was more likely to be lower than that reported by participants with less severe obsessions.

Differentiating Fat Necrosis from Recurrent Malignancy in Fat Grafted Breasts After Breast Reconstruction: An Imaging Classification System

Rajiv P. Parikh, BA⁽¹⁾; Erin L. Doren, MD⁽¹⁾; Blaise Mooney, MD^(2,3); Weihong V. Sun, MD, MS⁽³⁾; Christine Laronga, MD, F.A.C.S.⁽³⁾; Paul D. Smith, MD^(1,3) ⁽¹⁾Division of Plastic Surgery, Department of Surgery, University of South Florida, Tampa, Florida ⁽²⁾Department of Radiology, H. Lee Moffitt Cancer Center, Tampa, Florida ⁽³⁾Comprehensive Breast Program, H. Lee Moffitt Cancer Center, Tampa, Florida University of South Florida Morsani College of Medicine Surgery

Keywords: Breast Reconstruction; Cancer; Imaging; Fat Grafting; Palpable Nodule

Objective: In breast reconstruction patients undergoing autologous fat grafting (AFG), concerns persist about differentiating palpable masses representing fat necrosis from palpable masses representing recurrent cancer. Our objective is to develop standardized imaging classifications to distinguish benign from malignant lesions after AFG.

Methods: An IRB approved database of 286 breast reconstruction patients undergoing AFG from 2006 to 2011 was retrospectively reviewed to identify patients with imaging of clinically palpable masses. All images were independently reviewed by a radiologist blinded to prior results. Lesions were characterized using ACR BI-RADS ultrasound (US) lexicon and classifications were developed: (A) Solid mass, hypoechoic, (B) Solid mass, isoechoic, (C) Solid mass, hyperechoic, (D) Solid mass, complex echogenicity, (E) Anechoic mass with posterior acoustic enhancement, (F) Cystic mass with internal echoes, and (G) Negative. Evolutions in lesions on follow-up US were recorded. Images were correlated with histopathologic results.

Results: 66 lesions were visualized in 37 patients with palpable masses. 22/66 (33%) were BIRADS category 4 lesions; all were biopsied. Histopathologic results revealed: 85.7% (6/7) with classification D and 100% with classifications A, B, C, E, F, and G were fat necrosis. The one malignant lesion (classification D) exhibited vascularity and angular margins on US, and was not in the location of AFG. NPV of avascularity and circumscribed margins for malignancy was 100%. Follow-up US of 29 lesions at median 6.5 months revealed no masses increased in size or developed vascularity.

Conclusion: US analysis with a standardized classification system is reliable at differentiating benign from malignant lesions after AFG in breast reconstruction.

Research supported by:

Modification of the A-Constant to Optimize Refractive Outcome for Patients Undergoing Cataract Surgery

H R Patel Morsani College of Medicine, C K Patel Oxford Eye Hospital University of South Florida Morsani College of Medicine Ophthalmology

Keywords: ophthalmology, eye, surgery, cataract, lens

Objective: To determine an effective way to measure and modify the surgeon specific A-constant of the LW575 IOL cataract implant with the objective to better refractive outcomes for patients undergoing cataract surgery.

Methods: A retrospective analysis of forty cataract surgeries was performed using biometry data obtained by Carl Zeiss IOLMaster V 7.1. Preoperative and postoperative lens position, manifest refraction, and visual analysis. The parameters included target refractive error and a target refraction, white-to-white distance, best corrected visual acuity, uncorrected visual acuity, K1/K2, and axial length. The Holladay IOL Consultant Software & Surgical Outcomes Assessment was used to analyze this data. In addition, the T2 formula calculator version 1.1 was used and directly substituted for SRK/T.

Results: Using the Holladay IOL Consultant analysis, the surgeon specific A-constant for this lens was determined to be 118.8.

Conclusion: Using an optimized A-constant to ensure a precise lens choice helps to provide the best possible care to patients undergoing cataract surgery. For a limited population, lens options may not as broad and lesser known lenses such as the LW575 IOL may be used. It is not uncommon for these lenses to not have an established optimized A-constant. Therefore, this A-constant may prove to be beneficial to other surgeons currently utilizing this lens.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine.

Changing Face of Acoustic Neuroma Treatment and Symptomatology: 25 Year Trends from Analysis of Patient Surveys from the Acoustic Neuroma Association

Jaymin Patel, Vasani, R, Sweeney, JM, Youssef, A. Samy, Van Loveren, H, Agazzi, S University of South Florida Morsani College of Medicine, Dept. of Neurosurgery and Brain Repair

Keywords: Patient-perspective Acoustic Neuroma Review

Objective: To utilize the 1983-1998 and 2008 Acoustic Neuroma Association (ANA) patient surveys to report trends and evolution in Acoustic Neuroma (AN) presentation, treatment, and treatment related outcomes on a national level.

Methods: The results of the ANA surveys were reviewed to determine respondent's pre- and postoperative symptoms and treatment. The responses were analyzed to detect trends between presenting symptoms, tumor size, treatment modality, and treatment outcomes including persisting symptoms. Results of the 2008 survey were compared to the 1998 survey to establish 25 year trends in patient presentation and care. SPSS software was used to conduct statistical analysis.

Results: Patients with AN most commonly presented with hearing loss (2008-88%; 1998-88%), tinnitus (2008-73%; 1998-64%) and balance disturbance (2008-59%; 1998-64%). In the last decade, tumor size at diagnosis decreased significantly (1998: 23% < 1.5cm; 2008: 38% < 1.5cm). From 1998 to 2008, the use of microsurgery (85%), radiosurgery/radiotherapy (5%), and observation (4%) showed a decrease in microsurgery (60%) and increase in radiosurgery/radiotherapy (20%) and observation methods (20%).

Conclusion: While acoustic tumor size at diagnosis has decreased in the past 10 years, patient symptomatology has remained largely unchanged. This national level, patient driven review also confirms that management of acoustic tumors has seen significant decline in microsurgical treatment while radiation therapy/radiosurgery and observation have gained popularity. Persisting patient morbidities may merit a reevaluation of the shift in treatment strategy. This review provides a glimpse into the changing face of acoustic tumor management from a patient's perspective over a 25 year period.

Evaluation of a Universal-Sample Transport Optimized Platform (U-STOP) for the Storage and Identification of Dengue Virus Infection in Clinical Samples

Vishal Patel B.S.¹, Dr. Alberto van Olphen D.V.M. M.S. Ph.D.², Dr. Juan Miguel Pascale M.D. Ph.D.³, Dr. M. Theresa Trindade Ph.D.², Health Yamilka Diaz B.S.³ ¹University of South Florida Morsani College of Medicine, ²University of South Florida, College of Public Health, Department of Global Health, ³Gorgas Institute of Health, Dept of Virology and Genomics

Keywords: Dengue, U-STOP, ELISA, serum, transport

Objective: The current method of infectious disease diagnosis in remote areas of the world involves collecting and transporting temperature-sensitive, potentially biohazardous patient serum samples to a centralized facility. This method is unavailable in most parts of the world. The aim of this study is to develop and field evaluate a new efficient, yet inexpensive, Universal-Sample Transportation Optimized Platform (U-STOP), which permits the transport of potentially infectious agents from remote areas without temperature regulation or biohazardous containment, strengthening disease surveillance programs worldwide.

Methods: The device developed involves chemically treated filter paper capable of inactivating the viral particles in serum while still effectively preserving the molecular and immunological identification markers. Serum samples collected from Dengue virus infected individuals were incubated on U-STOP cards, tested using ELISA and compared to traditional sample collection methods.

Results: This study shows that the developed U-STOP is able to inactivate the pathogenic components of the virus as demonstrated in cell cultures. The presence of viral particles is demonstrated by virus specific serum immunoglobulin IgM, IgG in addition to the intracellular non-structural protein, NS1. Identification through RT-PCR has not yet produced viable results due to the protocol's inability to detect the decreased viral loads.

Conclusion: The developed U-STOP provides an improved method of patient sample transport for remote area disease surveillance by allowing collection and analysis of samples without the need to maintain a cold-chain or for transporting potentially hazardous viral particles while also preserving the samples for extended periods.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

The Causes of ALTEs (Apparent Life-Threatening Events) in Infants Evaluated at a Community Hospital

Jonathan G. Pavlinec MSII, Dr. James Orłowski M.D., Florida Hospital Tampa, University of South Florida, Morsani College of Medicine, Dept. of Pediatrics

Keywords: Retrospective Chart Review ALTE GERD

Objective: An ALTE is defined as an episode that is frightening to the observer and is characterized by some combination of apnea, color change, change in muscle tone, and choking or gagging. Current medical literature suggests approximately 30-40% of ALTEs are due to gastro-esophageal reflux, while up to 50% of cases remain unexplained. As the vast majority of research on the causes of ALTEs comes from tertiary care centers, the results may be distorted by referral patterns for varying etiologies. Our study examines the diagnoses and risk factors associated with ALTEs at a community hospital.

Methods: All known cases of ALTEs were identified, from January 2005 to May 2011. These were split into in-patient, ER, and SIDS records. Statistical analysis was performed, focusing on discharge diagnoses and potential risk factors. Based on physician observation, our hypothesis was that closer to 80-90% of ALTEs at a community hospital would be associated with gastro-esophageal reflux.

Results: A total of 333 charts were evaluated for potential ALTEs during the study period, with 154 cases included. Overall, gastro-esophageal reflux was seen in 127/154 ALTE cases (82.5%). Of the 70 inpatient cases, 68 (97.1%) were associated with some level of reflux. Potential risk factors were evaluated in the in-patient group and included smoke exposure (44.3%), pet exposure (30%), cardiac defects (20%), prematurity (18.6%), and URIs (15.71%).

Conclusion: Gastroesophageal reflux is the principle etiology of ALTEs in pediatric patients presenting at the community hospital level. Consequently, children with a history of GERD may be at increased risk for an ALTE. In addition, smoking, pet exposure, cardiac defects, prematurity, and URIs may exacerbate or increase the likelihood of an ALTE.

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Obesity and the Incidence of Skin Cancer in US Caucasians

Salma Pothiwala^{1,2}, Abrar A. Qureshi^{2,3}, Yunhui Li³, Jiali Han^{2,3,4}, ¹Department of Dermatology & Cutaneous Surgery, University of South Florida College of Medicine, Tampa, FL, USA; ²Clinical Research Program, Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; ³Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; ⁴Department of Epidemiology, Harvard School of Public Health, Boston, University of South Florida Morsani College of Medicine Dermatology

Keywords: Skin cancer; melanoma; squamous cell carcinoma; basal cell carcinoma; obesity, BMI, prospective cohort

Objective: The objective of this study was to examine the association between obesity and the risk of both melanoma and non-melanoma skin cancers.

Methods: Using pooled data the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS), we prospectively examined the incidence of melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) among participants who were grouped according to their body mass index (BMI). BMI values were calculated for participants based on height and weight measurements reported at the start of the cohort study and subsequently updated biennially. Participants were followed up on their diagnosis of incident skin cancer from 1980 to 2006. Cox proportional hazards models, adjusting for age, skin cancer risk factors, sun exposure at different ages, state of residence, and physical activity, were used to estimate the relative risk and 95% confidence intervals (CI) for each type of skin cancer.

Results: Participants with a BMI in the obese range had a 32% lower risk of developing SCC and those with a BMI in the morbidly obese range greater had a 37% lower risk of developing SCC. The decrease in SCC risk was limited to women. Those with a BMI in the obese range had a 19% lower risk of developing BCC, and those with a BMI in the morbidly obese range or greater had a 29% lower risk of developing BCC. The risk of developing melanoma did not statistically differ by BMI grouping. The results were similar using BMI measurements obtained 10 years prior to the diagnosis of skin cancer.

Conclusion: These results suggest that there is no association between obesity and melanoma risk. Being obese is associated with a decreased risk of both SCC and BCC.

Research supported by: Brigham and Women's Hospital

Are African American Men Represented in Prostate Cancer Randomized Controlled Trials? A Systematic Review.

Sanja Galeb, Moffitt Cancer Center, Tea Reljic, University of South Florida, Benjamin Djulbegovic, Moffitt Cancer Center, University of South Florida, Clement Gwede, Moffitt Cancer Center, Nagi B. Kumar, Moffitt Cancer Center, Ambuj Kumar, Moffitt Cancer Center, University of South Florida, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: External validity, Health disparities, Systematic review

Objective: African American (AA) men bear a disproportionate burden of incidence and mortality from prostate cancer compared to other racial groups. The clinical applicability of randomized controlled trials (RCTs) depends on whether the sample of patients represents the disease population. Underrepresentation of AAs in RCTs could impact the external validity of their findings.

Methods: We searched Medline and Cochrane databases to identify all prostate cancer RCTs for the years 2005-2009. Phase III trials conducted in North America which evaluated prostate cancer prevention, screening, or treatment were included. Dual extraction was undertaken on patient characteristics, interventions, controls, outcomes and study quality. Meta-analysis using random effects model was performed to assess overall outcomes according to AA participation.

Results: Our search identified 1206 citations of which 20 (29 comparisons) met inclusion criteria. Overall quality of included studies was high. Only 55% (11/20) of studies reported data on racial composition. Among those, 1 reported 30%, 4 reported 10-20%, and 6 reported <10% AA enrollment. Nine studies reported survival data. Pooling data by AA participation showed no difference in survival. The pooled hazard ratio (95% CI) in trials with >10% AA participation was 0.94 (0.87, 1.02), 0.97 (0.92, 1.03) in trials with <10% AA participation and 0.92 (0.80, 1.07) in trials with no reporting of race data.

Conclusion: AA men are underrepresented in prostate cancer RCTs in contrast to their disproportionate disease burden. Despite the conventional belief that AA men have poorer outcomes compared with other racial groups, our results show no difference in outcomes in prostate cancer RCTs.

Research supported by: Center for Equal Health

Sexual Health in Individuals with Intellectual Disabilities and Autism

Jacquelyn Selbst, MS¹, Nila Benito², Laurie Woodard, MD^{1,2} ¹University of South Florida, Morsani College of Medicine, Dept. of Family Medicine, ²Florida Center for Inclusive Communities, (University Center of Excellence in Developmental Disabilities, University of South Florida

Keywords: Intervention, sexual health, intellectual disabilities

Objective: Individuals with intellectual & developmental disabilities (IDD) are at high risk for sexual abuse partly because sexual health education in this population is often neglected. Caregivers & health providers often feel unskilled or uncomfortable in dealing with this topic. By teaching ways to promote good sexual health in people with IDD we hypothesize that comfort & knowledge among caregivers & health providers will improve leading to healthier, safer outcomes for people with IDD.

Methods: Based on literature review & clinical experience we developed a 45-minute learning module which was presented as a webinar (x1) & live (x3). Audiences included caregivers & health providers. Attendees were asked to complete a 5-question pre- & post-test about knowledge & comfort.

Results: 153 participants have completed the pre-test, 42 have completed the post-test. Each question showed improvement in either knowledge or comfort, indicating effectiveness of the presentation. Preliminary findings show that discomfort is greater among family members of people with IDD, educators, & paid caregivers compared to IDD professionals or university faculty.

Conclusion: Attending a short learning module about teaching sexuality in the IDD population has shown to improve knowledge & comfort in caregivers & providers with this topic which we believe will improve health & safety for people with IDD. Our study is limited by the lower response rate in the post-test compared to the pre-test which we attribute to lack of participatory reward & inability to require participation, especially during online sessions. By reviewing pre- & post-test surveys we will tailor the presentation to different audiences, maximizing its effectiveness by keeping the presentation focused & relevant.

Research Supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Analysis of Tolerability and Toxicity of Intraperitoneal Chemotherapy in Advanced-Stage Ovarian, Peritoneal and Fallopian Tube Cancers

Patrick Teefey, MD, Nadim Bou Zgheib, MD¹, Patricia L. Judson, MD^{1,2,3}, Jesus Gonzalez-Bosquest, MD, PhD^{1,3}, Sachin M. Apte, MD^{1,3}, William Roberts, MD^{1,3}, Johnathan M. Lancaster, MD, PhD^{1,2,3}, and Robert M. Wenham, MD^{1,2,3}

¹Department of Women's Oncology, ²Experimental Therapeutics Program, ³Department of Oncologic Sciences, H. Lee Moffitt Cancer Center & Research Institute, University of South Florida Morsani College of Medicine Obstetrics & Gynecology

Keywords: intraperitoneal, chemotherapy, ovarian, carcinoma, fallopian Chart Review

Objective: Intraperitoneal (IP) chemotherapy for ovarian cancer has been associated with a high rate of grade 3/4 toxicities preventing patients from completing all 6 IP cycles. Despite major benefit in overall survival, these toxicities have been implicated as the cause of the lack of acceptance and widespread utilization of the IP regimen over the traditional intravenous method. The objective of this study is to evaluate the tolerability and toxicities of the use of IP regimen at Moffitt Cancer Center, for patients with stage IIC-IV ovarian, fallopian tube and peritoneal carcinoma.

Methods: Using Moffitt database, we evaluated the outcomes of all patients who underwent primary optimal cytoreduction for stage IIC-IV ovarian, tubal, and peritoneal carcinoma followed by IP chemotherapy regimen consisting of: Day 1, IV paclitaxel, Day 2, IP cisplatin, and Day 8, IP paclitaxel every 21 days for 6 cycles.

Results: We identified 57 patients who received the IP regimen and completed their chemotherapy at the time of this report. The median age at diagnosis was 56 years (range 31-72). The most frequent grade 3/4 toxicity was: neutropenia, 19(33.3%); GI, 5 (8.8%), metabolic, 5 (8.8%) and fatigue, 4 (7.1%). All other grade 3/4 toxic events occurred in less than 5% of patients. There were 8 (14%) IP port related complications. Narcotics were required to manage abdominal pain in 14 (24.6%). Of the 57 total patients, 43(75.4%) completed 4 or more cycles of IP therapy while 38 (66.7%) completed all 6 IP cycles.

Conclusion: By acquiring familiarity with the IP regimen utilized in the Gynecologic Oncology Group study 172; our preliminary results reveal that convenience, tolerability, and toxicity appear improved.

Research supported by:

Designing Patient-Centric Applications for Chronic Disease Management

Athanasios Tsalatsanis¹, Laura Barnes¹, Eleazar Gil-Herrera², Ambuj Kumar¹, Rahul Mhaskar¹, Niel Matthiessen³, Benjamin Djulbegovic¹; ¹Center for Evidence-Based Medicine and Health Outcomes Research, University of South Florida; ²Dept. of Industrial and Management Systems Engineering, University of South Florida; ³University of South Florida St. Petersburg. University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: mHealth, health information technology

Objective: Chronic diseases such as diabetes and heart disease are the leading causes of disability and death in the developed world. Technological interventions such as mobile applications have the ability to facilitate and motivate patients in chronic disease management, but these types of interventions present considerable design challenges. The primary objective of this work is to present the challenges arising from the design and implementation of software applications aiming to assist patients in chronic disease management.

Methods: Through formative research we determined the features and characteristics that are most crucial to the successful operation of self-management applications and demonstrate their functionality in a diabetes management application. By surveying existing mobile self-management applications we identified strengths and weaknesses that cause an application to succeed or fail.

Results: We determined that the most crucial features of self-management applications are: design of user interface and application platform, ability to monitor and track user information, data security and patient privacy, mechanisms for user motivation and psychological support, evidence-based decision support capabilities, opportunities for self-education and communication protocols.

Conclusion: We present our preliminary work on the development of a patient-centric diabetes management application for young adults with which we plan to study the effects of mobile applications in cultivating positive behaviors and education.

Research supported by: This work was supported by a grant from Bringing Science Home at USF Health. Bringing Science Home is supported by the Patterson Foundation.

Pediatric Intracranial Aneurysms: Current National Trends in Patient Management and Treatment

Jaymin Patel, Vasan, R, Sweeney, JM, Youssef, A. Samy, Van Loveren, H, Agazzi, S University of South Florida, Morsani College of Medicine, Dept. of Neurosurgery & Brain Repair

Keywords: Pediatric Intra-cranial Aneurysms

Objective: Investigate the national trends of ruptured and unruptured pediatric intracranial aneurysms regarding costs, hospital experience and procedural management of this condition.

Methods: The national Healthcare Cost and Utilization Project (HCUP) Kid's Inpatient Dataset (KID) was queried using the online HCUPnet system. Overall trends in length of stay (LOS), associated charges, and in-hospital deaths were analyzed for both SAH and non-ruptured aneurysms from 1997-2009 and trends in the type of procedure, associated LOS and charges were analyzed for subarachnoid hemorrhage (SAH) from 2003-2009. SPSS software was used to conduct statistical analysis.

Results: Patients with SAH had a longer mean LOS (11.5-14.2 days) compared to shorter LOS of non-ruptured aneurysm patients (4.0-6.6 days). The utilization of endovascular strategies for SAH increased from 10.0%-19.8% from 2006 to 2009 while the surgical management has remained steady (2003-6.2%; 2006-8.6%; 2009-6.7%). The costs of endovascular procedures rose 50% (2006-2009) while the cost of surgical procedures increased 6% (2003-2009). The mean LOS has increased for endovascular procedures (16.5-17.2 days) and decreased for surgical procedures (20.4-14.7 days). No significant decline in in-hospital mortality was noted from 2003 to 2009.

Conclusion: The national trend in management of pediatric intracranial aneurysms and SAH has not seen significantly decline in in-hospital mortality, despite dramatic increases in hospital charges and utilization of endovascular treatment strategies. Endovascular treatment LOS is extended and cost of procedure is increasing at an expedited rate while surgical procedures have seen a modest increase in cost while maintaining a fairly constant utilization and decreasing LOS.

Omentectomy in Colorectal Resection: Does it Affect Complications?

Willet, Stephanie. L.; Campbell, Michael L.; Sanchez, Jaime E.; Rasheid, Sowsan H.; Marcet, Jorge E. All: University of South Florida Morsani College of Medicine Surgery

Keywords: omentectomy; colorectal; morbidity, mortality, infection

Objective: Preservation of the greater omentum in animal studies has been shown to reduce the formation of intestinal adhesions and enhance peritoneal defense mechanisms, yet its influence is understudied in human subjects. The purpose of our study is to evaluate whether infection rate, post-operative morbidity, and mortality in humans are affected by omentectomy in colorectal resection.

Methods: 674 patients underwent colorectal surgery for malignancy, benign tumor, colonic Crohn's disease, ulcerative colitis, or colonic inertia between January 2004 and September 2011. 39 patients underwent omentectomy (OM) during colorectal resection, and 407 patients did not (NO group). Clinical outcomes measured were rate of wound infection, bowel obstruction, re-operation, post-operative sepsis, post-operative ileus, length of stay (LOS), and mortality.

Results: Overall complication rates were statistically similar in both groups: 33% in the OM group vs. 32% in the NO group. Wound infection rate was also similar in both patient groups (18% in both groups). Bowel obstruction at the anastomotic site, however, was 5.1% in the OM group vs. 1.5% in the NO group (p not significant). Post-operative sepsis (0% vs. 0.5%) and mortality (2.6% vs. 3.2%) were found to be minimal and similar in both groups. The re-operative rate was 7.7% in the OM group vs. 9.8% in the NO group (p not significant). Patients undergoing omentectomy had longer length of stay than the control group (mean of 7.6 days vs. 6.5 days; p=0.044).

Conclusion: Despite its immunological and barrier properties, removal of the greater omentum does not seem to significantly alter clinical outcome in human subjects, but does seem to lengthen LOS. This topic warrants future large-scale clinical trials for further evaluation.

Research supported by: Research Scholarly Concentrations at USF Health Morsani College of Medicine, University of South Florida

Hepatic-Specific Deletion of Lipin-1 Aggravates Alcoholic Fatty Liver in Mice

Ming Hu (¹); Ray Zhang (¹); Christopher Q. Rogers (¹); Brian N. Finck (²); Mayurranjan S. Mitra (²); Xiaomei Liang (¹); Hannah E. Everitt (¹); Huquan Yin (¹); Joanne M. Ajmo (¹); Laura A. Flatow (¹); and Min You (¹) University of South Florida Health Sciences Center, Tampa, FL. (²) Washington University School of Medicine, St. Louis, MO University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology and Physiology

Keywords: Liver, ethanol, lipid metabolism, AFL

Objective: In the present study, using a liver specific Lipin-1 knockout (Lipin-1LKO) mouse model, we sought to investigate the functional role of Lipin-1 in the development of alcoholic fatty liver and explore the underlying mechanisms.

Methods: Alcoholic fatty liver was achieved by pair feeding wild-type (WT) and Lipin-1 liver-specific knock-out (LKO) mice with modified Lieber-DeCarli ethanol-containing low fat diets for 4 weeks.

Results: Deletion of hepatic of Lipin-1 resulted in significant elevation of serum liver enzymes, accompanied by markedly increased hepatic pro-inflammatory cytokine expression in mice fed with or without ethanol, indicating an essential role of Lipin-1 in regulating the inflammatory process and liver injury. Of note, ethanol-fed KO mice showed a dramatic increase of hepatic fat accumulation than the WT as observed by histological analysis and enzymatic colorimetric quantification of hepatic triglycerides and cholesterol. Mechanistic studies revealed that hepatic Lipin-1 ablation augmented ethanol-induced impairment of hepatic fatty acid oxidation, reducing the generation of ketone bodies, suppressing VLDL secretion, and exacerbating alcoholic liver steatosis largely via impairment of hepatic PGC-1 α signaling.

Conclusion: In conclusion, our findings demonstrate that liver-specific Lipin-1 deletion in mice leads to rapid onset and progression of alcoholic fatty liver. Pharmacological or nutritional modulation of hepatic Lipin-1 may be beneficial for the prevention and/or treatment of human alcoholic fatty liver disease.

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Graphene-Based Electrochemical DNA Biosensing Platforms

Subbiah Alwarappan^{1,2}, Ashok Kumar¹, Shyam S Mohapatra² ¹Nanotechnology Research and Education Center, ²Nanomedicine Research Center, Morsani College of Medicine, University of South Florida, Tampa, FL

Keywords: Biosensors, Graphene, Voltammetry, Impedance, DNA

Objective: Graphene-based biosensing platforms have been used for rapid, robust, ultrasensitive electrochemical detection systems, but have not been used for DNA detection. Herein we applied graphene technology to design an ultrasensitive, low-noise array for detection of DNAs in nL sample volumes.

Methods: Graphene nanosheets were obtained by chemical vapor deposition. A multi-electrode graphene DNA biosensor array consisting of 6 to 30 working electrodes, a reference and an auxiliary electrode was fabricated by sputtering technology. The graphene surface of the electrodes was then modified by covalent modification or through π - π stacking. DNA from patient samples was allowed to hybridize with the capture oligonucleotides for 10 minutes and the extent of hybridization was measured by electrochemical voltammetry and electrochemical impedance technique.

Results: Raman spectroscopic analysis clearly indicated high quality graphene on nanosheets. High resolution transmission electron microscopy indicated the presence of 3-10 layers of graphene. Electrochemical characterization indicated that the graphene obtained in our work possessed the surface cleanliness and structure requisite for use as an electrode platform for the electrochemical detection of DNA mutations.

Conclusion: Our results show that a graphene-based biosensor array can detect DNAs in the sub-femtogram range, which to the best of our knowledge is the lowest level of detection ever reported. Additional optimization of the biosensor and improvement of the surface chemistry is expected to further improve the performance of this platform as a diagnostic tool for multiplex DNA analysis.

Effect of Molecular Crowding on Aggregation of Disordered Proteins

Leonid Breydo, Krishna Reddy, Vladimir Uversky Department of Molecular Medicine, University of South Florida Morsani College of Medicine Cardiology

Keywords: Intrinsically disordered proteins, protein aggregation, molecular crowding, α -synuclein

Objective: Aggregation of intrinsically disordered proteins is associated with several human diseases. The precise mechanism of protein aggregation is still poorly understood. The problem is further complicated by the fact that the in vivo environment is very crowded with macromolecules occupying up to 30% of the available volume. Earlier studies of the crowding effects on protein aggregation have used flexible, spherical polymers. However, a variety of biopolymers are present in vivo including rigid, rod-like polymers. Here we investigate the effects of both spherical and rod-like polymers (polysaccharides) on the kinetics and mechanism of aggregation of α -synuclein and insulin in the conditions where these proteins are unfolded.

Methods: Kinetics of protein fibril formation was measured using ThT fluorescence. Structure of the fibrils was assessed using CD and FTIR spectroscopy. Aggregate morphology was analyzed by electron microscopy, and their stability towards denaturation by denaturation in the presence of guanidinium thiocyanate.

Results: We found that spherical polymers promoted protein fibril formation while rod-like polymers promoted fibril formation at low concentrations and inhibited it at higher concentrations. Morphology, secondary structure and stability of the protein fibrils were also altered depending on the shape of the crowding agent.

Conclusion: We have shown that spherical and rod-like polymers have different effects on protein aggregation and their effects are likely due to interplay between excluded volume and viscosity effects.

Abstract #: 148**Presented by: Carrie Butler, BS, Graduate Student*****Identifying Novel Pan-apicomplexan Protozoan Cell Cycle Genes***

Carrie Butler¹, Olivier Lucas¹, Stefan Wuchty², Bin Xue¹, Vladimir Uversky¹, Michael White¹ ¹Molecular Medicine, University of South Florida, Tampa, FL, USA ²National Institute of Health, Bethesda, MD, USA, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Toxoplasma gondii, toxoplasmosis, Plasmodium falciparum, apicomplexa, cell cycle

Objective: Apicomplexa parasites are major causes of disease. Toxoplasmosis is a serious infection of immune compromised individuals, while Plasmodium falciparum (Pf) causes the most lethal form of malaria. Both Toxoplasma gondii (Tg) and Pf cause disease by rapid intra-cellular replication and lysis of host cells. Our goal is to identify novel pan-apicomplexan genes essential to parasite replication, upon which new therapeutic targets to prevent or reduce parasite burden might be developed.

Methods: We combined comparative and functional genomics datasets to generate a list of cell division cycling (CDC) genes shared by Tg (Behnke et al., 2010) and Pf (Bozdech et al., 2003). This list was curated to discover the subset of CDC genes present only in apicomplexan parasites. Endogenous epitope tagging was then performed on a subset of genes in order to validate their expression and cell cycle timing, and determine protein subcellular localization.

Results: 20 uncharacterized genes were selected from 679 pan-apicomplexan CDC mRNAs. These 20 orthologs possess dynamic mRNA expression profiles, conserved timing of expression and similar predicted protein folding. These genes represent a range of protein lengths (142-4,956 AA) and are distributed through the cell cycle. Immunofluorescence assays of the tagged proteins revealed proteins that localize to the parasite invasion apparatus including the apical and inner membrane complex structures.

Conclusion: Cell cycle timing, relative abundance, and protein topology is conserved between hypothetical Tg and Pf genes indicating these genes may be required for all apicomplexan cell cycles. Future knockouts of the genes will provide additional insights into the roles these proteins serve in the growth of both Pf and Tg.

Research supported by: NIH

Intracellular Degradation/Retention of Mutant C-terminal Truncated Decorin in Human Congenital Stromal Corneal Dystrophy

Shoujun Chen¹, Mei Sun¹, David E Birk¹ University of South Florida, Morsani College of Medicine, Dept. of Pathology and Cell Biology

Keywords: decorin, Human Congenital Stromal Corneal Dystrophy

Objective: We established a transgenic mouse model that recapitulated the pathophysiology of Human Congenital Stromal Corneal Dystrophy (HCSCD) caused by a mutation resulting in a C-terminal truncated decorin. The purpose of this work is to characterize the cellular/molecular mechanisms whereby C-terminal truncated decorin leads to HCSCD.

Methods: The mouse model combined with an in vitro system, where HEK293 cell lines were transfected with wild type decorin or 952delT mutant decorin were utilized.

Results: In vivo, the extracellular content of mutant decorin was significantly lower than wild type decorin. Histological analysis of mutant corneas showed altered keratocyte morphology exhibiting an increased number of vesicles, suggesting an alteration of intracellular processing of mutant decorin that may affect keratocyte function. In transfected HEK293 cell lines, the intracellular expression of mutant decorin was comparable with that of wild type decorin. However, mutant decorin expression in the cell medium was significantly lower than the expression of wild type decorin, an observation that was consistent with our in vivo study. The intracellular mutant decorin was significantly decreased compared to wild type decorin 12 hours after protein synthesis inhibition in cell lines. However, a proteasome inhibitor did not increase mutant decorin expression, suggesting that increased intracellular degradation may be through an autophagy-lysosome pathway.

Conclusion: Truncation of the C-terminus may decrease decorin stability, increase its degradation/retention and reduce its secretion, all of which affect intracellular homeostasis, and in turn may affect the expression of extracellular matrix components, as we observed in our transgenic mouse model of HCSCD.

Noninvasive Remote-Controlled Release of Drugs from a Nanogel Triggered by Near IR

Vignesh Chinnasamy-Staff, Chunyan Wang-Post doc and Subhra Mohapatra-PI, Molecular Medicine Department and Nano-medicine Research center University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: remote control release, nanogel, drug delivery

Objective: Some serious medical conditions, such as cancer, diabetes and chronic pain, require medications on an as-needed basis over a long period of time. Thus, it is necessary to develop a delivery system to allow remote, repeatable, and reliable switching of drug release. The goal of this study is to develop a drug delivery system based on a thermosensitive nanogel incorporating graphene that allows loading of a large quantity of drug that can be released on-demand by near IR laser.

Methods: The nanogel was prepared from monomers, acrylated-chitosan modified graphene nanosheets, N-isopropylacrylamide, and crosslinker PEG-diacrylate by radical polymerization. Doxorubicin was loaded into the nanogel by equilibrium partitioning. The photothermal behavior of the nanogel was tested with an 800 nm laser. The drug release kinetics were determined by loading the drug into dialysis tubing and incubating at 37°C and 42°C and pH medium after using the laser to switch on the release for several cycles. The cellular uptake of Cys5.5 modified nanogels was tested on human embryonic kidney (HEK293) cells.

Results: The nanogel prepared by radical polymerization was characterized by Fourier transform infrared spectrometry, scanning electron microscopy and Doppler laser scanning (DLS). The DLS results showed that the size of the nanogel decreased from 330-270 nm when the temperature was increased from 37°C to 42°C, which is desired for the remote control release. The drug was released mostly at 42°C and pH 6.0 but little at 37 °C, pH 7. The nanogel was taken up by HEK293 cells.

Conclusion: These results demonstrate that acrylated chitosan-graphene nanogels can be used for on-demand drug release, which can be triggered by a near IR laser.

Research supported by: NIH and Florida Biomedical Research Funds

Erythroid 5-Aminolevulinatase Synthase Variants Cause Porphyrin Accumulation in HeLa Cells

Erica J. Fratz, Gregory A. Hunter, and Gloria C. Ferreira. University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: 5-aminolevulinatase synthase, heme, porphyrin

Objective: 5-Aminolevulinatase synthase (ALAS) catalyzes the reaction of succinyl-CoA with glycine to produce 5-aminolevulinatase, carbon dioxide, and CoA, the first and rate-limiting step of the heme biosynthetic pathway in animals. Erythroid ALAS (ALAS2) is negatively regulated by heme at the level of mitochondrial import and, in its mature form, certain mutations of the murine ALAS2 active site loop result in an increase in porphyrin production. Moreover, various mutations in the C-terminus of human ALAS2 have recently been found to be associated with the disease X-linked dominant erythropoietic protoporphyria (XLDPP), in which patients accumulate the photosensitizer protoporphyrin IX (PPIX). The objective of this study was to analyze and compare the effects of ALAS2 variants *ex vivo* in order to begin investigation of the underlying mechanism of ALAS2 in XLDPP and to assess the potential utility of ALAS2 variants in PPIX production for photodynamic therapy.

Methods: HeLa cells were transfected with plasmids encoding ALAS2 variants and PPIX fluorescence was analyzed using flow cytometry.

Results: Expression of murine ALAS2 with a mutated presequence increases PPIX in comparison to expression of wild-type ALAS2 and "empty" vector control, and additional mutation of the active site loop adds significantly to the PPIX accumulation. However, expression of human ALAS2 XLDPP variants did not result in significant PPIX accumulation as anticipated.

Conclusion: Transfection of murine ALAS2 hyperactive variants into HeLa cells causes accumulation of PPIX, but the XLDPP variant enzymes must be further analyzed in order to understand the mechanism underlying the PPIX accumulation as seen in patients with XLDPP.

Research supported by: The American Heart Association Grant #10GRNT4300073

Dietary Indole 3, 3'-Diindolylmethane Protects Cultured Human Alveolar Epithelial Cells From Oxidative Stress Induced Cell Death

Lakshmi Galam, Prasanna Tamarapu Parthasarathy, Asfiya Younis, Amanda Hodgkins, Gurukumar Kollongod Ramanathan, Ruan R Cox Jr, Venugopal Rajanbabu, Anu Stephan, Richard F. Lockey and Narasaiah Kolliputi
University of South Florida Morsani College of Medicine Internal Medicine

Keywords: Dietary indoles, Acute lung injury, Oxidative stress, DIM

Objective: Dietary indoles like indole-3-carbinol (I3C) and its derivative, diindolylmethane (DIM) are found in cruciferous vegetables and have been known for their anti cancer and anti-inflammatory properties. Oxidative stress and alveolar epithelial cell death play a key role in the pathogenesis of several pulmonary diseases. However, effect of DIM in pulmonary diseases and alveolar epithelial cell death is not known. We investigated whether DIM has the protective ability to ameliorate oxidative stress and alveolar epithelial cell death *in vitro*.

Methods: Human type II alveolar epithelial cells (A549) were treated with an inducer of oxidative stress, in the presence and absence of DIM. In another set of experiments, we first induced apoptosis by starvation in epithelial cells and the starved cells were post treated with DIM to determine whether DIM can reverse epithelial cell apoptosis. qPCR was performed to assess the expression levels of Epithelial sodium channels (ENaC) in starved A549 cells after treatment with difference concentrations of DIM.

Results: Our results showed that H₂O₂ induced a significant alveolar epithelial cell necrosis and apoptosis. In contrast, epithelial cells treated with DIM inhibited H₂O₂ induced cell necrosis and apoptosis. In addition, DIM also reverses cell death and protects alveolar epithelial cells from starvation induced cell damage and cell death. DIM treated A549 cells showed an increase in ENaC α and ENaC β levels indicating a probable restoration of fluid balance.

Conclusion: For the first time our data demonstrated that the natural dietary compound DIM attenuates oxidative stress induced epithelial cell death.

Research supported by: AHA Grant09SDG2260957 and NIH R01 HL105932

A Macroporous Graphene Hydrogel Matrix for the Differentiation of Mesenchymal Stem Cells

Ujjwala sree Garapati^{1,2,4}, Chunyan Wang^{1,2,4}, Jaya Mallela^{1,2,4}, Vignesh Chinnasamy^{1,2,4}, Frantz Jean Louis^{1,2,3,4} and Subhra Mohapatra^{1,2,3,4} ¹Department of Molecular Medicine, ²Nanomedicine Research Center, ³Signature Program in Allergy and Immunology, ⁴University of South Florida, Tampa, Florida University of South Florida Morsani College of Medicine Cardiology

Keywords: Stem cell differentiation, 3D hydrogel, Chondrogenesis, Osteogenesis, Adipogenesis

Objective: Cell-based therapies using mesenchymal stem cells (MSCs) have great potential in tissue regeneration. Therapeutic efficiency is critically dependent on the mode of delivery and viability of transplanted MSCs at the implantation site. We reasoned that a biocompatible three-dimensional matrix might prime the differentiation of MSCs toward multiple lineages. To test this hypothesis, we synthesized a graphene-based hydrogel system and evaluated its potential to differentiate bone marrow (BM) MSCs.

Methods: BM MSC culture: Mesenchymal stem cells (MSCs) have been isolated and cultured from C57BL/6 mouse femurs and tibias based on the cells' adherence to plastic surfaces. Viability: MSCs plated on hydrogels were incubated overnight and live/dead assays were performed to assess viability. Preparation of hydrogel: The hydrogel was prepared from acrylated chitosan modified graphene nanosheets by radical polymerization at room temperature. The swelling kinetics of the hydrogel was tested. Differentiation: The potential of MSCs to differentiate along multiple mesenchymal lineages was tested with end-point and time-course experiments.

Results: BM MSCs grown on hydrogels were viable. Differentiation on hydrogel was confirmed with various mesenchymal characteristics. Time course experiments indicated that cell differentiation was significantly faster and more efficient in hydrogels than on monolayers.

Conclusion: Graphene-based hydrogels support MSC survival and differentiation to mesenchyme. This can be utilized as a versatile matrix for study and to enhance priming of MSCs toward various cell types for regenerative therapies.

Research supported by: NIH and Florida Biomedical Research Funds.

Alteration of Cholesterol Enhances JAK Inhibitor Therapy in Myeloproliferative Neoplasms

Lori N. Griner^{1,2}, Kathy L. McGraw^{1,2}, Joseph O. Johnson², Alan F. List², Gary W. Reuther², ¹University of South Florida, ²Moffitt Cancer Center. University of South Florida, College of Arts and Sciences, Dept. of Cell Biology, Microbiology & Molecular Biology

Keywords: Lipid Rafts, Statins, Myeloproliferative Neoplasms

Objective: To elucidate the role of lipid rafts in JAK2-V617F-driven myeloproliferative neoplasms (MPNs).

Methods: Co-localization of JAK2 and lipid rafts is done using immunofluorescence with confocal microscopy. Disruption of lipid rafts with methyl-beta cyclodextrin and filipin complex in JAK2-V617F-positive cell lines is demonstrated through western blot techniques. Lipid rafts are isolated using a iodixanol gradient separation method followed by ultracentrifugation. We used trypan blue exclusion in our cell proliferation analysis of JAK2-V617F-positive cell lines treated with cholesterol lowering statins and JAK inhibitor, INCB018424. The effects of statins on primary JAK2-V617F-positive MPN patient cells were analyzed by colony formation of endogenous erythroid colonies (EECs). Apoptosis analysis is achieved by PARP cleavage and Annexin V staining.

Results: Our work shows JAK2-V617F co-localizes with lipid rafts. In addition, lipid raft disrupting agents reduce JAK2 and STAT5 activation in JAK2-V617F-positive cell lines. For long-term raft disruption, we use statins to demonstrate a decrease in proliferation in JAK2-V617F-positive cell lines, with an enhanced reduction in proliferation with the combination of statins and JAK inhibitors. Further, we show an increased induction of apoptosis of JAK2-V617F cells after statin and INCB018424 treatment, compared to single agent treatment. In addition, primary cells from JAK2-V617F-positive MPN patients show a reduction in EECs with low dose statins, while normal controls are unaffected.

Conclusion: Our data shows JAK2-V617F driven JAK-STAT pathway activation is vulnerable to lipid raft disrupting agents and suggest lipid raft integrity as a therapeutic target for JAK2-V617F-positive MPNs.

Development of a Sensitive Gel-Based Assay to Measure Protein Palmitoylation

Laura Hamel, David Mitchell, Robert Deschenes Molecular Medicine, Morsani College of Medicine, University of South Florida University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: Ras, Palmitoylation, CaaX, Post-translational Modifications, Fluorescence tagging

Objective: Protein palmitoylation plays a key role in subcellular trafficking, protein-protein interactions, and protein stability. Current analysis involves 3H-palmitate, which is limited by low sensitivity and efficiency. We have developed a procedure using a bodipy-C12-CoA to mimic palmitate; overcoming 3H-palmitate limitations. This assay is used for screening of palmitoylating and depalmitoylating enzymes and for the identification of palmitoylating enzyme/protein pairs. Of particular interest is identifying the enzyme that depalmitoylates Ras. Ras isoforms are implicated in ~30% of all known cancers and up to 90% in specific cancer types. Modulators of Ras palmitoylation are therefore promising new therapeutic cancer targets.

Methods: Bodipy-C12-CoA will be incubated with mCherry-Ras2 and Erf2•Erf4 (the enzyme complex that palmitoylates Ras2) for 30 minutes, and separated by SDS-PAGE. Bodipy fluorescence will be visualized to observe a shift from bodipy-enzyme intermediate to bodipy-Ras2, indicating the acylation of Ras2. Western Blot analysis confirms the presence of the palmitoylating enzyme and Ras2.

Results: We have optimized and can consistently produce 2.5mg/ml of highly pure Erf2•Erf4. In preliminary studies, bodipy-C12-CoA co-migrates with mCherryRas2, indicating that acylation is occurring. A non-palmitable Ras2 mutation does not get acylated by bodipy-C12-CoA, supporting the idea that bodipy-C12-CoA mimics palmitate in vitro. Multiple carbon-chain lengths for the bodipy-CoA were screened, and bodipy-C12-CoA mimics palmitate best in both specificity and action.

Conclusion: A gel-based assay can utilize bodipy-C12-CoA to overcome the limitations of a 3H-palmitate-based assay to observe protein acylation.

Research supported by: NIH Grants CA50211 and GM73976

Manganese Oxide Lipid Nanoparticles (MLNs) For Use As A T1 MRI Contrast Agent And Gene Delivery

Vehicle Mark Howell (1), Chunyan Wang (1), Suraj Dixit (2), Shyam Mohapatra (1,2,3) and Subhra Mohapatra (1,2,3)
(1) Department of Molecular Medicine, (2) Nanomedicine Center, University of South Florida Morsani College of Medicine, (3) James A Haley VA Hospital, Tampa, FL

Keywords: Manganese, Nanoparticles, Lipids, Micelles, and Multifunctional

Objective: Magnetic resonance imaging (MRI) of the lung is more difficult than in other organs. Our research goal was to design a multifunctional nanoparticle for T1-weighted MRI contrast enhancement and DNA delivery to assist in lung cancer diagnosis and treatment. Manganese oxide (MnO) nanoparticles were chosen as a T1 contrast agent, due to the intrinsic properties of manganese. To confer biocompatibility to the MnO nanoparticles they were encapsulated in lipid micelles, allowing MLNs to bind stably, protect, and deliver DNA into target cells.

Methods: Oleic acid coated MnO nanoparticles were synthesized via thermal decomposition of an Mn-oleate precursor in a high boiling point solvent. These hydrophobic nanoparticles were then encapsulated in micelles composed of varying amounts of PEG-2000 PE, cationic DC-cholesterol, and DOPE. We tested these MLNs' ability to act as a T1 contrast agent and DNA delivery vehicle using in vitro MRI studies and cellular transfections.

Results: Size and morphology of MLNs were determined using dynamic light scattering and transmission electron microscopy. In vitro phantom MRI results confirmed MLNs were able to provide enhanced T1 MRI contrast. Transfection studies using HEK 293 and A549 cells proved that MLNs were capable of protecting and delivering DNA to cells in vitro, as well as or better than Lipofectamine.

Conclusion: Our in vitro studies showed that these MLNs can improve lung cancer diagnosis and treatment via T1 MRI contrast enhancement and can serve as a delivery vehicle for DNA gene therapies. Future studies will determine their potential use in vivo.

Research supported by: The National Institute of Health (NIH) supported this work.

Plac1 (Placenta-Specific 1) is Paternally Imprinted and Necessary For Normal Placental and Embryonic Growth.

Suzanne Jackman, M.D.¹, Xiaoyuan Kong, M.D.¹, Michael Fant, M.D.^{1,2,3} ¹Department of Pediatrics, ²Obstetrics and Gynecology, ³Pathology and Cell Biology University of South Florida Morsani College of Medicine Pediatrics

Keywords: placenta, X-inactivation, knock out mouse

Objective: The aim of this study was to determine the role of imprinting on Plac1 function during development.

Methods: Plac1 was deleted in murine ES cells and bred against a C57BL/6 background. Timed matings were established between wild type (WT) or hemizygous males and heterozygous (het) or WT females. Placentae were obtained at various gestational ages. Placental morphology was analyzed using IHC and Plac1 mRNA expression was assessed by Q-RT-PCR. Embryos were genotyped using a PCR-based strategy.

Results: Plac1 deletion resulted in placentomegaly in Plac1-null mice as well as hets where the mutant allele was inherited from the mother (XPlac1X). This was associated with expansion and disorganization of the junctional zone. By contrast, het placentae where the mutant allele was inherited from the father (XXPlac1) were indistinguishable from WT consistent with preferential inactivation of the paternal X-chromosome. Growth dynamics, however, suggested that paternally expressed Plac1 escaped complete X-inactivation. XPlac1X placentae peaked in weight at e16.5 followed by a slight decline thereafter. By contrast, KO placentae continued to increase in weight after e16.5 suggesting a gene dosage effect. Q- RT-PCR confirmed that XPlac1X placentae expressed Plac1 although at lower levels than XXPlac1 placentae. Additionally, IHC analysis indicated that paternally-derived Plac1 is expressed only in labyrinthine trophoblasts.

Conclusion: Plac1 is essential for normal placental and embryonic growth. It is paternally imprinted but exhibits partial escape from X-inactivation. Additionally, paternally-derived Plac1 appears to be expressed in a trophoblast lineage-specific manner.

Research supported by: March of Dimes #6-FY09-503

Purification of the Erf2•Erf4 Protein Acyl Transferase Complex from Yeast Membranes

Yiping Ling, David A. Mitchell and Robert J. Deschenes University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Purification, DHHC, Membrane Protein, Palmitoylation

Objective: One key to improve the success in obtaining pure membrane protein for biochemical and structure analysis is sufficient yields of protein and ordered crystals. Membrane spanning proteins, for example, are rigorously monitored by sensitive cellular quality control mechanisms that can limit the expression level and trigger degradation pathways the extent of their expression. We are working to develop improved protocols for expression and purification of membrane protein in the yeast *Saccharomyces cerevisiae*.

Methods: The recombinant protein was expressed under the control of a galactose-inducible promoter in the yeast. In this system, epitope-tagged fusion proteins are expressed using the tightly regulated GAL1,10 promoter.

Results: We have genetically altered the yeast strain to raise the level of the limiting component of the galactose utilization pathway to increase the overall expression of the protein of interest.

Conclusion: Here we present the over-expression and purification of a tetra-membrane spanning subunit of the DHHC enzyme family, Erf2, and its associated subunit, Erf4. Using our system, we are able to recover 6-7 milligram quantities of this enzyme at about 80% purity from as little as 3 liters of cell culture.

Research supported by: NIH Grants CA50211 and GM73976

Distinct Progenitor Cell Populations in Mouse Achilles Tendon and Epitenon

Michael J. Mienaltowski, Sheila M. Adams, David E. Birk. Morsani College of Medicine, Department of Pathology & Cell Biology, University of South Florida, Tampa, FL.

Keywords: Achilles tendon, stem cells, progenitor cells, niche

Objective: The purpose of this study is to characterize tendon stem/progenitor cell populations to determine if they express unique markers. We hypothesize that progenitor cells from within the tendon and the surrounding epitenon are alternatively recruited in unique healing mechanisms; thus, each population will possess distinct features.

Methods: Cells isolated from within the tendon and the epitenon of mouse Achilles tendons were characterized by colony forming unit and multipotency assays, real-time quantitative polymerase chain reaction, and flow cytometry.

Results: Data indicate that two distinct stem cell populations exist within the tendon center versus the epitenon. Cells from both regions were multipotent, but more progenitor colonies were observed for the tendon than the epitenon ($3.92 \pm 1.55\%$ vs. $0.24 \pm 0.26\%$, $p < 0.01$). Relative to those of the epitenon, tendon progenitors had increased expression of tenomodulin ($22.6x$, $p = 0.031$) and scleraxis ($5.9x$, $p = 0.047$), indicative of a tendon origin. Moreover, while progenitor markers were detected for cells from both regions, cells from the epitenon demonstrated relative increases in vascular (Emcn: $2.3x$, $p = 0.016$) and pericyte (Cd133: $2.2x$, $p = 0.078$) markers consistent with a progenitor class recruited during extrinsic repair.

Conclusion: These findings demonstrate that separate progenitor populations exist in and around the Achilles tendon niche. Distinct profiles lend support to the argument that each progenitor pool may contribute differently within intrinsic and extrinsic tendon repair mechanisms. Further studies are required to localize these cell populations in situ and to determine their roles during repair in vivo.

Research supported by: This project was supported by Grants #AR058027 (MJM) and #AR044745 (DEB) from NIAMS/NIH.

Acute Mitochondrial Modulation Activates Airway Sensory Nerves via TRP Channels

Lika Nesuashvili, Stephen Hadley, Parmvir Bahia, Thomas Taylor-Clark, University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: Mitochondria, lung, sensory nerve excitability

Objective: Mitochondrial dysfunction, which is common in inflammatory diseases, forms reactive oxygen species (ROS). ROS activate nociceptive sensory nerves, via transient receptor potential ankyrin 1 (TRPA1) ion channels. We hypothesize that acute modulation of mitochondrial function will activate airway sensory nerves. Antimycin A (AA), an electron transport chain protein complex III inhibitor, induces superoxide production selectively in the mitochondria.

Methods: Ex vivo bronchopulmonary C-fiber extracellular recordings, patch clamp and Ca^{2+} imaging.

Results: AA ($20\mu M$) activated nociceptive (i.e. TRP vanilloid1 (V1)-expressing) bronchopulmonary sensory nerves, but failed to activate non-nociceptive nerves. The response to AA was significantly greater in TRPA1-expressing nociceptors. Activation was reduced by TRPA1 and TRPV1 receptor antagonists HC-030031 and I-RTX, respectively. AA ($20\mu M$) increased cytosolic $[Ca^{2+}]$ only in neurons expressing TRPA1 and/or TRPV1. Responses were reduced with TRPA1 and TRPV1 receptor antagonists and abolished in the absence of extracellular Ca^{2+} . AA increased cytosolic $[Ca^{2+}]$ in TRPA1- and TRPV1-expressing human embryonic kidney (HEK) cells and failed to activate nontransfected HEK cells. AA activated currents in TRPA1- and TRPV1-expressing HEK cells, but not in nontransfected HEK cells. Currents were reduced with TRP channel blocker Ruthenium Red. Oxygen deprivation or reducing agent dithiothreitol blocked TRPA1 responses to AA. Antioxidants: Mito-Tempo, Tempol, Pegylated-Catalase, MnTMPyP and Trolox failed to do so.

Conclusion: Acute modulation of nerve terminal mitochondria activates nociceptive nerve subtypes by gating TRPA1 and TRPV1 ion channels.

MicroRNA-16 Modulates the Expression Of EnaC, Tgf β And Its Targets In Human Alveolar Epithelial Cells

Prasanna Tamarapu Parthasarathy, Gurukumar Kollongod Ramanathan, Lakshmi Galam, Asfiya Yunus, Ruan R. Cox Jr, Venugopal Rajanbabu, Richard F. Lockey and Narasaiah Kolliputi University of South Florida Morsani College of Medicine, Dept of Internal Medicine

Keywords: Acute lung injury, Micro RNA-16, SERT, ENaC, Hyperoxia

Objective: MicroRNAs (miRNAs) have emerged as a novel class of gene regulators which play a critical role in complex diseases like acute lung injury (ALI). Our miRNA profiling studies identified that several miRNAs like miR-146a, miR-16 and miR-155 were dysregulated in animal models of ALI. These changes in miRNA expression are associated with immune response, inflammation and pathogenetic severity of ALI. The aim of this study is to investigate the effects of miR-16 on human alveolar epithelial cells (A549) in vitro.

Methods: Human alveolar epithelial cells (A549) were commercially obtained and cultured according to the manufacturer instructions. Cells were transfected with plasmid containing miR-16 or control vector by Lipofectamine. Post transfection, cells were treated with serotonin and qPCR was performed to assess the effects of miR-16 on serotonin transporter (SERT) and other downstream signalling molecules like Transforming growth factor β (TGF β) and Epithelial sodium channel (ENaC).

Results: A549 cells transfected with miR-16 decreased the expression levels of SERT when compared to controls. Dose dependant regulation of SERT was observed in untransfected A549 cells treated with serotonin. Expression of TGF β and ENaC were also altered in miR-16 over expressed A549 cells in the presence of serotonin.

Conclusion: miR-16 over expression can alter serotonin transporter, TGF β and ENaC expression in human alveolar epithelial cells. Targeting ALI using miR-16 as a novel therapeutic approach is very promising and could be a potential candidate to treat ALI.

Research supported by: NIH-R01-HL105932 and AHA-09SDG2260957

Multifunctional Multilayered Mag-micelle Nanoparticles (4M-NPs) for Prostate Cancer Targeted Gene Therapy and MR Imaging

Sowndharya Ravi¹, Chunyan Wang^{1,2}, Vignesh Chinnasamy¹, Subhra Mohapatra^{1,2,3} ¹Molecular Medicine Department, ²Nanomedicine Research Center, College of Medicine, University of South Florida, 12901 Bruce B. Downs Blvd., Tampa, FL, 33612, USA ³James A Haley VA Hospital, 12902 Bruce B. Downs Blvd., Tampa, FL, 33612, USA University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: targeted gene delivery, prostate cancer, MRI

Objective: Prostate cancer is second leading cause of cancer death among US men. Our lab is investigating nonviral gene therapy for prostate cancer, combining targeted gene delivery to prostate cancer cells with real-time in vivo monitoring. We report the development and characterization of multifunctional multimodal mag-micelle nanoparticles (4M-NPs) for prostate cancer targeted gene therapy and MRI.

Methods: 4M-NPs were conjugated with prostate stem cell antigen (PSCA) antibody and modified with Cys5.5. In vitro uptake of nanoparticles and in vitro transfection efficiency of TRAMP-C1 cells were evaluated by microscopy. In vivo MRI was done using Agilent ASR 310 7 Tesla MRI high-field scanner. In vivo gene delivery was visualized by fluorescent microscopy 48 hours after i.v. administration.

Results: PSCA antibody conjugated 4M-NPs demonstrated much higher cellular uptake and transfection efficiency than 4M-NPs without PSCA peptide. In vivo MRI of prostate cancer mice showed contrast enhancement starting from 7.7 min post i.v. injection of PSCA-4M-NPs. Moreover, i.v. administration of PSCA-DNA-4M-NPs expressed red fluorescent protein (tdT) with high efficiency in the prostate tumors of TRAMP mice at 48 hours.

Conclusion: These results demonstrate that PSCA-4M-NPs can target delivery of genes for prostate cancer and enhance MRI contrast.

Research supported by: NIH and Florida Biomedical Research Funds.

PLAC1 (Placenta Specific-1) Expression is Differentially Affected by Labor in Distinct Trophoblast Populations

Yahdira Rodriguez, M.D.¹, Xiaoyuan Kong, M.D.¹, Michael Fant, M.D., Ph.D.^{1,2,3} ¹Department of Pediatrics, ²Obstetrics and Gynecology, ³Pathology and Cell Biology University of South Florida Morsani College of Medicine Pediatrics

Keywords: PLAC1, placenta, fetal membranes, labor, parturition

Objective: PLAC1 is an X-linked gene whose expression is restricted primarily to cells of trophoblast lineage. It is essential for normal placental development but its role there has not been defined. The objectives of this study were to examine the expression of PLAC1 by human trophoblasts derived from chorionic villus tissue and the chorion laeve, and determine the effect of labor on its expression.

Methods: Chorionic villus tissue and fetal membranes were obtained from normal, human placentae at term delivered in the presence or absence of labor. PLAC1 mRNA was measured by Q-RT-PCR. Paraffin-embedded sections were analyzed by IHC.

Results: PLAC1 expression in chorionic villus tissue was 100% higher in the absence of labor than in the presence of labor. There was no difference in expression associated with spontaneous or induced labor. Additionally, PLAC1 was expressed in fetal membranes where it localized to trophoblasts of the chorion laeve. Its expression there, however, was not influenced by the presence or absence of labor.

Conclusion: PLAC1 is expressed by trophoblasts of the chorion laeve as well as the chorionic villi, extending its role at the maternal-fetal interface to include the fetal membranes. PLAC1 mRNA expression in the chorionic villi was significantly lower in pregnancies associated with spontaneous or induced labor, suggesting that PLAC1 expression decreases in response to labor. The significance of this observation to parturition is not known but is consistent with a role for PLAC1 in the maintenance of the maternal-fetal interface. Future efforts are aimed at defining the functional role(s) of PLAC1 at the cellular level.

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An Integrin Network Tethers The Regulatory Collagen V to the Fibroblast Surface in Developing Tendon

Simone M. Smith, PhD, David E. Birk, PhD University of South Florida, Morsani College of Medicine Dept. of Pathology and Cell Biology

Keywords: Collagen V, Tendon Development, Adhesion, Ehlers Danlos Syndrome

Objective: To define the cellular localization and the binding partners of collagen V, a regulatory collagen in developing tendon.

Methods: Collagen V was localized in mouse flexor tendons (FDL) by immunofluorescence. Binding partners were identified by co-immunoprecipitation (co-IP) followed by proteomic identification. Western blots were used to confirm the interactions. In vitro focal contact formation and adhesion assays were used to characterize the integrin-mediated attachment of tendon fibroblasts.

Results: Collagen V is enriched at the fibroblast surface in early (P4), but not late developing (P15) or mature (P30) tendons. Proteomic analysis identified fibronectin and integrins in a Collagen V co-IP assay from tendon. A Western Blot of this precipitate confirmed fibronectin and integrin beta 1 binding to collagen V. By immunofluorescence, these molecules and integrin alpha 2 were localized spatially with collagen V. Additionally, tendon fibroblasts isolated from early developing FDL formed focal adhesions and adhered in an integrin-specific manner to fibronectin, collagens I and V, but not collagen XI, indicating a specific, functional collagen V/integrin interaction.

Conclusion: The cell surface enrichment identified, suggests collagen V (with no transmembrane domains) in P4 tendons is interacting with a membrane molecule, integral or peripheral. This allows a retention of collagen V at the cell surface during this critical period for collagen fibril assembly. Our finding that collagen V interacts with fibronectin and integrins provides a mechanism for tethering this collagen to the cell surface, allowing it to effectively regulate fibril initiation using the newly processed collagen secreted pericellularly.

Research supported by: NIH/NIAMS Grants AR044745(DEB), AR056937(SMS)

Recycling of the Large Conductance Calcium-Activated Potassium Channel by the GTPase Rab11b

Sophia Sokolowski, Margaret Harvey, Yoshihisa Sakai, Amy Jordan, Bernd Sokolowski, University of South Florida, Morsani College of Medicine, Dept. of Otolaryngology - Head and Neck Surgery

Keywords: cochlea, sensory cells, ion channels, protein-protein interactions

Objective: The large conductance calcium-activated potassium channel underlies increased hearing sensitivity in the cochlea. Previously, we used a high-throughput screening method that included LC-MS/MS to determine putative interacting partners with the BK channel (Kathiresan et al., 2009). These studies suggested an interaction with the small GTPase, Rab11b. Rabs are master regulators of endosomal trafficking, involved in: protein transport to the cell membrane (early endosome), recycling from and to the membrane (recycling endosomes), and protein transport for degradation in the lysosome (late endosomes). Previous studies suggest Rab11b is involved with either late or recycling endosomes.

Methods: Interactions of Rab11b with BK were examined by using reciprocal coimmunoprecipitation, immuno-electron microscopy, yeast two-hybrid assays, and by silencing and overexpressing Rab11b in a heterologous expression system.

Results: Results showed that Rab11b colocalizes with BK in endosomes of cochlear hair cells, when double-labeled with colloidal gold for immuno-electron microscopy. This GTPase interacts with the N-terminus of the BK channel. The Rab11b gene, cloned from mouse cochlea, has a similarity greater than 97% to Rab11b from human, cow, mouse, rat, and goat. Knockdown and overexpression of Rab11b in CHO cells resulted in a decrease and increase in hemagglutinin-tagged BK expression, respectively.

Conclusion: These data suggest that Rab11b recycles the BK channel back to the membrane as opposed to transporting BK to the lysosome for degradation. Of future interest will be the role of Rab11b in regulating BK under different conditions of auditory stimulation, such as in noise-induced hearing loss.

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5-Aminolevulinate Synthase: Structure-Function Studies Related to the Enzymatic Succinyl-CoA Binding Site

Bosko M. Stojanovski*, Gregory A. Hunter*, and Gloria C. Ferreira**[^] *Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa, Florida 33612 **Department of Chemistry, College of Arts and Sciences, University of South Florida, Tampa, Florida 33612 [^]H. Lee Moffitt Cancer Center and Research Institute, University of South Florida, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: ALAS, Heme Biosynthesis, Succinyl-CoA, Kinetics, CAST

Objective: 5-Aminolevulinate synthase (ALAS) catalyzes the condensation of glycine with succinyl-CoA to yield 5-aminolevulinate (ALA), coenzyme A, and CO₂. The reaction catalyzed by ALAS is the first and regulatory step in heme biosynthesis. The crystal structure of ALAS reveals that the adenosyl moiety of succinyl-CoA interacts with amino acids constituting a hydrophobic pocket located on the surface of the enzyme, whereas the succinate group of succinyl-CoA interacts with amino acids that are part of a glycine-rich stretch deep in the active site. To examine how permissive specific amino acids of the hydrophobic pocket and glycine-rich stretch of ALAS are to substitutions by other amino acids,

Methods: combinatorial active-site saturation test (CAST) was used to introduce mutations to specific set of amino acids in the hydrophobic pocket (i.e., at positions I214/K221) and glycine-rich stretch (T148/N150) of the enzyme.

Results: The mutagenic process generated 49 functional variants at positions I214/K221 and 15 functional variants at positions T148/N150. Differences in the steady-state kinetic parameters and catalytic efficiencies of selected variants as compared to the wild-type enzyme indicate that the mutations affect the catalytic functioning of the variants. Further, the transient-state kinetic parameters of selected variants and wild-type ALAS were examined under multiple-turnover conditions, indicating differences in the observed rate constants assigned to the steps of quinonoid intermediate formation and decay.

Conclusion: In conclusion, mutations in amino acids in the hydrophobic pocket and glycine-rich stretch of ALAS involved in the binding of succinyl-CoA affect the enzymatic steady and transient-state kinetic parameters.

Research supported by: American Heart Association

Multilayered Multifunctional Magnetic Micelle Nanoparticles (4M-NPs) for MRI and Gene Delivery Chunyan Wang(a,b), Sowndharya Ravi(a), Gary.V. Martinez(c), Vignesh Chinnasamy(a), Mark Howell(a), Yvonne Davis(a), Mohindar S. Seehra(d), Subhra Mohapatra(a,b,e) (a) Molecular Medicine Department, (b) Nanomedicine Research Center, Morsani College of Medicine, University of South Florida, Tampa, FL (c) H.Lee Moffit Cancer Center and Research Institute, Tampa, FL (d) Department of Physics, West Virginia University, Morgantown, WV (e) James A Haley VA Hospital, Tampa, FL

Keywords: multilayered multifunctional magnetic micelle nanoparticle (4M-NPs), magnetic resonance imaging (MRI), super paramagnetic iron oxide nanoparticles (SPIONs), gene delivery, theranostics

Objective: Gene therapy is a promising therapeutic approach for treating disease, but the efficient delivery of drugs to desired locations with minimal side effects remains a challenge. Herein, we report on the development of novel 4M-NPs that can deliver nucleic acid-based therapeutic agents and also provide magnetic resonance imaging (MRI).

Methods: The 4M-NPs were prepared by a multi-step reaction and characterized by FTIR, NMR, TEM, DLS and MRI. The cellular uptake of 4M-NPs was tested with TEM and confocal microscopy. The gene transfection efficiency was tested with luciferases assay. Cytotoxicity was tested on HEK293 and PC3 cells by WST assay. The biodistribution of 4M-NPs in mice was determined by Xenogen IVIS. The toxicity and in vivo gene delivery efficiency was tested in mice with H&E staining and fluorescent microscopy.

Results: These 'theranostic' 4M-NPs are composed of monodisperse hydrophobic superparamagnetic iron oxide nanoparticles (SPIONs) loaded into the cores of micelles that are self-assembled from a block copolymer of mPEG-PLA. The T2 relaxivity of micelles was similar to 4M-NPs confirming that coating with cationic polymers did not alter magnetism. 4M-NPs showed highly efficient transfection efficiency in HEK293, 3T3 and PC3 cells. 4M-NPs are biocompatible, can be delivered to various organs and are nontoxic. Genes delivered in vivo by 4M-NPs continued to be expressed for at least one week.

Conclusion: Our results demonstrate that a structural reinforcement of SPIONs loaded into the core of an mPEG-PLA micelle coated with cationic polymers provides efficient DNA delivery and enhanced MRI potential, and affords a promising candidate for theranostics in the future.

Research supported by: NIH and Florida Biomedical Research Funds

Phosphorylation of HDAC6 C-terminus by ERK1 Affects its Function and Interaction with its Cytoplasmic Substrates.

Kendra A. Williams, Mu Zhang, Shengyan Xiang, Bin Fang*, John Koomen*, Santo V. Nicosia, Wenlong Bai and Xiaohong Zhang. Morsani College of Medicine, Department of Pathology & Cell Biology. *Moffitt Cancer Center. University of South Florida, Morsani College of Medicine, Dept. of Pathology and Cell Biology

Keywords: histone deacetylase 6, migration, tubulin.

Objective: Histone deacetylase 6 (HDAC6) is involved in many biological processes including cell migration. Post-translational modification of HDAC6 emerges as an important mean to regulate HDAC6 function. This study aims to identify novel kinases which target HDAC6 and to study the biological consequences of HDAC6 phosphorylation.

Methods: Novel phosphorylation sites of HDAC6 were identified by mass spectrometry. In vitro kinase assay was performed to determine whether ERK1 phosphorylates HDAC6 in vitro and ERK inhibitors were used to determine whether ERK1 phosphorylates HDAC6 in vivo. Deacetylase assays of HDAC6 towards α -tubulin were performed using reconstituted microtubules as substrates. Binding of HDAC6 and its phosphorylation/dephosphorylation mimicking mutants to its cytoplasmic substrates α -tubulin was determined using immuno-complexes obtained from 293T cells transfected with Flag-tagged HDAC6 or mutants. HDAC6 deficient mouse embryonic fibroblast cells (MEFs) stably expressing Flag-tagged HDAC6 or mutants were used in transwell assays to determine how phosphorylation of HDAC6 affects cell migration.

Results: Serine1035 of HDAC6 was identified as a novel phosphorylation site targeted by ERK1 both in vitro and in vivo. HDAC6 S1035 mutant mimicking dephosphorylation harbors higher deacetylase activity and higher affinity towards α -tubulin compared with the phosphorylation-mimicking mutant. However, HDAC6 null MEFs rescued with phosphorylation mutant exhibit increased cell migration compare with cells expressing the dephosphorylation mimicking mutant.

Conclusion: This study illustrates that phosphorylation of HDAC6 by ERK1 increases HDAC6-mediated cell migration, which might be through novel substrates other than α -tubulin.

Research supported by: James & Ester King Biomed

Roles of Local Structural Flexibility in Methionine Oxidation

Kuiran Xu(Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa), Vladimir N. Uversky(Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa; Institute for Biological Instrumentation, Russian Academy of Sciences, 142290 Pushchino, Moscow Region, Russia), and Bin Xue(Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa) University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Methionine oxidation, intrinsic disorder, disorder score, flexibility, solvent accessible surface area

Objective: All amino acid residues in proteins are susceptible to oxidation, with methionine and cysteine residues being extremely sensitive to various reactive oxygen species (ROS). Methionine oxidation leads frequently to destabilization and inactivation of proteins. The oxidatively modified proteins can even accumulate under oxidative stress, in various diseases, and during the process of aging. Although the oxidation efficiency of a given methionine can depend on its solvent accessibility (evaluated from a protein structure as the accessible surface area of the corresponding methionine residue), the oxidation rate and oxidation sites in many experiments can not be unequivocally explained by the methionine solvent accessible surface area alone. New theories need to be developed to explain other possible mechanisms.

Methods: Bioinformatics analyses were implemented on a set of oxidized methionines contained in thirty-one proteins.

Results: In all the oxidized methionines, 41% of the methionines are exposed, 15% are buried but with various degree of flexibility, and the rest 44% are buried and structured. Buried but highly flexible methionines can be oxidized. Buried and less flexible methionines can acquire additional local structural flexibility from flanking regions to facilitate the oxidation. Oxidation of buried and structured methionine can also be promoted by the oxidation of neighboring methionine that is more exposed and/or flexible.

Conclusion: Our data are consistent with the hypothesis that protein structural flexibility represents another important factor favoring the oxidation process.

Impairment of Neurotransmitter and Neurotrophin Receptor Localization and Function in Alzheimer's Disease Caused by Inhibition of Kinesin Eg5

Csilla Ari, Sergiy I. Borysov: USF Byrd Alzheimer's Institute; Department of Molecular Medicine, Morsani College of Medicine; Eric Pfeiffer Suncoast Alzheimer's Center; Moffitt Cancer Center, Tampa, FL. Jiashin Wu: Department of Molecular Pharmacology and Physiology, Morsani College of Medicine, Jaya Padmanabhan, Huntington Potter: USF Byrd Alzheimer's Institute; Department of Molecular Medicine, Morsani College of Medicine; Florida Alzheimer's Disease Research Center, University of South Florida, Tampa FL; Eric Pfeiffer Suncoast Alzheimer's Center; Moffitt Cancer Center, Tampa, FL

Keywords: NMDA, p75, monastrol

Objective: Previous work showed that APP over-expression or A β treatment causes defects in the cell cycle (chromosome missegregation and aneuploidy), and also disrupts the cellular MT network and causes mis-localization of Low Density Lipoprotein Receptor (LDLR) in cultured neurons. Furthermore, polymorphisms linked to Eg5/KIF11 have been shown to increase AD risk. Our objective was to test whether amyloid- β or mutant PS/APP induced microtubule dysfunction causes impaired cell surface neurotransmitter and neurotrophin (such as p75 or NMDA) receptor localization and function and to identify the mechanism underlying this defect.

Methods: To test the effect of A β on receptor localization, H4 APP cells or A β -treated primary neurons in culture were examined by quantitative confocal microscopy. Immunoprecipitation was performed on Xenopus egg extract, mouse (E18) primary neurons and on the brain of PS1/APP transgenic mice. LTP was measured after monastrol or A β treatment. PC12 cells were used for neurite outgrowth experiments.

Results: In this study we found that the inhibition of neuronal Eg5 with either A β or Monastrol significantly reduced cell surface levels of neurotrophin (p75NTR) and neurotransmitter (NMDA) receptors and caused decreased neurite outgrowth and LTP.

Conclusion: These data imply that A β may prevent many key receptors from localizing effectively to the cell surface, including those for neurotrophins and neurotransmitters, potentially leading to the loss of learning and memory function in neurodegenerative diseases.

Research supported by: This study was supported by the Byrd Institute startup funds and the Eric Pfeiffer Chair and currently supported by NIH grants. SIPIN grant provided partial funding. We thank Michelle Norden for assistance with the surgical procedures.

Selective HDAC6 Inhibition Improves Spatial Memory Deficits in rTg4510 Mouse Model

Leif Benner¹, Jay Hans Kalin PhD², Alan Kozikowski² PhD, Marcia N Gordon PhD¹, Dave Morgan PhD¹, Maj-Linda B Selenica PhD¹ ¹ Byrd Alzheimer's Institute and Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa FL, USA. ²College of Pharmacy, Dept of Medicinal Chemistry and Pharmacognosy (MC 781), 833 South Wood Street Chicago, Illinois_University of South Florida

Keywords: HDAC, TAU, acetylation, microtubules, aggregation.

Objective: Histone deacetylases (HDACs) are a class of enzymes that regulate the removal of acetyl groups from histone and non-histone proteins. These changes are believed to regulate many vital cellular processes, implicated in many types of cancer and neurodegenerative disease. HDAC6 plays a key role in deacetylation of microtubules, which is believed to destabilize microtubules and promote pathological changes in tau protein causing intracellular aggregation. In this study we will determine the effect of a selective HDAC6 inhibitor on tau phosphorylation and aggregation. We will also determine the role of HDAC6 in neuroprotection and cognitive performance.

Methods: We used the rTg4510 mouse model that overexpresses the P301L mutant human Tau protein, as well as non-transgenic (WT) littermates. We treated half the mice in each group with either Tubastatin A, or .9% saline. The drug was administered through i.p. injection every day over a two month period. A battery of behavior tests was performed during the last two weeks of treatment.

Results: We found that mice treated with Tubastatin A performed significantly better on a spatial memory test (Two Day Radial Arm Water Maze, RAWM) than saline treated rTg4510 mice, $p = .0171$. There was a genotype specific effect on RAWM Reversal, Rotarod, and Open Pool, while no differences were found in Y-Maze. We have also performed immunohistochemical staining to assess the phosphorylation of tau by utilizing several p-tau epitopes, as well as aggregated tau (Gallyas). These are yet to be quantified.

Conclusion: Our data so far suggests that HDAC6 inhibition ameliorates memory deficits in the rTg4510 mouse model, positioning HDAC6 as a therapeutic target for AD and tauopathy.

Abstract #: 172**Presented by: Jessica Chang, PhD, Postdoc****TRAF6 and ALS**

Jessica N. Chang, Carrie L. Butler, Haris Hatic, and Bruce A. Citron Laboratory of Molecular Biology, Research and Development, Bay Pines VA Healthcare System and Department of Molecular Medicine, University of South Florida Morsani College of Medicine, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: ALS, motor neuron, TRAF6, TDP-43, NSC34

Objective: Amyotrophic lateral sclerosis (ALS) is a degenerative disease where motor neurons in the spinal cord selectively die for unknown reasons. Recently familial ALS mutations have been identified in the gene that encodes the TDP-43 protein. Model mice with these mutations also demonstrate progressive neuronal death. In these patients, model mice, and sporadic ALS cases, TDP-43 is misprocessed, forming toxic C-terminal fragments, and mislocalized to cytoplasmic aggregates. We seek to elucidate the responsible molecular mechanisms. TRAF6 is an E3 ubiquitin ligase that may participate in TDP-43 processing.

Methods: We measured the expression of TRAF6 in the spinal cords of TDP-43 A315T mutant mice with Western blots and monitored localization by immunohistochemistry. In culture, TRAF6 was overexpressed in the NSC34 model motor neurons and monitored for susceptibility to oxidative insult by propidium iodide staining.

Results: We observed elevated TRAF6 expression in the spinal cord of both male and female ALS model mice. The expression appeared to be predominantly cytoplasmic, but also involved the nucleus. Overexpression of TRAF6 protected the model neurons from oxidative stress.

Conclusion: The overexpression of TRAF6 in TDP43 mutant animals suggests that TRAF6 could play a role in motor neuron survival. TRAF6 may contribute to the misprocessing or mislocalization of TDP-43. Cell culture experiments indicate that TRAF6 is neuroprotective. Because TRAF6 is a known E3 ligase it may function to poly-ubiquitinate dysregulated TDP-43 resulting in its clearance from the cell.

Research supported by: Department of Veterans Affairs, The Bay Pines Foundation, and The James and Esther King Biomedical Postdoctoral Fellowship.

Overexpression of μ -Calpain in HEK293 Cells Increases the Secretion of Beta-Amyloid Precursor Protein

Huey T Nguyen, Darrell R Sawmiller and Ming Chen* Aging Research Laboratory, Bay Pines VA Healthcare System, University of South Florida Morsani College of Medicine Molecular Pharmacology & Physiology

Keywords: calcium, calpain, amyloid, aging, Alzheimer

Objective: A major mystery in the study of brain aging is the regulatory mechanism of alpha-processing of beta-amyloid precursor protein (APPs secretion). This process is highly sensitive to a wide variety of regulatory compounds, and many of which activate Ca^{2+} signaling and calpain, a Ca^{2+} -dependent protease. We therefore suggested that calpain is involved in APP alpha-processing. To test this idea, we transferred the u-calpain catalytic subunit gene into HEK293 cells and determined how this affected the calpain activity in the transfected cells and the levels of APPs secretion from the cells.

Methods: construction of the u-calpain gene-containing vector; gene transfection and calpain overexpression; assay for calpain enzymatic activity in situ and measurement of APPs secretion by Western blotting.

Results: (1) transfection of the u-calpain gene in HEK 293 cells resulted in a 2.1-fold overexpression of the enzyme levels compared to wild-type cells. (2) The calpain catalytic activity in the transfected cells is significantly increased over wild-type cells both in the resting cells or in the cells stimulated by nicotine, glutamate and PDBu (a phorbol ester), which are known for activating calpain in the cell. (3) APPs secretion in the transfected cells was robustly increased in the resting cells and upon stimulation by nicotine, glutamate and PDBu.

Conclusion: These data are consistent with the hypothesis that calpain somehow mediates APP α -processing. The information will help for an in-depth understanding of the mechanisms of amyloid plaque formation in the aging brain and developing new intervention strategies for delaying senile dementia.

Research supported by: Merit Review program from The US Department of the Veterans Affairs

Immediate, but not Delayed, Microsurgical Skull Reconstruction Exacerbates Brain Damage in Experimental Traumatic Brain Injury Model

Loren E. Glover*, Naoki Tajiri*, Tsz Lau, Yuji Kaneko, Harry van Loveren, Cesar V. Borlongan University of South Florida, Morsani College of Medicine, Dept. of Neurosurgery & Brain Repair

Keywords: TBI

Objective: Moderate to severe traumatic brain injury (TBI) often results in skull malformations. Aesthetic surgical maneuvers may normalize skull structure, but inconsistent surgical closure of the skull area accompanies TBI. We examined whether wound closure by replacement of skull flap and bone wax would allow aesthetic reconstruction of the TBI-induced skull damage without causing any detrimental effects to the cortical tissue.

Methods: Adult male Sprague-Dawley rats were subjected to TBI using the controlled cortical impact (CCI) injury model. Immediately after the TBI surgery, animals were randomly assigned to skull flap replacement with or without bone wax or no bone reconstruction; then euthanized five days post-TBI for pathological analyses.

Results: The skull reconstruction provided normalized gross bone architecture, but 2,3,5-triphenyltetrazolium chloride and hematoxylin and eosin staining results revealed larger cortical damage in these animals compared to those that underwent no surgical maneuver at all. Brain swelling accompanied TBI, especially the severe model, that could have relieved the intracranial pressure in those animals with no skull reconstruction. In contrast, immediate skull reconstruction produced an upregulation of the edema marker aquaporin-4 staining, probably preventing the therapeutic benefits of brain swelling resulting in larger cortical infarcts.

Conclusion: TBI animals introduced to a delay in skull reconstruction (i.e., 2 days post-TBI) showed significantly reduced edema and infarcts compared to those exposed to immediate skull reconstruction. That immediate, but not delayed, skull reconstruction may exacerbate TBI-induced cortical tissue damage warrants a careful consideration of aesthetic repair of the skull in TBI.

Multilayered Multifunctional Magnetic Micelle Nanoparticles for Delivery of DNA to Brains of Rats with Mild Traumatic Brain Injury

Mahasweta Das^{1,2}, Chunyan Wang^{1,3}, Subhra Mohapatra^{1,3,4}, and Shyam Mohapatra^{1,2,4} USF Morsani College of Medicine, Nanomedicine Research Center¹, Department of Internal Medicine Division of Translational Medicine², Department of Molecular Medicine³, and James A Haley Veteran's Hospital and Medical Research Center⁴, Tampa, FL

Keywords: Traumatic brain injury, nanoparticle, blood brain barrier, cortex.

Objective: Traumatic brain injury (TBI) causes significant mortality, long term disability and psychological symptoms; however, the mechanism underlying TBI pathogenesis is poorly understood. Although severe TBI compromises the blood-brain barrier, drug delivery to the brain remains a challenge with mild TBI. Here we tested multilayered multifunctional magnetic micelle nanoparticles (4MNPs) to deliver DNA to the brain after mild TBI.

Methods: Adult male SD rats were subjected to mild TBI using a lateral fluid percussion injury device or sham operated. 4MNPs were made according to Chunyan et.al, 2010 (USF Research day poster) and complexed with a plasmid expressing red-fluorescent protein (TdTomato). 4MNP-DNA complexes were injected intraperitoneally or given intranasally immediately after TBI or sham surgery. 24 or 48 hours later, rats were transcardially perfused with 4% PFA, brains were removed and sections stained with Fluoro-Jade to show neuronal injury or anti-DsRed antibody to see plasmid expression.

Results: Among different 4MNP-tdT conjugates, rats injected with 4M551-tdT showed plasmid expression in the choroid plexus while intranasally administered 4M551-tdT was expressed in the cortex 48 hours after TBI. The expression was more pronounced in the brain parenchyma of the olfactory lobe and in the rostral cortex of the ipsilateral side compared to more caudal areas or the contralateral side. Sham animals did not show any expression.

Conclusion: These results suggest that 4M551 can effectively carry DNA to the brain following mild TBI and can be used as potential diagnostic and therapeutic agent in TBI.

Research supported by: Veterans Reintegration Grant

Autoreactive-Abeta Antibodies Promote APP Beta-secretase Processing

Juan Deng^{1,2}, Huayan Hou¹, Brian Giunta^{1,3,7}, Takashi Mori⁴, Yan-Jiang Wang², Frank Fernandez^{1,3}, Sascha Weggen⁵, Wataru Araki⁶, Demian Obregon^{1,7}, and Jun Tan^{1,7,1} Rashid Laboratory for Developmental Neurobiology, Department of Psychiatry and Neurosciences, Morsani College of Medicine (MCOM), University of South Florida (USF), Tampa, ²Department of Neurology, Daping Hospital, Third Military Medical University, Chongqing, China ³Neuroimmunology Laboratory, Department of Psychiatry and Neurosciences, MCOM, USF, Tampa, ⁴Departments of Biomedical Sciences and Pathology, Saitama Medical Center and Saitama Medical University, Kawagoe, Saitama, Japan ⁵Department of Neuropathology, Heinrich-Heine-University, Düsseldorf, Germany ⁶Department of Demyelinating Disease and Aging, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Kodaira, Tokyo, Japan ⁷James A. Haley Veterans' Administration Hospital, Tampa, University of South Florida, Morsani College of Medicine, Dept. of Psychiatry and Neuroscience

Keywords: Alzheimer's disease; auto-Abeta antibodies; APP amyloidogenic processing; anti-N-terminal Abeta antibodies; Abeta40, 42 peptides

Objective: not only bind to Abeta, but bind also to APP, and while the concentrations and binding of anti-Abeta antibodies to Abeta have been extensively studied, knowledge of their functional effects on APP processing is unknown. □ Many autoantibodies targeting Abeta

Methods: We screened serum autoantibodies from AD patients and non-demented age-matched controls for their ability to alter APP processing in Chinese hamster ovary (CHO) cells engineered to overexpress Swedish mutant APP and human wild-type presenilin-1 (PS1wt)(CHO/APPswe/PS1wt). Monoclonal antibodies to various regions of Abeta were also screened for APP processing effects in CHO/APPswe/PS1wt cells. We delivered monoclonal antibodies targeting this Abeta1-17 region via intracerebroventricular (ICV) injection into transgenic AD model mice overexpressing both APPswe and mutant human PS1 (PSAPP mice).

Results: We show that naturally occurring Abeta-reactive autoantibodies isolated from AD patients promote beta-secretase activity in cultured cells. Further, using monoclonal antibodies to various regions of Abeta, we found that antibodies generated against the N-terminal region, especially Abeta1-17, dose dependently promoted amyloidogenic processing of APP via beta-secretase activation.

Conclusion: This property of certain autoantibodies in driving Abeta generation could be of etiological importance in the development of sporadic forms of AD. Future passive or active anti-Abeta immunotherapies must consider potential off-target effects resulting from antibodies targeting the N-terminus of Abeta, as co-binding to the corresponding region of APP may actually enhance Abeta generation.

Research supported by: supported by the NIH/NIA (R01AG032432 and R42AG031586, J.T.) and a Veterans Affairs Merit grant (J.T.)

Activity-dependent Expression of Ube3a.

Irina Filonova, Edwin J. Weeber USF Health Byrd Alzheimer's Center, Department of Molecular Pharmacology and Physiology, University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: Angelman syndrome, Ube3a, activity-dependent expression, imprinting

Objective: Angelman Syndrome is a devastating neurological disorder caused by defects in Ube3a gene. The absence of Ube3a is linked to severe neurological symptoms in humans, abnormal spine development and defects in synaptic plasticity in mice. Although localization and expression profiles of Ube3a have been extensively evaluated, the mechanism whereby Ube3a deficiency results in AS is an enigmatic. Present work focuses on the investigation of neuronal activity-dependent alteration in Ube3a expression that will expand our current knowledge of Ube3a and Ube3a gene product and allows us to investigate new therapeutic targets for AS treatment.

Methods: Using in vitro systems (primary neuronal culture, acute hippocampal slices) we have determined changes in Ube3a during neuronal activation. Our in vivo (fear conditioning paradigm) studies have addressed temporal and regional alteration in Ube3a protein during learning and memory formation.

Results: Using in vitro and in vivo systems we found dramatic changes in the expression of Ube3a following synaptic activation and memory formation. These observations showed a potential dynamic nature to Ube3a gene which has been previously thought to have static expression. We further found that Ube3a is subjected to temporal and spatial regulation during neuronal activity in mouse brain. In addition, we demonstrated that imprinted paternal Ube3a copy has an expressional profile similar to the maternal gene that could be activated by neuronal stimulation.

Conclusion: This work expands our knowledge about activity-dependent Ube3a expression. It is important to understand changes induced by synaptic stimulation not only in total Ube3a protein, but also changes in both maternal and paternal Ube3a gene products.

Characterization of the Mechanism of Production and Functional Significance of a Novel, Caspase-Dependent Fragment of Amyloid Precursor Protein

Tina Fiorelli, Lisa Hornbeck, Jaya Padmanabhan, Department of Molecular Medicine, University of South Florida, USF Health Byrd Alzheimer's Institute, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Apoptosis Caspase Alzheimer's Disease Amyloid Neurodegeneration

Objective: Variation in the processing of the amyloid precursor protein (APP) is considered one of the central aspects of Alzheimer's disease (AD) pathogenesis. Our lab has observed the production of a novel, 207 amino acid C-terminal fragment of APP (C207) generated under DNA-damaging conditions. Here, we investigate the mechanism by which this fragment is generated, as well as the functional significance of C207.

Methods: Lysates from camptothecin (CPT) treated H4 neuroglioma cells overexpressing APP were analyzed by western blot. Candidate caspases were identified after bioinformatic analysis of the APP sequence and inhibited using small peptides and shRNA. Localization of the caspases and APP in primary neurons was observed by immunocytochemistry (ICC) and differential centrifugation followed by western blot. Finally, C207 expressing HEK-293 cells were analyzed by western blot.

Results: Treatment with CPT results in production of a novel peptide fragment detectable by three independent APP antibodies. Bioinformatic analysis identified caspases 3 and 7 as capable of generating this fragment. Inhibition of these caspases results in decreased production of C207. Subcellular localization suggests that this cleavage may occur in an intracellular compartment. Expression of the C207 fragment suggests that its further processing may be relevant to AD pathogenesis.

Conclusion: APP is cleaved by a group II caspase in the extracellular domain. Subcellular localization of caspase 7 during apoptosis is consistent with cleavage occurring within an intracellular compartment. The C207 fragment can then be further processed into C99 and amyloid beta, suggesting that the C207 fragment may contribute to AD pathology development.

Research supported by: NIH, Alz. Assoc., USF/Byrd

Neonatal Rat Brain Mounts A Rapid Endogenous Anti

Loren E. Glover, Naoki Tajiri, Jared Ernhart, Jun Tan, Yuji Kaneko, Cesar V. Borlongan, Department of Neurosurgery and Brain Repair, University of South Florida College of Medicine, 12901 Bruce B. Downs Blvd, Tampa FL 33612, University of South Florida, Morsani College of Medicine, Dept. of Neurosurgery & Brain Repair

Keywords: cerebral palsy, stem cell transplantation, inflammation, neuroprotection

Objective: In a recent study we reported the importance of timing of therapeutic intervention in experimental traumatic brain injury (TBI) (Glover et al., 2012 in press), accompanied by genetic and histologic inflammation and apoptosis (Borlongan and colleagues, 2009, 2010) in early stage of the injury. Although the immediate cell death cascade accompanies adult models of TBI, the pathophysiology of the neonatal TBI is poorly understood. The present study examined the role of cytokine regulation following TBI in neonatal rats.

Methods: Seven-day old Sprague-Dawley rats were subjected to TBI using the controlled cortical impact (CCI) injury model. Age-matched littermates exposed to sham surgery served as controls. Within 15 minutes after TBI, rats were euthanized, and their brains and plasma processed for a BioRad 23-Plex cytokine assay.

Results: To our surprise, 18 of the 23 cytokines analyzed were significantly downregulated in the hemisphere contralateral to the TBI impacted hemisphere. IL-5, IL-6 and MIP-3a were significantly suppressed in both hemispheres of TBI rats compared to controls, indicating a massive cytokine downregulation. Plasma assay revealed no significant alterations in any the same cytokines examined here.

Conclusion: In stark contrast to the early upregulation of inflammatory response markers in adult TBI, the neonatal brain downregulated brain cytokine levels, suggesting a robust endogenous anti-inflammatory response that was mounted unexpectedly by a brain area remote from the site of injury, i.e., the contralateral hemisphere. The plasticity of the neonatal brain, shown here to be equally capable of cytokine regulation following TBI, may be responsible for the supra-acute regenerative process.

Research supported by: USF Department Neurosurgery & Brain Repair

Genomic Instability in Human and Mouse Neurodegenerative Tauopathies, Frontotemporal Dementia and Niemann-Pick Disease Antoneta Granic (^{1,2,4}), Michelle Norden (^{1,2}), Dennis W. Dickson (⁵), and Huntington Potter (^{1,2,3,4}) (¹)Byrd Alzheimer's Center and Research Institute at USF Health; (²)Department of Molecular Medicine, Morsani College of Medicine at USF Health; (³)Eric Pfeiffer Suncoast Alzheimer's Center, USF Health; (⁴)School of Aging Studies, College of Behavioral and Community Sciences, USF; (⁵) Department of Neuroscience (Neuropathology), Mayo Clinic, Jacksonville

Keywords: aneuploidy, microtubule dysfunction, fluorescence in situ hybridization (FISH)

Objective: This study sought to investigate the novel role of protein tau in genomic stability and mitosis in two human tauopathies, frontotemporal dementia (FTD) and Niemann-Pick disease (NPC). We hypothesized that, as in Alzheimer's disease (AD), microtubule (MT) dysfunction may be a common pathological trait of other neurodegenerative diseases that leads to chromosomal instability and aneuploidy, and results in apoptosis-prone neurons, tauopathy and cognitive impairments.

Methods: To investigate the levels of chromosomal instability in FTD and NPC we used FISH analysis and DNA probes for chromosome 21 and 12 on 1) brain cells of patients diagnosed with FTD and age-matched controls; 2) spleen and brain cells of 8 months old mice harboring the P301S Tau mutation; 3) human cells with normal karyotype transiently transfected with mutant Tau genes; and 4) neurons, glia and fibroblasts of NPC patients with NPC1 mutation.

Results: Our data indicate that, similar to familial AD caused by mutations in APP and PS, mutated Tau and NPC1 genes also participate in mitosis, and contribute to genomic instability, including trisomy 21 mosaicism in FTD and NPC. Brain cell from FTD patients harbored up to 6.5% aneuploidy, and mice expressing the P301S Tau mutation developed a 2-fold increase in trisomy 16 in spleens and brains. NPC neurons, glia and fibroblasts developed a 4- to 6-fold increase in trisomy 21 compared to control cell.

Conclusion: These results indicate that the presence of MT dysfunction in FTD and NPC, and consequent mitotic spindle errors may lead to chromosomal instability and development of aneuploid apoptotic neurons and neural progenitors, contributing to neurodegeneration.

Research supported by: Eric Pfeiffer Chair for Research on Alzheimer's Disease, NIA (AG025711, AG037942)

Minocycline Ameliorates Cognitive and Motor Deficits in the Angelman Syndrome Mouse Model

Joseph Grieco, Erika Donaldson, Ashley Sponaugle, Justin Roger, Edwin Weeber University of South Florida, Morsani College of Medicine, Department of Molecular Pharmacology and Physiology

Keywords: Minocycline, Angelman, Syndrome, synaptic plasticity, tetracycline

Objective: The objective of this study is to determine if minocycline has the ability to ameliorate the cognitive and motor deficits experienced by the Angelman syndrome mouse.

Methods: Minocycline was injected into a murine model of AS for a period of 21 days. A battery of behavioral testing including open field, rotorod, prepulse inhibition and associative fear conditioning was performed. The animals were then euthanized and acute hippocampal slices were made for electrophysiological testing.

Results: The results of these studies show a marked improvement in synaptic function in CA1 region of the hippocampus following high frequency stimulation. A profound defect in hippocampal LTP induction is seen in saline injected AS mouse model controls. In comparison, MC treated mice show hippocampal LTP equal to that of wild type littermate controls. The motor coordination defect determined by latency to fall on an accelerating rotorod was improved and equivalent to that of wild type controls. Finally, an increase in freezing behavior to the context is indicative of increased memory retention. These three parameters represent the strongest changes in behavioral and physiologic phenotypes of the AS mouse model with a brief exposure to MC.

Conclusion: The administration of minocycline recovered the motor coordination and associative learning deficits in the AS mouse model. Take together with an observed increase in long term potentiation, the results indicate minocycline may normalize synaptic plasticity and improve cognitive function in the AS mouse model.

Research supported by: The Foundation for Angelman Syndrome Therapeutics. Edwin Weeber, Ph.D., Principal Investigator

Modulation of Transcription Factors in Traumatic Brain Injury

Haris Hatic¹, Lital Rachmany³, Vardit Rubovitch³, Chaim G. Pick³, Jessica N. Chang^{1,2}, Bruce A. Citron^{1,2} ¹Laboratory of Molecular Biology, Research & Development 151, Bay Pines VA Healthcare System, Bay Pines, FL 33744 ²Department of Molecular Medicine, University of South Florida Morsani College of Medicine ³Department of Anatomy and Anthropology, Sackler School of Medicine, Tel Aviv University University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: Traumatic Brain Injury, Transcription Factor, Neuroprotection, Nrf2, Apoptosis

Objective: Traumatic brain injury (TBI) is currently untreatable, afflicts approximately 1.4 million people annually in the United States, and has a worldwide incidence of about 0.5% per year. We have identified several regulatory molecules important to the health of neurons in the brain. We hypothesize that modulation of certain inflammatory responsive transcription factors after TBI may be neuroprotective.

Methods: We tested tissue culture and mouse models of mild TBI. SH-SY5Y neuroblastoma cells were mechanically injured and evaluated with Annexin staining, metabolic (MTS), and cell lysis (LDH release) assays. The effects of tBHQ (tert-butylhydroquinone), an activator of Nrf2, were analyzed with EMSAs, Western immunoblots, immunohistochemistry, and qRT-PCR. A closed head injury of mice was tested for the effects of tBHQ treatment on visual memory tests and the expression of HSP70.

Results: We found that injured cells that were treated with tBHQ displayed improved cellular viability. tBHQ also increased overall Nrf2 expression and nuclear translocation and resulted in elevated expression of downstream genes Trx1, Trx2, and HSP70. Inhibition of HSP70 caused greater neuronal loss after injury, even in the presence of tBHQ. In mice, we found that tBHQ enhanced post-mTBI visual memory and the expression of HSP70 in the brain.

Conclusion: Nrf2 activation may be neuroprotective after mild TBI through the induction of HSP70. The insights gained from the mouse and tissue culture models can aid in the identification of useful and effective therapeutic interventions to protect the brain from injury.

Research supported by: Department of Veterans Affairs, Florida Department of Health, USF Signature Interdisciplinary Program in Neuroscience, and the Bay Pines Foundation.

Gastric CO₂ Output Via the Esophagus Increases During Systemic Hypercapnia in Anesthetized Cat

Heather E. Held¹, Jay B. Dean¹, Bruce G. Lindsey, Teresa C. Pitts², Melanie J. Rose², Ashley Mortensen², Justine N. Nicholas², David Baekey, Paul Davenport², Donald C. Bolser²: ¹Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL, ²Department of Physiological Sciences, University of Florida, Gainesville, FL, University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: hypercapnia, gastric acid production, gastric ventilation

Objective: The stomach extracts arterial CO₂ during respiratory acidosis to produce HCl & HCO₃⁻, which react in the lumen to re-form CO₂. This study tested the hypothesis that hypercapnia stimulates gastric CO₂ removal via the esophagus.

Methods: Tracheal and esophageal CO₂ (PEsCO₂) and flows were measured in 13 anesthetized, pyloric occluded cats. Tracheal and gastric CO₂ output (VGCO₂) and gastric minute ventilation (VG) were calculated during tracheal air breathing for 30min (Control) and CO₂ breathing: 10%CO₂ in air (1hr), recovery in air (30min), followed by 6x10min alternating paired bouts of 10%CO₂ and air (10CO₂, 10air).

Results: CO₂ breathing increased PEsCO₂ above control 77% after 1hrCO₂ and 123% during 10CO₂. Coughing revealed more CO₂ was present in the stomach: PEsCO₂ increased 134% (in air) and 115% (after 1hrCO₂) compared to pre-cough PEsCO₂. VGCO₂ ranged from 0-15% (=2.5%) of total CO₂ output during 1hrCO₂-2. VG was 27% higher during 10CO₂ versus 10air. Relative to control, VG increased 95% after 1 hrCO₂ and 148% after the first bout of 10minCO₂.

Conclusion: The results show a dynamic, supplemental CO₂-eliminating response by the gastroesophageal system during systemic hypercapnia.

Research supported by: NIH HL89104, HL103415 & ONR

Microvascular Impairment in the Brain and Spinal Cord of ALS Patients

Diana G Hernandez-Ontiveros¹, Maria CO Rodrigues¹, Aric Frisina-Deyo¹, Cesario V Borlongan^{1, 2}, Paul R Sanberg^{1, 2}, Svitlana Garbuzova-Davis^{1, 2, 1}: ¹Center of Excellence for Aging and Brain Repair, ²Department of Neurosurgery and Brain Repair, University of South Florida, College of Medicine, Tampa, USA, University of South Florida, Morsani College of Medicine, Dept. of Neurosurgery & Brain Repair

Keywords: Amyotrophic Lateral Sclerosis, blood-brain barrier, blood-spinal cord barrier, vascular pathology.

Objective: ALS is a neurodegenerative disease characterized by motor neuron degeneration in the brain and spinal cord resulting in progressive muscle weakness, paralysis and death. Blood-brain barrier (BBB) and blood-spinal cord barrier (BSCB) impairment has been suggested as a key factor involved in ALS pathogenesis. In the G93A SOD1 rodent model of ALS, structural and functional alterations of the BBB/BSCB have been detected in the pre-symptomatic disease stage, worsening with disease progression. We hypothesized alterations to the microvascular integrity of the BBB/BSCB in ALS patients.

Methods: Capillaries in grey and white matter of medulla, cervical and lumbar spinal cord post-mortem tissues, obtained from tissue banks, from 25 ALS patients and 18 age-matched control subjects were analyzed for structural (electron microscopy) and functional integrity (immunohistochemistry). Tight junction protein expressions were also evaluated (Western blot).

Results: Ultrastructural analysis of capillaries in ALS tissues confirmed endothelial and pericyte cell damage, intra- and extra-cellular edema, and a large accumulation of collagen around the basement membrane. Western blot analysis revealed downregulation of tight junction proteins in both gray and white matter capillaries. IgG vascular leakage was detected by immunohistochemistry, indicating BBB/BSCB disruption. Staining for CD31 (PECAM-1) and CD105 (endoglin) revealed ill-defined vessel margins and discontinuities in the endothelial lining accompanied by asymmetrical increases in the capillary wall extensions.

Conclusion: These results demonstrate brain & spinal cord microvascular alterations in ALS that could indicate substantial BBB/BSCB impairment.

Research supported by: Supported by the Muscular Dystrophy Association (Grant #92452).

Molecular Determinants of Intracellular Calcium Dysregulation During Concurrent Ischemia and Acidosis in Neurons

Whitney Hethorn, Geoffrey Ciarlone, Lisa Kirouac, Christopher Katnik, Javier Cuevas, College of Medicine, Department of Pharmacology and Physiology; University of South Florida, Tampa, FL University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: Ischemia, Acidosis, Stroke, Calcium Dysregulation

Objective: During ischemic stroke, cells in the region affected by loss of perfusion experience ischemia and acidosis. Our laboratory has shown these two factors act synergistically to promote an influx of calcium into the neurons, depolarizing the cells, and causing cell death. Experiments were performed in rat cortical neurons to determine the molecular mechanisms responsible for the $[Ca^{2+}]$ dysregulation. We used a pharmacological approach to determine if HCN, TASK or TRPM7 channels are involved in the synergistic effect.

Methods: Cultured cortical neurons from embryonic rats were exposed to ischemia and/or acidosis. Calcium imaging was carried out to assess the effects of three ion channel blockers: cesium, barium, and 2-APB on the ion channels HCN, TASK, and TRPM7, respectively. Fura-2 dye was utilized in fluorescent imaging to measure the amount of cytosolic free- Ca^{2+} . Patch-clamp electrophysiology was carried out to measure ischemia and acidosis activated membrane currents.

Results: Compared to the control, Ba showed a significant decrease in the area and peak levels, as well as an increase at baseline. Cs showed a decrease in the peak. A combination of Cs and Ba only showed an increase in baseline $[Ca^{2+}]$. 2-APB revealed a significant decrease in the area as well as the peak.

Conclusion: The increases in $[Ca^{2+}]$ at baseline indicate that these drugs also block some K^{+} channels, leading to depolarization of the cell. A significant decrease of intracellular $[Ca^{2+}]$, as measured by the area under the curve, was seen in Ba and 2-APB. This decrease in $[Ca^{2+}]$ provides insight into what ion channels may be contributing the influx of Ca^{2+} (TASK and TRPM7 channels), and a potential target for further studies and possible therapies.

Research supported by: Supported in part by an AHA GIA to JC

Cyclosporine a Treatment Abrogates Ischemia-Induced Neuronal Cell Death By Preserving Mitochondrial Function By Upregulating The Parkinson's Disease Protein DJ-1

Yuji Kaneko, Naoki Tajiri, Loren E. Glover, and Cesar V. Borlongan University of South Florida Morsani College of Medicine Neurosurgery & Brain Repair

Keywords: Cyclosporine A, Parkinson's disease, DJ-1, stroke, mitochondrial function

Objective: Under hypoxic ischemia condition, the mitochondrial membrane potential ($\Delta\psi_m$), respiratory-related enzymes, and mitochondrial DNA deteriorate resulting in the aberrant accumulation of free radicals and reactive oxygen species. CsA, an immunosuppressant drug, has been shown as a potent neuroprotectant against neuronal cell death. However, the molecular mechanism by which CsA interacts with mitochondrial membrane-associated proteins remains not fully understood. Using the in vitro stroke model of oxygen glucose deprivation (OGD), we examined this interaction between CsA and the Parkinson's disease protein DJ-1, which has been recently implicated in the regulation of mitochondrial function.

Methods: Primary rat neurons were exposed to the OGD and processed for immunocytochemistry and ELISA to reveal the role of DJ-1 in CsA modulation of mitochondrial function. ATP content, hexokinase activity, and mitochondrial DNA (mtDNA) stability were measured by a bioluminescence assay kit.

Results: Administration of CsA before stroke onset, but not after stroke, afforded significant neuroprotective effects, characterized by the following cellular and molecular events: 1) CsA prevented the mitochondria-dependent cell death signaling pathway involved in cytochrome c induced apoptosis; 2) CsA protected cellular ATP decline without altering the hexokinase activity and the $\Delta\psi_m$; (3) blocked mtDNA degradation, and; 4) enhanced secretion of DJ-1 into neighboring cells.

Conclusion: These novel observations indicate that CsA- and DJ-1-neuroprotection amplify the maintenance of mitochondrial function, and that mitochondria-based treatments targeting the early phase of disease progression may prove beneficial in stroke.

Research supported by: USF Department of Neurosurgery and Brain Repair Funds

Cell Cycle Mediated Hyperphosphorylation of APP and its Role in Alzheimer's Disease Pathogenesis

Lisa Kirouac, Tina Fiorelli, Jaya Padmanabhan, Department of Molecular Medicine, University of South Florida, USF Health Byrd Alzheimer's Institute, University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: Amyloid Precursor Protein Cell cycle Alzheimer's disease A β C-terminal APP

Objective: Aberrant expression of cell cycle regulatory proteins in vulnerable neuronal populations plays a key role in Alzheimer's disease (AD) pathogenesis. Our studies show that amyloid precursor protein (APP) is phosphorylated in a cell cycle-dependent manner. Here, we examined if cell cycle activation is necessary for the phosphorylation and processing of APP.

Methods: H4 neuroglioma cells overexpressing APP (H4-APP) were synchronized by serum starvation and treated with various cell cycle inhibitors in the presence and absence of serum. Western blotting was used to analyze total APP, phosphorylated APP (P-APP), A β , and C-terminal fragment of APP (C-APP) using antibodies. Immunostaining analysis was performed to visualize cellular distribution of phosphorylated APP under different treatment conditions.

Results: Phosphorylation of APP was evident only in cells stimulated with serum. Cells arrested in the G2/M phase of cell cycle showed maximum phosphorylation, with nocodazole treatment showing significantly higher levels of P-APP. Similarly, generation of C-APP was visible only in serum stimulated cells with an increase in nocodazole and taxol treated cells. These findings were further supported by immunostaining analysis.

Conclusion: Our studies show that phosphorylation and processing of APP are cell cycle-dependent. Analysis of phosphorylation in cells arrested at different phases of cell cycle reveals that maximum phosphorylation at Thr668 occurs in G2/M phase of cell cycle. Further, immunostaining analysis suggests that phosphorylation of APP occurs as cells enter cell cycle indicating neurons that are subjected to any cell cycle deregulation may show altered processing of APP and associated neurodegeneration.

Research supported by: NIH, Alzheimer's Association, USF/Byrd

Neuronal Nicotinic Acetylcholine Receptors (nAChRs) Are Involved in Nicotine-Mediated Reversal of Ataxia in an Animal Model

Chase S Lambert, Rex M Philpot, Melanie E Engberg, Lynn Wecker, University of South Florida, Department of Psychiatry and Neurosciences, Tampa, FL. University of South Florida, Morsani College of Medicine. Dept. of Molecular Pharmacology & Physiology

Keywords: Neuronal Nicotinic Acetylcholine Receptors; Ataxia

Objective: Clinical data indicate that the neuronal nicotinic acetylcholine receptor (nAChR) partial agonist varenicline ameliorates abnormalities in gait and balance in patients with spinocerebellar ataxia type 3, but the mechanisms involved have not been investigated. The goal of this study was to determine whether nicotine (Nic) could improve gait in an animal model of ataxia and whether this effect was mediated by an action at nAChRs.

Methods: Following baseline assessment of locomotor activity and gait, male Sprague-Dawley rats received injections of the neurotoxin 3-acetylpyridine (3-AP) to preferentially destroy the olivocerebellar pathway, and behaviors were reassessed one week later. Subsequently, animals received daily injections of either saline or mecamylamine (Mec, 1 mg/kg), followed 30 minutes later by either saline or Nic (1 mg/kg) for 1 week.

Results: The administration of 3-AP led to a 21-23% decrease in distance moved and velocity of movement, an 8% decrease in hindpaw stride length and a 25% increase in stride width. Nic administration for 1 week did not alter locomotor activity or velocity, but did improve hindpaw stride length and width, effects that were prevented by prior Mec administration.

Conclusion: Results indicate that activation of nAChRs are of benefit in an animal model of olivocerebellar degeneration. Current experiments include determining the specific nAChRs involved, the cellular mechanism mediating this effect, and further investigating changes in gait following 3-AP and drug treatment with the use of a treadmill.

Research supported by: Supported by NIH #NS072114-01

Human Apolipoprotein E Isoform-Dependent Changes Amyloidogenic Processing of Amyloid Precursor Protein in a Mouse Model of Alzheimer's Disease.

Qingyou Li¹, Justin. H. Trotter¹, Mindy Peters¹, Jennifer Voegler¹, Erika Donaldson¹, MaryJo LaDu² and Edwin.J. Weeber¹. ¹Department of Molecular Pharmacology and Physiology, USF Health Byrd Alzheimer's Disease Institute, University of South Florida, Tampa, FL ²Department of Anatomy and cell biology, University of Illinois at Chicago, Chicago, IL University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology

Keywords: Alzheimer's disease, Amyloid beta, ApoE, APP, Tg mouse

Objective: Increased production or decreased clearance of Amyloid β (A β), which derive from the amyloidogenic process of amyloid precursor protein (APP) by two proteases, β - and γ -secretases, induce the amyloid plaque pathological hallmark of Alzheimer's disease (AD). Apolipoprotein E (apoE) is involved in the both processes as an isoform-dependent manner. In contrast to an established role of apoE isoforms in clearance of A β the extent to which apoE isoforms influence the processing of APP is unclear. To investigate how the human apoE isoforms alter the production of A β , by modulating APP processing,

Methods: we bred mice of apoE target-replacement (TR) to mice expressing 5 familial Alzheimer's Disease mutations (5XFAD) generating apoE-TR/5XFAD (EFAD) mice in which each isoform of human apoE (as well as no apoE) express with a massive A β production.

Results: We first evaluated whether apoE respond to the processing of APP or A β and found that apoE protein level was increased by 12% in E2FAD, 54% in E3FAD and 123% in E4FAD when compare with the apoE isoform matched apoETR littermates. We next assess whether presence or absence of apoE changes the amyloidogenic processing of APP and found that apoE2 and apoE3 lower the level of full length APP, delay A β burden in brain of young EFAD mice relative to apoE-null-FAD mice. And in contrast to apoE4, the apoE2 as well as E3 decrease APP, β -CTF level and A β deposition through modulating the β -site APP cleaving enzyme 1, a major β -secretase in 12-month-old EFAD mice.

Conclusion: Taken together, these data indicate that human apoE isoforms differentially alters accumulation of A β by affecting on processing of APP and changes in AD pathogenesis.

Temperature-Dependent Hypothermia Reduces Mitochondrial Dysfunction after Neonatal Encephalopathy

Mayo-Perez, Amora, MS.,¹ Kaneko, Yuji, Ph.D.,¹ Tajiri, Naoki, P. T., Ph.D.,¹ Glover, Loren E, MS.,¹ and Borlongan, Cesar V., Ph.D.¹ ¹Center of Excellence for Aging & Brain Repair, Department of Neurosurgery & Brain Repair, University of South Florida College of Medicine, University of South Florida, Morsani College of Medicine, Dept. of Neurosurgery & Brain Repair

Keywords: cerebral palsy, hypothermia, neuroprotection, animal model, translational medicine

Objective: Neonatal encephalopathy (NE) is a serious condition that can lead to mortality and long term disability. Recent clinical trials have shown that hypothermia provides neuroprotection in infants suffering from NE. However, the optimal regimen of hypothermia for treating NE remains not fully determined. Here, the optimal temperature for hypothermia treatment was evaluated in vitro using primary neuronal cells exposed to oxygen-glucose deprivation (OGD).

Methods: Primary rat neuronal cells (gestational age day 18) were exposed to OGD to model NE. After OGD treatment, the cells were exposed to normal oxygen and glucose concentrations for 5 hours (short-term) and 24 hours (long-term) at temperature 25°C, 34°C and 37°C which corresponded to severe hypothermia, moderate hypothermia, and normothermia, respectively. Mitochondrial activity of each temperature condition was measured at 5 hours and 24 hours post-OGD to assess the secondary energy failure through ATP production of the cells, a key component in cell death.

Results: Moderate hypothermia attenuated the OGD-induced reduction in mitochondrial activity, whereas severe hypothermia worsened the dysfunctional mitochondrial activity after OGD compared to OGD under normothermic condition. Moderate hypothermia was shown to reduce secondary energy failure in primary rat neuronal cells exposed to OGD.

Conclusion: This temperature-dependent therapeutic benefit of hypothermia likely capitalizes on the relationship between temperature and metabolic rate. Further studies are underway to reveal the optimal timing of initiation of hypothermia post-OGD in NE models.

Research supported by: USF Department of Neurosurgery and Brain Repair

Differential Regulation of Adult Hippocampal Neurogenesis by an NMDAR Antagonist: Protective and Toxic Effects

Shonali Midha¹, Dolores L. Collado-Morente², Sally Wingsze Leung³, Elizabeth M. Sajdel-Sulkowska, DSc², Bruno A. Benítez, MD⁴, Gabriel A. de Erausquin, MD, PhD¹, Daniel G. Herrera, MD, PhD² ¹University of South Florida, Morsani College of Medicine, Dept. of Psychiatry and Neurosciences, ²Brigham and Women's Hospital, ³SUNY Downstate College of Medicine, ⁴Washington University in St. Louis

Keywords: Neurogenesis, dentate gyrus, MK-801, NMDA, EGCG

Objective: Adult neurogenesis in the dentate gyrus (DG) has been shown to be enhanced by a mechanism thought to involve N-methyl-D-aspartate receptor (NMDAR) blockade and adrenal steroids. However, administration of NMDAR antagonists has been shown to both stimulate and impair neurogenesis. Our study was designed to resolve this apparent contradiction by testing the hypothesis that acute or chronic NMDAR antagonist administration at various times after cell birth would result in differential effects on neurogenesis. We further hypothesized that this effect is due to increased oxidative stress and therefore, should be prevented by antioxidants.

Methods: Adult male mice were treated under acute and chronic paradigms with the NMDAR antagonist MK-801, and survival of proliferating neurons was measured after exposure to cell proliferation marker 5-Bromo-2-deoxyuridine (BrdU). Neurogenesis and characterization of specific cellular sub-populations were determined by immunohistological staining for BrdU, Ki67, DCX, PSA-NCAM, and neuronal degeneration was estimated with Fluorojade C.

Results: Neuronal precursors were found to be most vulnerable following chronic MK-801 administration in the second week after cell birth. In addition, we found that chronic administration of MK-801 increases hippocampal oxidative stress. The impairment in neurogenesis could be prevented by concurrent administration of (-)-epigallocatechin gallate (EGCG).

Conclusion: Our data indicate that the effects of NMDAR antagonists on proliferation of new neurons is dependent on the maturational stage of new neurons. These results have important implications for the understanding of neuropsychiatric disorders in which neurogenesis is altered as well as for the clinical applications of NMDAR antagonists.

Abstract #: 192**Presented by: Raffaele Pilla, PhD, Staff*****Pseudoephedrine (PSE) Enhances Seizure Onset During Deep Dives at 5 Atmospheres Absolute (ATA) in Unanesthetized Rats***

Raffaele Pilla, Heather E. Held, Carol S. Landon, and Jay B. Dean University of South Florida Morsani College of Medicine Molecular Pharmacology & Physiology

Keywords: Pseudoephedrine, Dive, Oxygen Toxicity, Seizures, Hyperbaric

Objective: PSE salts (hydrochloride and sulfate) are commonly used as nasal and paranasal decongestant by scuba divers. PSE is rapidly reduced, resulting in a stimulant action due to direct and indirect activation of α - and β -adrenoceptors. This stimulation causes vasoconstriction, due to muscle contraction. Prior to a deep dive breathing pure O₂ (i.e., Nitrox or rebreather), PSE can augment the risk of CNS oxygen toxicity (CNS-OT; i.e., seizures), according to anecdotal reports from Divers Alert Network (DAN). We hypothesized that high doses of PSE reduces latency to seizure in unanesthetized rats breathing a toxic dose of hyperbaric O₂ (5 ATA)

Methods: 54 Adult male Sprague-Dawley rats (200-300 grams) were implanted with a radio-transmitter for recording EEG, core body temperature, and physical activity. After ≥ 7 day recovery, rats were administered with saline solution (control) or PSE hydrochloride intragastrically 2hr prior to "diving" at the following doses (mg PSE/Kg): 0 (control), 80, 100, 120, 160 & 320 (9 rats/group). Rats were placed into a sealed chamber inside a hyperbaric chamber, which were pressurized in parallel with pure O₂ and air, respectively, to 5 ATA (132 feet of seawater) until the onset of seizure

Results: Our results show a significant dose dependent decrease in LS, compared to the control, at doses of 100-320 mg/Kg, as well a significant decrease in body temperature after the administration of PSE, independently from the given dose

Conclusion: Our findings show that high doses of PSE should be avoided in deep dives breathing pure O₂ as it increases the risk for CNS-OT. In addition, the animal body temperature decrease and the latency to seizure may be correlated

Research supported by: DAN (Divers Alert Network) and ONR (Office of Naval Research)

Effect of Ketone Treatment and Glycolysis Inhibition in Brain Cancer Cells (U87MG) and Rat Primary Cultured Neurons Exposed to Hyperbaric Oxygen and Amyloid BetaAngela Bennett¹, Csilla Ari³, Shannon Kesl¹, Jaimie Luke¹, David Diamond^{2,4}, Jay Dean¹, Dominic D'Agostino¹.¹Molecular Pharmacology and Physiology, ²Department of Psychology, University of South Florida, Tampa, FL, ³Byrd Alzheimer's Institute, Tampa, FL, ⁴James A. Haley Veterans Hospital, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Molecular Pharmacology & Physiology**Keywords:** ketone, hyperbaric oxygen, cancer, Alzheimer**Objective:** Mild ketosis from caloric restriction or the ketogenic diet confers a therapeutic effect against a wide range of pathologies, including brain cancer and Alzheimer's disease. Based on previous work, we hypothesized that supplemental ketones, glycolysis inhibition (lonidamine) and hyperbaric oxygen (HBO) would decrease viability of U87 MG cells. Furthermore, we hypothesized that ketones would prevent oxidative stress in primary neurons associated with amyloid beta (Ab) toxicity and HBO.**Methods:** LDH assays were used to measure cell viability in response to ketones (1-10mM), lonidamine (glycolysis inhibitor) and HBO (3atm, 60min.) Rat primary neurons were treated with 10nM A β 42 for 24 hours (with and without HBO) and superoxide anion production was measured with dihydroethidium (DHE).**Results:** Lonidamine and HBO increased U87 MG cell death in cultures exposed to acute drug treatment (1hr). Ketone treatment in primary neurons decreased superoxide anion production by 20.5% and 36.2% in normobaric treatment (NBO) and HBO, respectively. Ketone treatment in A β 42 treated neurons reduced superoxide by 23% and 16.5% in NBO and HBO, respectively.**Conclusion:** We conclude that glycolysis inhibition decreases viability in U87 MG cells and that supplemental ketones reduce superoxide production in primary rat neurons exposed to HBO and A β . These observations support a therapeutic effect of ketones in brain cancer and Alzheimer's disease.**Research supported by:** Signature Interdisciplinary Program in Neuroscience (SIPIN), Office of Naval Research (ONR)***Reelin Supplementation Enhances Cognitive Ability, Synaptic Plasticity and Dendritic Spine Density***Justin T. Rogers^{1,2,6}, Ian Rusiana^{1,2}, Justin H. Trotter^{1,2,6}, Lisa Zhao³, Erika Donaldson^{1,2,6}, Daniel T.S. Pak⁴, Lenard W. Babus⁵, Melinda Peters^{1,2}, Jessica L. Banko^{2,6}, Pascale Chavis^{7,8,9}, G. William Rebeck¹⁰, Hyang-Sook Hoe¹¹, Edwin J. Weeber^{1,2,6}¹Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL, ²Department of Molecular Biophysics and Physiology, Vanderbilt University Medical Center, Nashville, TN ³Department of Pharmacology, Georgetown University, Washington DC ⁴Department of Neuroscience, Georgetown University, Washington DC ⁵Department of Molecular Medicine, University of South Florida, Tampa, FL ⁶USF Health Byrd Alzheimer's Institute, Tampa, FL ⁷Inserm Unité 901, Marseille, 13009, France⁸Université de la Méditerranée, UMR S901 Aix-Marseille 2, 13009, France ⁹INMED, Marseille 13009, France¹⁰Department of Neuroscience, Neurology, Georgetown University, Washington DC ¹¹University of South Florida, Morsani College of Medicine, Dept of Molecular Pharmacology & Physiology**Keywords:** Low Density Lipoprotein Receptors, Hippocampus, Long-term Potentiation, and Learning and Memory.**Objective:** Apolipoprotein receptors belong to an evolutionarily conserved surface receptor family that has intimate roles in the modulation of synaptic plasticity and is necessary for proper hippocampal-dependent memory formation. The known lipoprotein receptor ligand Reelin is important for normal synaptic plasticity, dendritic morphology and cognitive function; however, the in vivo effect of enhanced Reelin signaling on cognitive function and synaptic plasticity in wild-type mice is unknown. The present studies test the hypothesis that in vivo enhancement of Reelin signaling can alter synaptic plasticity and ultimately influence processes of learning and memory.**Methods:** Purified recombinant Reelin was injected bilaterally into the ventricles of wild-type mice.**Results:** We demonstrate that in vivo single Reelin injection increases activation of adaptor protein Disabled-1 and cAMP-response element binding proteins after 15 minutes. These changes correlated with increased dendritic spine density, increased hippocampal CA1 LTP and enhanced performance in associative and spatial learning and memory.**Conclusion:** The present study suggests that an acute elevation of in vivo Reelin can have long-term effects on synaptic function and cognitive ability in wild-type mice.**Research supported by:** Supported by P01AG030128

Stress and DNA Damage in Experimental Stroke Kazutaka Shinozuka, Naoki Tajiri, Nathan Weinbren, Yuji Kaneko, and Cesar V. Borlongan Department of Neurosurgery and Brain Repair, University of South Florida, Morsani College of Medicine, Tampa FL

Keywords: stroke, stress, pain, immune system, DNA damage

Objective: Stress has been implicated as a major determinant of stroke pathological manifestations including immune response. The present study was designed to investigate relationships between stroke, stress, and DNA damage in the thymus, an important organ for immune-defense system.

Methods: Fifteen SD rats received middle cerebral artery occlusion (MCAo). Thirteen rats served as intact control subjects. Routine behavioral and histological assays were performed to determine stroke symptoms. The subjects were videotaped before and after MCAo and sacrificed to collect their thymus at day 3. Subjects' pain perception, which is considered as one of post-stroke stressors, was analyzed from the video in accordance with Rat Grimace Scale (Sotocinal et al. Mol Pain 2011, 7:55). DNA damage in the thymus was analyzed by immunostaining with gamma-H2AX antibody, which is known as DNA double strand break marker.

Results: Stroke animals displayed the characteristic motor asymmetry and cerebral infarction, whereas intact subjects exhibited normal behaviors and non-detectable pathological damage to the brain. Stroke subjects showed significantly higher pain scores than those in intact subjects after MCAo. Gamma-H2AX immunoreactive cells were localized at the boundary between medulla and cortex of the thymus, and were highly expressed in the stroke group than the control group.

Conclusion: The present study demonstrated that the typical stroke symptoms produced by MCAo were accompanied by a pain response and an increased DNA damage in the boundary area of the thymus. These results suggest that care and management of stroke patients, at least in the acute setting, may benefit from a careful consideration of treating stressors.

Research supported by: USF Department of Neurosurgery and Brain Repair Funds

Neuroprotective Effects of Bone Marrow Stromal Cells in Co-cultures of Fetal Dopaminergic Neuronal Cultures

Shijie Song a, b, Amanda Rowe b, c, Kunyu Li b, Vasyl Sava b, Juan Sanchez-Ramos a, b, c, * a James A Haley Veterans Affairs Medical Center, Tampa, FL, USA; b Department of Neurology, University of South Florida, FL USA; c Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL, USA University of South Florida, Morsani College of Medicine Dept. of Neurology

Keywords: mesenchymal stem cells, Methyl phenylpyridinium (MPP+), growth factors, cell fusion, transdifferentiation

Objective: Objectives: The primary goal of this in vitro cell culture study was to determine if direct contact of bone marrow stromal cells (BMSC) with fetal midbrain (MB) neuronal cultures is necessary to confer neuroprotection against the neurotoxicant MPP+.

Methods: Methods & Results: Results presented here demonstrate that diffusible growth factors, and not direct cell contacts, were responsible for mitigating neurotoxicity. When compared to the effects of MPP+ on MB monolayer cultures,

Results: the neurite length and functional activity indicated by [3H]-DA uptake of DA neurons was significantly greater in bilayer cultures where there was no contact between the green fluorescent protein expressing (GFP+) BMSC layer and the MB cell culture layer. Mixed co-cultures, (with MB and GFP+ BMSC in direct contact) were also protected against MPP+ to the same extent as in the bilayer cultures. There was no evidence of fusion of tyrosine hydroxylase expressing (TH+) neurons with GFP+ BMSC despite careful search for doubly labeled dopaminergic cells in the mixed cultures. A small fraction (7-10%) of neurons co-expressed GFP and NeuN (neuron specific nuclear antigen) suggesting possible fusion of GFP+ BMSC with non-TH+ neurons, a finding that does not explain the neuroprotective effects observed in the bilayer cultures.

Conclusion: Summary: In summary, the neuroprotection conferred by BMSC in mono-and bilayer cultures can be attributed to elaboration of neurotrophic and other unknown factors which enhance neurite sprouting and improve DA neuron function.

Research supported by: VA Merit Review Grant (to SS and JSR) and the Helen Ellis Endowed Chair Research Fund (JSR).

Combination Treatment of Moderate Hypothermia and Mesenchymal Stem Cell Amplifies Neuroprotection in Vitro Model of Hypoxic-Ischemic Injury: Relevance to Neonatal Encephalopathy Naoki Tajiri, Yuji Kaneko, Loren E. Glover and Cesar V. Borlongan University of South Florida Morsani College of Medicine Neurosurgery & Brain Repair

Keywords: Hypoxic-ischemic encephalopathy (HIE), hypothermia, Primary rat neuronal cells, human mesenchymal stem cells (hMSCs), mitochondrial dysfunction

Objective: Hypoxic-ischemic encephalopathy (HIE), a subset of neonatal encephalopathy, has caused infant mortality and severe long-term neurological disorders. Although treatment of neonatal encephalopathy in newborns 6 hours after birth with brain cooling (hypothermia) has significantly increased survival rate, approximately 40% of these babies sustain serious neurologic disability and continue to deteriorate [Glass HC et al., 2011]. To this end, the current hypothermia treatment protocol may benefit from combination therapeutic strategies [Higgins RD et al., 2011]. To define the optimal regimen for hypothermia treatment in combination with stem cell therapy for ameliorating neonatal encephalopathy.

Methods: Primary rat neuronal cells (gestation age day 18) were exposed to oxygen-glucose deprivation (OGD) condition [Matsukawa N et al., 2009], a model of HIE, then incubated at 25°C (severe hypothermia), 34°C (moderate hypothermia), and 37°C (normothermia). Cells were subsequently co-cultured with human mesenchymal stem cells (hMSCs), and thereafter cell viability (calcein assay [Bell E et al., 2003]) and mitochondrial activity (MTT Assay [Borlongan CV et al., 2010]) of each condition were measured.

Results: Combination of moderate hypothermia and hMSCs treatment significantly improved cell survival and protected against mitochondrial dysfunction after OGD.

Conclusion: These results support combination therapy of hypothermia and stem cells for hypoxic-ischemic injury, which may have direct impact on current trials using stand-alone hypothermia or stem cells for treating newborn encephalopathy.

Research supported by: USF Department of Neurosurgery and Brain Repair Funds

Tau Regulation by Hsp90 and FKBP51

Kellen Voss¹, Shannon Hill², Umesh Jinwal³, Bina Nayak⁴, Laura Blair¹, Bryce Nordhues¹, Alex Barrett⁴, Zach Davey¹, Martin Muschol², Gary Daughdrill⁴, Chad Dickey¹ ¹Dept. of Mol. Med., USF Health Byrd Alzheimer's Institute, Tampa, FL ²Dept. of Physics, USF College of Arts and Sciences, Tampa, FL ³College of Pharmacy, USF Health Byrd Alzheimer's Institute, Tampa, FL ⁴Dept. of Cell Biology, Microbiology and Molecular Biology, USF Center for Drug Discovery and Innovation, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: molecular chaperones, tau, Alzheimer's disease

Objective: Alzheimer's disease (AD) is the most prevalent tauopathy, and molecular chaperones have been shown to play a large role in the progression of the disease. Pin1 is a peptidyl-prolyl isomerase (PPIase) that alters the conformation of phosphorylated tau to promote dephosphorylation and has been shown to have a role in the progression of AD. We have previously shown FK506 binding protein-51 (FKBP51), which binds heat shock protein 90 (Hsp90) through a tetratricopeptide repeat (TPR) domain and also possesses a peptidyl-prolyl isomerase domain, is involved in regulating tau phosphorylation and stability in cells. However, little is known about how FKBP51 coordinates with Hsp90 to regulate tau. We therefore examined this role and how disruption of the complex affects tau biology.

Methods: We examined the interactions of tau, Hsp90 and FKBP51 through the use of NMR, CD, in vitro aggregation, cell culture and transgenic mouse models.

Results: We found structural changes as a result of tau and FKBP51 interactions. In examination of how Hsp90 affects tau levels in conjunction with FKBP51, we found that FKBP51 reduction alone reduces tau levels, but reduction of FKBP51 and Hsp90 simultaneously preserves tau levels. This indicates Hsp90 is involved in the FKBP51-mediated turnover of tau. Finally, we found that FKBP51 on its own cannot influence tau aggregation in vitro. However, FKBP51 attenuated the ability of Hsp90 to modify tau aggregation in vitro.

Conclusion: The interaction of Hsp90 and FKBP51 through the TPR domain is important for the regulation of tau in vitro and in vivo. Further investigation into the interactions of FKBP51, tau, and Hsp90 should provide more specific targets for the treatment of tauopathies and Alzheimer's disease.

CS-oxidant Signaling and Adenosine A2B Receptor Activation Alters Adenosine A2A-mediated Airway Wound Repair

Diane Allen-Gipson, Ph.D, University of South Florida Health, College of Pharmacy and Pharmaceutical Sciences, Tampa, Florida USA; Hui Zhang, MD, Pulmonary, Critical Care, Sleep & Allergy Medicine Section, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE USA; Todd Wyatt, Ph.D, Pulmonary, Critical Care, Sleep & Allergy Medicine Section, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE

Keywords: cigarette smoke, adenosine, airway wound repair, oxidant

Objective: Cigarette smoke (CS) is responsible for a number of pulmonary diseases. Adenosine (ADO) a nucleoside is elevated in asthma and chronic obstructive pulmonary disease (COPD) suggesting ADO serves a regulative role. Both A2A and A2B adenosine receptor (A2AAR; A2BAR, respectively) have protective effects in tissue; however, A2BAR activation has destructive effects. We revealed ADO acting at the A2AAR promotes wound closure in human bronchial epithelial cells however, little is known of CS effects on ADO's role in maintaining and repairing the airway. Because CS-oxidant signaling contributes to the deregulation of the A2A reparative processes we hypothesize that, cigarette smoke exposure shifts the oxidant/antioxidant balance and activates A2BAR altering A2AAR-mediated airway wound repair.

Methods: To test this hypothesis, human bronchial epithelial cell line, Nuli-1 cells were exposed to 5% cigarette smoke extract (CSE) for 24 hours and A2B knockout (A2BKO) and C57BL/6 (wild-type; WT) mice were exposed to whole body CS exposure for 6 weeks. In vitro wounding studies were assessed via the electric cell-substrate impedance sensing (ECIS). For in vivo studies, lung tissue were collected and analyzed.

Results: ECIS revealed CSE blunts A2AAR-mediated wound closure and was associated with reduced glutathione (GSH) levels and marked generation of hydrogen peroxide (H₂O₂) as compared to media control. PCR revealed a marked increase in A2B mRNA in WT mice whereas there was a slight increase in A2A mRNA in A2BKO mice as compared to WT mice exposed to CS. CS exposure decreased the level of GSH in lungs from wild-type, but only minimally in the A2BKO mice.

Conclusion: The data suggest CS-oxidant signaling and A2BAR activation alters A2AAR-mediated airway wound repair.

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A Novel Method for Preparation and Application of Degraded Samples in STR Multiplex Amplification System

Yesha Amin (¹), Neel R. Nabar (¹), Liu Chao (²), Liu Changhui (²), Shu-Feng Zhou (¹)

¹ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

² Bureau of Public Security of Zhongshan City, Guangdong, Zhongshan

Keywords: STR, mini STR, degraded DNA

Objectives: Criminal investigations often use amplification of short tandem repeat (STR) markers present in the human nuclear DNA genome for individual identification. However, this process can be difficult when dealing with highly degraded evidentiary DNA samples. Different levels of DNA degradation require different procedures of DNA analysis; less degraded DNA can be analyzed via STRs, while shorter fragments must be analyzed via mini STRs or mtDNA. Thus, knowledge of the degradation state of DNA samples would allow for selection of a more effective analysis method.

Methods: We developed a novel method for extraction and purification of degraded DNA, while investigating the use of STR vs miniSTR analysis in degraded DNA. In this study, we extract and purify DNA from degraded tissues. DNA from 800bp, 600bp, 400bp and 200bp gel fragments were retrieved by low melting-point agarose gel electrophoresis. The resulting DNA extracts were quantified, and the rate of accuracy of DNA typing accuracy in low molecular weight DNA using commercial STR kits was compared with the rate of accuracy using available miniSTR kits.

Results: The results show that DNA in corrupted tissues were mainly fragments less than 200bp, while larger fragments were not very common. Furthermore, STR analysis was not effective in analysis of short, degraded DNA fragments (<200 bp), while mini STR analysis appears to work well.

Conclusion: This method of DNA extraction and preparation allows for differential analysis of different length DNA fragments, resulting in a more confident DNA profile for individual identification.

Improving in Vitro Dissolution Release Profiles of Nifedipine

Rebecca Andruski, Misty Muscarella, Sofonie Luinord, N. Langley*, Shaukat Ali* and Yashwant Pathak University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science, USF Tampa, FL, *BASF Corporation, New Jersey

Keywords: Nifedipine, dissolution, Lutrol

Objective: Nifedipine is a calcium-channel blocker used to treat hypertension and control angina. Its molecular weight is 346.3 and it is practically insoluble in water. Under BCS Nifedipine is typically categorized as a class II, having slow solubility and high permeability. This study attempts to improve the solubility of the drug by using the solid-solid dispersion of the drug in Poloxamer (Lutrols).

Methods: Poloxamer 188 (Lutrol F53), Poloxamer 227 (Lutrol F87), Poloxamer 338 (Lutrol F108) and Poloxamer 407 (Lutrol F127) were dissolved and used in formulation with Nifedipine in a 1:1 ratio. Melting process was used to incorporate Nifedipine in Poloxamer matrix. The formulations were characterized, and the dissolution tests were carried out under USP method 2. Nifedipine in hard gelatin capsules. The formulations were studied for their physicochemical properties by calorimetry, X-ray diffraction, high microscopy and in vitro dissolution studies.

Results: The in vitro studies showed improved dissolution of Nifedipine in combination with each Lutrol compared to the control Nifedipine, tested under identical conditions.

Conclusion: Poloxamers increased the solubility of Nifedipine when used in 1:1 combinations with the drug. The solubility enhancement of Nifedipine is due in part to increased surface active sites of drug in dispersions. Poloxamers' dispersions showed to be thermodynamically stable and had a continuous release of drug without precipitation. Poloxamers' matrix will enhance solubility, thus improve bioavailability, by maintaining such poorly soluble oral dosage forms, as Nifedipine, in the supersaturation state.

Research supported by: University of South Florida College of Pharmacy BASF Corporation

Screening of Novel Drugs for the Treatment of Parkinson's disease

Kaitlyn Braswell, Juan Zhang, Tina Patel, Juan Yu, Patrick Reid, Guang Y. Yang, Jessica Bencivenga, Twisha Jani, Daniel C. Lee, Umesh K. Jinwal, USF College of Pharmacy and Byrd Alzheimer's Institute, Calcul Laurent, Chandan Barhate, Jeremy Beau, Bill J. Baker -USF Department of Chemistry - USF College of Pharmacy and Byrd Alzheimer's Institute, University of South Florida College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Parkinson's disease, LRRK2, Drug Screen, Cell culture

Objective: Parkinson's disease (PD) is a disorder characterized by a gradual lack of controlled movements. It is the second most common neurodegenerative disease and nearly one million people are affected by Parkinson's in the United States alone. Symptoms of this disease include shakiness, slow movements, and eventually cognitive decline. Even though the cause of Parkinson's disease is unknown, scientists have identified certain genes related to familial cases that mutate and incorrectly code proteins. An example of one of these genes is leucine-rich repeat kinase 2 (LRRK2). Approximately 30% of PD patients found to have mutation in LRRK2 gene. Our main aim is to reducing the concentration of LRRK2 by using novel drugs.

Methods: To target LRRK2 we have used cell culture model expressing LRRK2. Cells were treated with various drugs for 24 hours. Samples were analyzed by Western blots, utilizing the LRRK2 antibody, and chemiluminescence.

Results: We have screened around 100 drugs and found several novel drugs showing potent reduction in the LRRK2 level.

Conclusion: Novel drugs identified by using cell culture model of LRRK2 could lead to the development of more stable, nontoxic drugs to slow progression and or cure PD.

Research supported by: USF College of Pharmacy Dean's Clinical and Research Pilot award for the Start-up & New Investigator Research Grant from Alzheimer's Association

Bioinformatic Prediction of microRNAs that Regulate Human Cytochrome P450 Genes

Helen Chew (¹), Zhi-Xin Wang (¹), Kevin B. Sneed (²), Jun Liang (¹) and Shufeng Zhou (¹) (¹) Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, Florida 33612 (²) Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida, Tampa, Florida, University of South Florida, College of Pharmacy Dept. of Pharmaceutical Science

Keywords: miRNA, CYP, regulation, prediction

Objective: miRNAs are involved in the regulation of a number of genes that are involved in development, cell proliferation and apoptosis, and carcinogenesis. There are limited data on how miRNAs regulate drug disposition in humans. This study investigated the miRNAs that probably regulated human CYP genes using a bioinformatic approach.

Methods: TargetScan was used to predict the miRNAs that probably regulated CYP genes.

Results: Among 57 functional human CYP genes, miRNAs regulating each of them were predicted by TargetScan, PicTar, EMBL, EIMMo, Miranda, miRBase Targets, PITA TOP, and mirWIP programs. Among all programs used, only TargetScan gave a comprehensive prediction. Among the 55 predictable CYP genes (no prediction data for CYP2C19 and 26C1), a total of 5,880 matching sites were found, with 106.9 sites for each gene. A total of 787 miRNAs were involved in the regulation of these 55 genes, with 647 (82.2%) miRNA being poorly conserved and 140 (17.8%) being conserved. Each CYP gene was regulated by 14.3 miRNAs. The TargetScan program predicted that CYP1A2, 2A6, 2B6, 2C9, 2C19, 2D6, 2E1, and 3A4 were regulated by 72, 18, 126, 34, 69, 4, 10, and 110 miRNAs, respectively. Conserved miRNAs included miR-16, miR-17, miR-141, miR-147, miR-1324, let-7a, etc, while examples of poorly conserved ones are miR-100, miR-105, and miR-1178. A single miRNA may regulate different CYP genes.

Conclusion: A small number of the miRNAs that were predicted to regulate human CYP genes have been confirmed by benchmarking studies. These studies provide initial insights into how CYPs genes are regulated by miRNAs.

Redox Changes and Pyridine Nucleotide Alterations: Role of Hypoxia and Hyperglycemia

Anastasia Groshev, Srinivas M. Tipparaju University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Potassium channel, pyridine nucleotides, hypoxia, Kv β subunit

Objective: Pyridine nucleotides function as essential coenzymes in a host of metabolic processes such as modification of proteins, regulation of glycolysis, and redox state of the cell. The goal of this study was to identify changes in concentration of pyridine nucleotides in hypoxic conditions to understand the physiological effect of oxidative stress on the cell. Pyridine nucleotides bind β -subunits of the voltage-gated potassium channels and alter Kv currents. Therefore we hypothesized that physiological changes in pyridine nucleotides levels will affect cell function via Kv channel.

Methods: Pyridine nucleotides were quantified by measuring fluorescence in HL-60 and COS-7 cells and standardized per protein content of the sample. The connection between oxygen availability and changes in pyridine nucleotides was assessed by subjecting cells to hyperoxic and hypoxic conditions for 30 minutes. Similarly, to understand the relationship of high glucose concentration and oxidative stress, pyridine nucleotides were quantified in cell subjected to hyperglycemic conditions for 30 minutes.

Results: Standard curve for the measurement of four pyridine nucleotides was obtained by use of micro plate reader assays. A range of 1-100 picogram for NAD(H) and NAD(P)H was established, proteins were quantified by using Pierce 660 assay. Presently we are utilizing assays to obtain the changes in the ratios of pyridine nucleotides in hypoxia. We expect a decline in concentration of NAD⁺ and increase in NADPH due to consummation of NAD⁺ in glycolysis and in conversion of pyruvate to lactate.

Conclusion: Ratios of NAD⁺/NADH and NADP⁺/NADPH concentrations respond to changes of intracellular environment, specifically to changes in oxygen and glucose.

Research supported by: NIH and USF-COP startup funds

A Review of Enhancing Membrane Permeability of Poorly Permeable Drugs by Carrier Mediated Prodrug Approach

Sheeba Varghese Gupta, Department of Pharmaceutical Sciences, College of Pharmacy, USF Health, Tampa, FL

Keywords: Prodrugs, PepT1, carrier-mediated, permeability

Objective: To analyse the application of carrier-mediated prodrug approach in the improvement of poorly permeable drugs

Methods: In the studied examples (gemcitabine and zanamivir) the amino acid prodrugs of poorly permeable drugs were synthesized in order to make them the substrates of intestinal amino acid transporter, PepT1. Prodrug's affinity for PepT1 was evaluated by inhibition of [3H]GlySar uptake in Caco-2 cells. The selective uptake of prodrugs by PepT1 was evaluated by uptake of the prodrugs in PepT1-transfected HeLa cells. Additionally, the permeability of the prodrugs were studied in Caco-2 monolayer assays and in-situ rat perfusion studies.

Results: The prodrugs have shown marked increase in the permeability as compared to the parent drugs. In case of zanamivir, The acyloxy ester prodrugs of zanamivir inhibited GlySar uptake in Caco-2 cells. The L-valine acyloxy ester of zanamivir (Zan-Val) had shown significant inhibition of GlySar uptake ($IC_{50} = 1.15 \pm 0.19$ mM) as compared to zanamivir which showed absolutely no inhibition. Zan-Val also exhibited approximately three fold uptake in hPEPT1/HeLa cells as compared to wild type. There was an increase in appearance of zanamivir in the basolateral compartment for Zan-Val compared to the parent drug in the Caco-2 permeability study ($P_{app} = 5.97662 \times 10^{-7} \pm 4.07244 \times 10^{-8}$ cm/sec). The Zan-Val prodrug further have shown increased permeability ($P_{eff} = 3.68 \times 10^{-5} \pm 2.23 \times 10^{-5}$ cm/sec) compared to parent drug which showed no permeability ($P_{eff} = -4.29 \times 10^{-5} \pm 5.33441 \times 10^{-5}$ cm/sec) in the in-situ rat perfusion studies.

Conclusion: Membrane permeability of poorly permeable drugs can be increased by carefully designed prodrugs. This approach can be used to increase the oral bioavailability of poorly absorbed drugs.

Development and Characterization of Amphotericin B bearing Emulsomes against Experimental Visceral Leishmaniasis

Swati Gupta^{1, 2, 3}, Anuradha Dube², Suresh P. Vyas¹, Yashwant Pathak³ ¹Drug Delivery Research Laboratory, Department of Pharmaceutical Sciences Dr. Hari Singh Gour Vishwavidyalaya, Sagar 470 003, INDIA ²Division of Parasitology, Central Drug Research Institute, Lucknow 226 001, INDIA ³College of Pharmacy, USF Health, Tampa, FL, University of South Florida. College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Emulsomes, amphotericin B, macrophages, targeting, visceral leishmaniasis

Objective: To develop emulsomes for effective and site specific localization of amphotericin B (AmB) inside the macrophages (MQs) to treat the visceral leishmaniasis (VL).

Methods: AmB loaded plain emulsomes (PE) and O-palmitoyl mannan coated emulsomes (CE) were prepared by cast film method followed by homogenization. The antileishmanial activity of amphotericin B-deoxycholate (AD), PE and CE was tested in vitro at different drug doses (0.03, 0.08, 0.13 and 0.2 µg/ml) in Leishmania donovani infected MQ-amastigote system (J774A.1 cells). L. donovani infected hamsters (weight 80-100 g) harboring 38-40 amastigotes/100 MQ nuclei were distributed (6 in each group, total 36, 3 control groups) for drug (equivalent to 0.5 mg/kg) treatment intracardially.

Results: 3.5% PI) ($p < 4.1\%$ PI) and AD (68.18% parasite inhibition, PI) over PE (83.27% PI). The in vitro antileishmanial activity showed higher efficacy of CE (93.06% PI) over AD (68.18% PI) ($p < 0.05$ for AD vs PE; $p < 3.4\%$ PI) ($p < 4.8\%$ PI) than PE (53.8% PI) ($p < 0.01$ for AD vs CE) [data at dose of 0.08 µg/ml]. Fluorescence microscopy study showed significant localization of fluorescein loaded PE and CE inside the liver and spleen cells of golden hamsters. Formulation CE eliminated L. donovani amastigotes within splenic MQs more efficiently (77.1% PI) ($p < 0.01$) or AD (33.1% PI) ($p < 0.001$).

Conclusion: 1) The proposed systems showed excellent potential for MQ targeting as shown by drug levels in liver and spleen. 2) The formulations could significantly modify the pharmacokinetics of AmB as compared to AD, providing prolonged action at comparatively low drug doses thereby reducing the toxicity problems like nephrotoxicity, cardiac arrhythmia etc.

Research supported by: University Grants Commission, New Delhi & Council of Scientific & Industrial Research, New Delhi, India

Bioinformatic Prediction of the microRNAs That Regulate ABC Transporter Genes

Kevin Guzman (¹), Zhi-Xin Wang (¹), Jun Liang (¹), Kevin Sneed (²), Shu-Feng Zhou(¹). (¹) Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, Florida 33612 (²) Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida, Tampa, Florida, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: microRNA, ABC Transporters

Objective: By targeting specific mRNA sequences, miRNAs regulate gene expression through RNA interference. Multiple studies have shown that miRNAs are responsible for the regulation of 30% of the human genome. Recently, there has been a limited amount of data regarding miRNA's role in the regulation of ATP-binding cassette transporters (ABC family). ABC transporters can carry many types of sterols, lipids, and drugs across membranes. This study investigated the miRNAs which are responsible for regulating the ABC transporter genes.

Methods: The miRNAs associated with regulation of ABC transporter genes were analyzed using TargetScan software.

Results: Among the 48 predicted ABC transporter genes, a total of 5,428 matching sites were found, which means there were around 113 candidate miRNAs for each gene. From the TargetScan data, ABCA4, ABCB2, ABCB9, ABCC3, ABCE2, and ABCG4 were regulated by 38, 132, 89, 181, 124 and 219 miRNAs, respectively. Conserved miRNAs included miR-124, miR-1271, miR-96, miR-182, and miR-495, while examples of poorly conserved ones are miR-17, miR-155, miR-23, miR-205 and miR-186. Also, it was shown that a single miRNA might regulate different ABC transporter genes. For example, miR-383 could regulate ABCA9, ABCC10, ABCC11, ABCG1, and ABCG5, as well as miR-1227 might regulate ABCA9, ABCA10, ABCB10, ABCC5, ABCG4, and ABCG8. Totally 682 miRNAs were involved in the regulation of these 48 ABC transporters genes.

Conclusion: This study shows the vast regulation of ABC transporter genes by miRNAs. Benchmarking studies are currently in progress to validate our computational data.

Proteomic Response to Acupuncture Treatment in Spontaneously Hypertensive Rats

Xin-Sheng Lai (¹), Jun Liang (²), Kevin B. Sneed (³) and Shufeng Zhou (²) (¹) College of Acupuncture and Moxibustion, Guangzhou University of Chinese Medicine, Guangzhou 510006, China (²) Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL 33612 (³) Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida, Tampa, Florida, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Acupuncture, hypertension, proteomics, LC/MS, rat

Objective: Previous animal and clinical studies have shown that acupuncture is a viable alternative or supplementary treatment to modern medicine in the management of hypertension. However, the mechanism of action through which acupuncture modulates blood pressure has not yet been explored. This study is the first to investigate the proteomic response in the nervous system to treatment at the Taichong (LR3) acupoint in spontaneously hypertensive rats (SHRs).

Methods: Unanesthetized rats were subject to 5-min daily acupuncture treatment for 7 days. Each day, blood pressure was measured 5 min after acupuncture. After euthanasia on the 7th day, rat medullas were dissected, homogenized, and subject to 2D gel electrophoresis and MALDI-TOF analysis.

Results: The results indicate that blood pressure stabilized after the 5th day of acupuncture, and compared with non-acupoint treatment, Taichong-acupunctured rat's systolic pressure was reduced significantly ($P < 0.01$), though not enough to bring blood pressure down to normal levels. The different treatment groups also showed differential protein expression: 2-DE image revealed 621 ± 30 proteins in normal SD rats' medulla, 621 ± 20 proteins in SHR's medulla, 621 ± 40 proteins in medulla of SHR after acupuncturing Taichong, and 621 ± 20 proteins in medulla of SHR after acupuncturing non-acupoint.

Conclusion: The results indicate an increase in antioxidant enzymes in the medulla of the SHRs subject to acupuncture, which may provide partial explanation for the antihypertensive effect of acupuncture. This study identifies proteomic responses as potential novel biomarkers for acupuncture treatment and helps optimize the treatment regimen of acupuncture.

Identification of Herbal Inhibitors for Human Cytochrome P450 1A2 and Implication in Herb-Drug Interactions

Phuong Le ⁽¹⁾, Dominique Nguyen ⁽¹⁾, Li-Ping Yang ⁽²⁾, Jun Liang ⁽¹⁾, Kevin B. Sneed ⁽³⁾ and Shufeng Zhou ⁽¹⁾ ⁽¹⁾ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa ⁽²⁾ Department of Pharmacy, Beijing Hospital of Health Ministry, Beijing 100730, China ⁽³⁾ Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida, Tampa, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: CYP1A2, inhibitor, liver microsome, herbal medicine, molecular modeling

Objective: Inhibition of CYP1A2 by herbal compounds may cause clinical herb-drug interactions. This study aimed to explore the binding mode of ligands with CYP1A2 and to screen potential inhibitors from a library of herbal compounds using computational and in vitro approaches.

Methods: Molecular docking was conducted using Discovery Studio and inhibitory studies were carried out using a high throughput screening kit.

Results: The heme prosthetic group and six residues including Thr124, Phe125, Phe226, Phe260, Gly316, and Ala317 in the active site of CYP1A2 were identified as important residues for ligand binding. Ala317 and Asp320 were highly conserved in most human CYPs with known crystal structures. In the in vitro inhibition studies, only tanshinone I, tanshinone IIA, and cryptotanshinone exhibited remarkable inhibition on CYP1A2, with IC₅₀ values of 0.027, 0.187 and 0.910 μ M, respectively. In addition, baicalein, osthole, quercetin, cordycepin, and sodium tanshinone IIA sulfonate showed moderate inhibition on the CYP1A2, with IC₅₀ values of 1.22, 1.49, 3.97, 6.69, and 7.08 μ M, respectively. In molecular docking, 19 of the 56 herbal compounds examined were identified as potential inhibitors of CYP1A2. Up to 21 of the 56 herbal compounds were hit by the pharmacophore model of CYP1A2 inhibitors developed and validated in this study. In the in vitro inhibition study, 8 herbal compounds were identified as moderate to potent inhibitors of CYP1A2. Five of the 8 herbal compounds predicted to be potential inhibitors were confirmed as CYP1A2 inhibitors in the in vitro study.

Conclusion: A combination of computational and in vitro approaches represents a useful tool to identify potential inhibitors for CYP1A2 from herbal compounds.

A High Throughput Screening Approach to Investigating How Nuclear Receptor Ligands Affect Human Cytochrome P450s

Ming-Hua Li ⁽¹⁾, Zhi-Xin Wang ⁽¹⁾, Jiazhi Sun ^(1,2), Jun Liang ⁽¹⁾, Kevin B. Sneed ⁽³⁾ and Shufeng Zhou ⁽¹⁾ ⁽¹⁾ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL 33612 ⁽²⁾ Department of Molecular Medicine, College of Medicine, University of South Florida, Tampa, FL 33612 ⁽³⁾ Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida, Tampa, FL, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: CYP, nuclear receptor, ligand, inhibitor

Objective: Nuclear receptors (NR) are a class of proteins which are responsible for sensing steroids, thyroid hormones and certain other molecules, and they work with other proteins to regulate the expression of target genes, thereby controlling the development, homeostasis, and metabolism of the body. This study investigated the effect of a library of nuclear receptor ligands (n = 80) on human CYP1A2, 2D6, 2C9 and 3A4 and the structure-inhibitory activity relationship.

Methods: The inhibitory effect of NRs on human CYPs was examined using high throughput screening kits with fluorescent probes as the model substrates. Selective inhibitors such as furafylline and quinidine were used as the positive controls. The SAR was studied using AutoDock and Discovery Studio software.

Results: The NR ligands exhibited differential inhibitory effect on CYP1A2, 2D6, 2C9 and 3A4, while some NR ligands showed activating effect on CYP2C9. For example, 6-formylindolo-[3,2-b]-carbazole was a potent inhibitor for CYP2D6 with an IC₅₀ of <1 μ M, but enhanced the activity of CYP2C9 3-fold. Among all the 80 NR ligands, about 10% showed significant inhibition (IC₅₀ ≤ 1 μ M) to CYPs; other NR ligands exhibited moderate to minor or negligible inhibitory effects on CYPs. Only taurocholic acid inhibited two CYPs - CYP 2C9 (IC₅₀ ≤ 1 μ M) and 3A4 (IC₅₀ = 1 μ M). Our docking studies demonstrated the tight binding of these inhibitors to respective CYPs.

Conclusion: The findings can be used to predict important drug interactions between NR ligands and other drugs whose disposition is regulated by NRs.

Novel Polymeric Nanoparticles Containing Tanshinone-IIA from Chinese Herbal Medicine: Preparation, Characterization, and Antitumor Activity

Qi Li ⁽¹⁾ and Shufeng Zhou ⁽²⁾ ¹ Department of Oncology, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 200062, P. R. China; ² Department of Pharmaceutics Science, College of Pharmacy, University of South Florida, Tampa, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Nanoparticles, tanshinone IIA, PLA, hepatoma

Objective: Our lab synthesized novel polylactic acid nanoparticles containing tanshinone IIA (TS-PLA-NPs) using a single oil-in-water emulsion/solvent evaporation method. This study aim to characterize these particles.

Methods: The optimized nanoparticles were characterized for morphology, mean particle size, zeta potential, entrapment efficiency, drug-loading content, X-ray diffractometer measurement, and in vitro release kinetics. The effect of TS-PLA-NPs on hepatoma was performed in murine models.

Results: The obtained nanoparticles were spherical and intact. The mean particle size was 192.5 nm with polydispersity index being 0.029 and zeta potential 226.27 mV. The mean entrapment efficiency and loading of tanshinone IIA (TSIIA) in TS-PLA-NPs were 86.35 and 1.61%, respectively. The in vitro release study showed the TSIIA sustained release from TS-PLA-NPs for more than 7 days. The mean in vitro cumulative release percentage of TSIIA from TS-PLA-NPs vs. time curve fitted well with the Higuchi Equation ($Q = 2.0365 + 13.564 \times t^{1/2}$; $r = 0.9950$). In pharmacokinetics studies, the concentrations of TSIIA were higher in hepatoma and lower in blood, heart, kidney, spleen, and lung at 2 hr after TS-PLA-NPs administration via caudal vein. TS-PLA-NPs were effective in destroying the human liver cancer cells as shown by an MTT assay, and the growth-inhibitory effect of TS-PLA-NPs on human liver cancer cells was concentration and time dependent. Mice studies showed TS-PLA-NPs were markedly more effective than both of TSIIA and blank PLA nanoparticles in preventing tumor growth and increasing survival time of mice with hepatoma.

Conclusion: This study provided support for the new paradigm, the application of TSIIA for the treatment of hepatoma.

Abstract #: 212

Presented by: Jun Liang, BS, Graduate Student

Osteogenesis of Goat Bone Marrow Mesenchymal Stem Cells Induced by Transfection of BMP-2 and Bfgf

Jun Liang ⁽¹⁾, Neel R. Nabar ⁽¹⁾, Qifeng Guo ⁽²⁾, Huihua Xu ⁽²⁾ and Shufeng Zhou ⁽²⁾ ⁽¹⁾ Department of Pharmaceutical Science, College of Pharmacy, University of South Florida, Tampa, FL ⁽²⁾ Department of Orthopedics, Guangzhou First Municipal People's Hospital Affiliated to Guangzhou Medical College, Guangzhou 510180, China, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Stem cells, osteogenesis, transfection, BMP, bFGF

Objective: The advent of tissue engineering and stem cell based regenerative medicine has provided hope for a novel approach to managing bone degeneration, since bone marrow mesenchymal stem cell (BMSC) strategies have shown promise in preliminary studies. Both bone morphogenetic protein-2 (BMP-2) and basic fibroblast growth factor (bFGF) have been implicated in inducing bone formation from BMSCs. However, exogenous bone induction factors easily lose activity through protease breakdown and thus cannot trigger continuous local stimulation and bone induction effect. On the other hand, gene therapy resulting in integration into the host genome can overcome these issues with direct application of exogenous growth factors. This study investigated the gene expression and bone formation of goat BMSCs transfected by adenovirus-mediated BMP-2 and bFGF.

Methods: After construction of a recombinant adenovirus Ad-BMP2-bFGF-GFP vector, goat BMSCs were transfected with Ad-BMP2-bFGF-GFP and Ad-GFP at different multiplicity of infection values. Expression levels of BMP-2 and bFGF were analyzed by ELISA and staining was performed to determine the level of osteoblast differentiation.

Results: After 48 hr, the results indicated significant expression of BMP-2 and bFGF within Ad-BMP2-bFGF-GFP group and differentiation of BMSCs of the Ad-BMP2-bFGF-GFP treatment group into osteoblasts as confirmed by ALP staining. The difference was most obvious 6 days after transfection, and was detected over a period of 20 days.

Conclusion: The data lay the foundation for bone regeneration through stem cell use, with the potential of increasing the efficacy of skeletal reconstructive treatments.

Enhancing the Solubility Profiles of Indomethacin Using Lutrols by Solid-Solid Dispersions

Sofonie Luinord, Misty N. Muscarella, Rebecca Andruski, N. Langley*, Shaukat Ali*, Yashwant V. Pathak, University of South Florida College of Pharmacy, Tampa, Florida, USA, *BASF Corporation, New Jersey, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: indomethacin, Poloxamers, invitro studies

Objective: Indomethacin is used to relieve swelling in the lining of joints from diseases such as osteoarthritis, rheumatoid arthritis etc. Indomethacin is a Class II drug, with a low solubility and highly varying pharmacokinetics. Enhancement of Indomethacin solubility will help in achieving reproducible blood levels. The purpose of the study is to enhance the solubility of indomethacin in pharmaceutically accepted Poloxamers (Lutrols) as solid-solid dispersions. The dissolution profiles of indomethacin were in a 1:1 ratio of the following Lutrols: F-68, 87, 108 and 127 in capsules

Methods: Four formulations were prepared by dissolving 1:1 (API:Lutrol) with each Lutrol F68, 87, 108, and 127. Melting process was used to incorporate indomethacin in Poloxamer matrix. The formulations were characterized, and the dissolution tests were carried out under USP II method specified for indomethacin in hard gelatin capsules. The formulations were studied for their physicochemical properties by calorimetry, x-ray diffraction, light microscopy and in vitro release profiles.

Results: The in vitro studies showed improved dissolution of indomethacin in combination with each Lutrol compared to indomethacin alone under identical conditions

Conclusion: Poloxamers increased the solubility of indomethacin when used in 1:1 combinations with the drug. The solubility enhancement of indomethacin is due in part to increased surface active sites of drug in dispersions. Poloxamers' dispersions showed to be thermodynamically stable and had a continuous release of drug without precipitation. Poloxamers' matrix will enhance solubility, thus improve bioavailability, by maintaining such poorly soluble oral dosage forms, as indomethacin, in the super saturation state.

Research supported by: USF College of Pharmacy, BASF Corporation

Metabonomics Study on Human Hepatocarcinoma Cells Treated with Tyrosine Kinase Inhibitors

Rui-Juan Luo ⁽¹⁾ and Shu-Feng Zhou ⁽¹⁾ ¹ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, University of South Florida, College of Pharmacy Dept. of Pharmaceutical Science

Keywords: HCC, Tyrosine-Kinase Inhibitors, Metabonomics

Objective: The molecular pathogenesis of hepatocellular carcinoma (HCC) is complicated, involving multiple signaling pathways and altered cellular behavior. However, early and timely diagnosis of HCC is difficult due to lack of selective biomarkers and specific clinical symptoms. In HCC, there is often increased expression of angiogenic factors including VEGFs, EGFs, and PDGF, which represent useful therapeutic targets that can be hit by tyrosine kinase inhibitors (TKIs). Metabolite profiles represent sensitive biomarkers of both genomic and phenotypic changes. We looked to metabonomic methods to find novel biomarkers and aid in TKI based drug development for HCC, including determining pharmacokinetic properties of these TKIs.

Methods: An HPLC-MS based metabonomics method was applied to monitor the endogenous metabolite profiling in HCC cell lines, HepG2, Hep3B and SK-HEP-1 upon treatment with commonly used TKIs.

Results: TKI drugs and their metabolites were quantified to establish pharmacokinetic concentration at cellular levels to clarify the effect of drug metabolism on therapeutic outcome and establish concentration-response relationships.

Conclusion: Concentration-response relationships were determined for each TKI tested. Our research shows metabonomics as a powerful method to determine pharmacokinetic and therapeutic properties of TKIs for HCC.

Solid-solid Dispersions of Theophylline Using Lutrol F 68, 87, 108, 127 to Improve In Vitro Dissolution Release Profiles

Misty Muscarella, Rebecca Andruski, Sofonie Luinord, N. Langley*, Shaukat Ali* and Yashwant Pathak, University of South Florida College of Pharmacy, Tampa, Florida, USA, *BASF Corporation, New Jersey, USA, University of South Florida College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: dissolution, poloxamer, solubility

Objective: Theophylline is a xanthine derivative naturally found in tea. This drug is used to treat asthma and bronchospasm by relaxing and opening the air passage way. It is poorly soluble, receiving classification from BCS as a class 1 drug having high permeability but low solubility. The study was aimed at creating solid-solid dispersions of theophylline in Lutrols, which improve the solubility profiles of hydrophobic drugs.

Methods: Poloxamer 188 (Lutrol F68), Poloxamer 227 (Lutrol F87), Poloxamer 338 (Lutrol F108) and Poloxamer 407 (Lutrol F127) were used as the matrix for theophylline. Four formulations were prepared by dissolving the API 1:1 with each Lutrol F68, 87, 108 and 127. Melting process was used to incorporate theophylline in Poloxamer matrix. The formulations were characterized and the dissolution tests were carried out under USP II method specified for theophylline in hard gelatin capsules. The formulations were studied for their physiochemical properties by calorimetry, x-ray diffraction, light microscopy and in vitro dissolution studies.

Results: The in vitro studies showed improved dissolution of theophylline in combination with each Lutrol compared to theophylline alone under identical conditions.

Conclusion: Poloxamers improved the solubility of theophylline when used in 1:1 combinations with the drug. The solubility enhancement of theophylline is due in part to increased surface active sites of drug in dispersions. Poloxamers' dispersions showed to be thermodynamically stable and had a continuous release of drug without precipitation. Poloxamers' matrix will enhance solubility, thus improve bioavailability, by maintaining such poorly soluble oral dosage forms, as theophylline, in the super saturation state.

Research supported by: USF College of Pharmacy, BASF

A Murine Study of a Novel Vaccine Using Mutated B-Amyloid Sensitized Dendritic Cells in Alzheimer's Disease

Neel Ravi Nabar ⁽¹⁾, Zhongqui Luo ⁽²⁾, Jialin Li ⁽²⁾, Xioyang Lin ⁽³⁾, Chuanhai Cao ^(1,3), Shu-Feng Zhou ⁽¹⁾. ¹ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL33612 ² Huanhu Hospital, Tianjin 300060, China ³ USF Health Byrd Alzheimer's Institute, University of South Florida Health, Tampa, FL, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: DC Vaccine, Alzheimer's Disease, Th1, inflammation, A β

Objective: In 2001, a clinical trial using a β -amyloid vaccine (human wild type A β peptide, AN-1792) showed promising results. Dementia scale scores of the active vaccine group were considerably lower than that of AD patients given the placebo. Unfortunately, severe adverse reaction occurred in about 6% of the patients, and after autopsy, one was confirmed to have died of meningoencephalitis due to an increased Th1 response. We investigated a safer method to obtain sufficient anti-A β antibody titer without the use of an adjuvant, eliminating the Th1 response. The developed method focused on use of dendritic cells (DCs), the most powerful antigen presenting cell in the immune system.

Methods: This study utilizes a mouse model (PDAPP) of AD to study this mutant A β 1-42 sensitized DC as a vaccine in vivo with regards to efficacy, safety, and mechanism of action through ELISA analyses, immunohistochemistry, and flow cytometry. The mutant A β 1-42 peptide contains the same epitopes as the full length A β peptide with T-cell epitope mutations.

Results: The results indicate that use of mutant A β 1-42 vaccine results in durable antibody production, but wild type vaccine does not induce antibody response at all. The antibody generated from antigen sensitized dendritic cells is against the same epitope as other A β vaccines. Our result also showed cognitive function benefit without the global inflammation seen in prior A β vaccines. Additionally, there was a significant reduction in A β burden, and the mechanistic studies implicated the LXR/ABC1 pathway in reduction of A β burden.

Conclusion: This treatment showed positive results in animal models and has many advantages over contemporary treatments. With further development, this vaccine may be a viable clinical treatment for AD.

A Novel, Multi-Component, Multi-Targeted "Cocktail" from Natural Products for the Treatment of Alzheimer's Disease

Jay Panchal (¹), Nickhil R. Nabar (¹), Neel Ravi Nabar (¹), Ge Bai (²), Chuanhai Cao (^{1,3}), Jun Liang (¹), Shu-Feng Zhou (¹)
¹ Department of Pharmaceutical Science, College of Pharmacy, University of South Florida, Tampa, ² Department of Chemistry, University of South Florida, Tampa ³ USF Health Byrd Alzheimer Institute, University of South Florida, Tampa, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Alzheimer's disease, Amyloid beta, drug design, cocktail

Objective: As Alzheimer's disease (AD) is a multifactorial, heterogeneous disorder involving multiple biochemical pathway changes, and a number of potential targets and signaling molecules have been identified as possible drug targets. Our approach focuses the discovery of a novel multi-component therapeutic ('cocktail') targeting multiple pathways for AD. β -Amyloid ($A\beta$), Tau hyperphosphorylation, and inflammation are considered to play a central role in the pathogenesis of AD. We postulate that targeting multiple pathogenic AD pathways will result in a synergistic effect, resulting in a treatment with better efficacy.

Methods: Panels of natural compounds were examined for their effect on AD using cellular (N2a APP Cells) and mouse AD models (P57/APP). ELISA, MTT Assays were used to determine effect of drug on cellular conditions. Studies on the signal transduction mechanisms in play were done using Western Blot.

Results: Four compounds (galangin, berberine chloride hydrate, indirubin-3'-monoxime, and honokiol) showed modulatory effects on the expression of $A\beta$ in N2a APP cells and were suitable for drug use based on ELISA and MTT assays. Mixtures of these four compounds showed varying effects on $A\beta$ aggregation.

Conclusion: Based on these results, various combinations of the four natural compounds will be investigated in N2a APP to determine the ratios that maximally suppress the expression of $A\beta$ while beneficially modulating the immune response. Our natural compound library will be expanded and screened. The optimal cocktail will be further tested on the animal model of AD.

Screening of Novel Drugs for the Treatment of Huntington's disease

Tina Patel, Jessica Bencivenga, Juan Zhang, Juan Yu, Kaitlyn Braswell, Twisha Jani, Cao Chuanhai, Umesh K. Jinwal USF College of Pharmacy and Byrd Alzheimer's Institute, Calcul Laurent, Chandan Barhate, Bill J. Baker, USF Department of Chemistry, - USF College of Pharmacy and Byrd Alzheimer's Institute, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Huntington's disease, Drug Screen, Cell culture

Objective: Mutations to the gene, HTT, encoding the huntingtin protein are caused by a repeat of the trinucleotide CAG. This is the known leading cause of autosomal dominant Huntington's disease (HD) cases. The function of the normal huntingtin protein is unknown, making it difficult to fully understand the mechanistic pathogenesis of the mutated version and how it causes neural dysfunction and cell death. As a result, there are no current effective drug therapies available. The aim of our research is to discover novel drugs that effectively reduce the mutant huntingtin protein in in-vitro cell culture model E3480 Q111/Q111, which has one hundred eleven CAG repeats in the cells' genes, and compare the identified drug to the wild type cell culture model E3482 Q7/Q7 to test whether this drug has any effect on wild type cells as compared to the Q111/Q111 cells.

Methods: Wild type and mutant Huntingtin expressing cells were treated with various drugs for 24 hours. Cell lysates were analyzed for protein levels by Western blots, utilizing the Huntingtin antibody, and chemiluminescence.

Results: Preliminary data from drug screen revealed several potential novel drug molecules for the regulation of Huntingtin protein level.

Conclusion: Further experimentation with these identified drugs may provide mechanistic insight into Huntington's disease and build a foundation upon which a novel HD therapy can be developed.

Research supported by: Research Support -USF College of Pharmacy Dean's Clinical and Research Pilot award for the Start-up & New Investigator Research Grant from Alzheimer's Association

Beclin 1 and Nuclear Factor-Kbp65 as Potential Biomarkers for Hepatocellular Carcinoma

Sarwadaman Pathak, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: BECN1, nuclear factor- κ B, immunohistochemistry, in situ hybridization, hepatocellular carcinoma.

Objective: There are no sensitive and specific biomarkers for the clinical diagnosis and prognosis prediction of hepatocellular carcinoma (HCC). This study was to determine the expression pattern of beclin 1 (BECN1) and nuclear factor-kappaB (NF- κ Bp65) in patients with (HCC) at both mRNA and protein levels.

Methods: We used immunohistochemistry and in situ hybridization to detect the expression of hepatic BECN1 and NF- κ Bp65. The expression patterns were compared to those of liver cirrhosis, hepatitis, and normal liver tissues.

Results: The expression of BECN1 protein in cancer tissues was significantly higher than that of cirrhosis tissue, hepatitis tissue, and normal tissue. The expression of BECN1 protein in hepatitis tissues was significantly higher than that of cirrhosis tissue and normal tissues. The expression of BECN1 mRNA in cancer tissue was significantly higher than that of cirrhosis tissues and normal tissues, and the expression of BECN1 mRNA in hepatitis tissues was significantly higher than that of cirrhosis tissues and normal tissues. The expression of NF- κ Bp65 protein in cancer tissue was significantly higher than that of cirrhosis tissue, hepatitis tissue and normal tissue. The expression of NF- κ Bp65 mRNA in cancer tissue was significantly higher than that of cirrhosis, hepatitis and normal tissues. BECN1 expression was positively correlated with the NF- κ Bp65 expression in HCC. The abnormal expression of BECN1 and NF- κ Bp65 was closely associated with the development of HCC.

Conclusion: These results suggest that BECN1 together with NF- κ Bp65 may serve as useful biomarkers for HCC.

Identification of Novel Genetic Polymorphisms in Short Tandem Repeat Loci in Two Ethnic Minority Populations in China

Neeti Pradeep (¹), Neel Nabar (¹), Chao Liu (²), Jun Liang (¹), Shu-Feng Zhou (¹) ¹ Department of Pharmaceutical Science, College of Pharmacy, University of South Florida, Tampa, FL ² Guangzhou Criminal Science & Technology Institute, Guangzhou 510030, China, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: STRs, non-CODIS, forensic science

Objective: DNA profiling for individual identification has been relatively well developed, however individual identification in complicated cases is still difficult. The Combined DNA Index System (CODIS), a database funded by the FBI, contains information on specific short tandem repeats (STRs) in the human genome that have been validated as useful and informative for forensic practice. In order to increase scope of individual identification, we are interested in validating non-CODIS STR loci as useful for forensic practice.

Methods: In this study, we investigated 9 polymorphic STR loci (D18S1364, D12S391, D13S325, D6S1043, D2S1772, D11S2368, D22-GATA198B05, D8S1132 and D7S3048), which are not included in the standard sets of forensic loci, in 181 Miao and 166 Gelao unrelated individuals in the Guangxi municipality, South China. Genepop V 4.0 was used to perform a Hardy-Weinberg equilibrium test after allelic identification using PCR. PowerStats V1.2 software was used to calculate forensic parameters with the cumulative matching probability of the 9 STR loci in Miao and Gelao population

Results: No deviations from Hardy-Weinberg Equilibrium were observed in these two populations. The cumulative matching probabilities of the 9 STR loci in the Miao and Gelao populations were calculated as 5.18×10^{-8} and 1.20×10^{-8} respectively. The cumulative exclusion powers were 0.9999894 and 0.9999064, individually.

Conclusion: Our study showed these 9 STRs as highly informative and suitable for use as candidate genetic markers in genetics and forensic practice. As these STRs are easily typed using commercially available kits, these STRs can serve as good and cogent biomarkers for complementary use with the CODIS STRs for individual identification.

Repositioning of the FDA-approved Tyrosine Kinase Inhibitors Targeting Histone Deacetylases, B-raf and Other Proteins

Jia-Zhi Sun (^{1,2}), L. Yang (³), M.H. Li (¹), Zhi-Xin Wang (¹), Elsa M. Wright (¹), C.E. Howell (¹), Kevin B. Sneed (⁴) and Shu-Feng Zhou (¹)
¹ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, Florida 33612 ² Department of Molecular Medicine, College of Medicine, University of South Florida, Tampa, Florida 33612 ³ Bio-X Center, Key Laboratory for the Genetics of Developmental and Neuropsychiatric Disorders, Shanghai Jiao Tong University, Shanghai, China ⁴ Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: drug repositioning, TKI, B-raf

Objective: Drug repositioning represents a fast, economic and effective approach in drug discovery. Tyrosine kinase inhibitors (TKIs) are an important group of drugs used in cancer treatment, and 12 TKIs have already been approved by FDA for clinical use. We hypothesize that these TKIs act on other molecular targets in addition to tyrosine kinases, facilitating cancer cell killing.

Methods: Using a simple docking approach with our established chemical-protein interactome (CPI) and 11 FDA-approved TKIs, we have identified 301 PDB-deposited proteins corresponding to 353 ligand binding pockets among a total of 1,780 PDB-deposited human protein entries.

Results: Sorafenib and dasatinib had a CPI binding score (ZZ_score) of -1.2903 and -1.0278 against histone deacetylase 7A, respectively. In addition, both TKIs achieved high ZZ scores against B-Raf and VDR-3, suggesting a high binding affinity of sorafenib and dasatinib with these proteins. Our preliminary studies have showed that both acetylated-lysine in α -tubulin and oncogenic Raf-signaling were inhibited significantly in human B-Raf (V600E) multiple melanoma 1205Lu cells by these two TKIs.

Conclusion: Taken together, FDA-approved TKIs may be repositioned to become a “magic bullet” concurrently targeting tyrosine kinase, HDAC, and BRAf, shedding a light for future broad-spectrum anti-cancer drug development. Further validation of additional “hot targets” such as HDAC, B-Raf, Akt and VDR-3 by TKIs are under study in our laboratory.

Improving In Vitro Dissolution Release Profiles of Fenofibrate Using Lutrol F 68, 87, 108, 127

Hardam H. Tripathi, Riana M. Elliott, Misty Muscarella, N. Langley*, Shaukat Ali* and Yashwant Pathak, University of South Florida College of Pharmacy, Tampa, Florida, USA, *BASF Corporation, New Jersey, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: solubilizer, solubility, dissolution, poloxamer, fenofibrate

Objective: Fenofibrate is a drug associated with cholesterol and lipid regulation. Taken with proper exercise and diet, it has shown to help lower fatty deposits and bad cholesterol, however, it does not repair any damage caused by heart problems. This antihyperlipidemic drug is classified by the Biopharmaceutics Classification System as a class 2 drug, meaning it has a low solubility and a high permeability. Because it's poorly soluble, we are using Lutrol, a hydrophilic polymer, to help improve the solubility profiles of the drug.

Methods: Poloxamer 188 (Lutrol F68), Poloxamer 237 (Lutrol 87), Poloxamer 338 (Lutrol 108) and Poloxamer 407 (Lutrol F127) were used in the matrix for fenofibrate. Four formulations were prepared by dissolving 1:1 (API:Lutrol) with each Lutrol F68, 87, 108, and 127. Mixing process was used to incorporate fenofibrate into the Poloxamer matrix. The formulations were characterized and the dissolution tests were carried out under USP II method specified for fenofibrate. The formulations were studied for their physiochemical properties by calorimetry, x-ray diffraction, light microscopy and in vitro dissolution.

Results: The in vitro studies showed improved dissolution of fenofibrate when combined with each Lutrol compared to the fenofibrate control under identical conditions.

Conclusion: The Poloxamers increased the solubility of fenofibrate when used in 1:1 combinations with Lutrol. The solubility enhancement of fenofibrate is in part due to its increased surface active sites of drug in dispersions. Poloxamers' matrix will enhance solubility by maintaining such poorly soluble oral dosage forms, as fenofibrate, in the supersaturation state. Overall, using Lutrol greatly enhanced the drug's solubility.

Research supported by: USF College of Pharmacy, BASF

Identification of Ligands for Human Cytochrome P450 2D6 using Virtual Screening and Molecular Modeling

Danielle M. Vachon ⁽¹⁾, Sui-Lin Mo ⁽²⁾, Kevin B. Sneed ⁽³⁾, Jun Liang ⁽¹⁾ and Shufeng Zhou ⁽¹⁾ ⁽¹⁾ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, Florida ⁽²⁾ The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, P.R. China ⁽³⁾ Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida, Tampa, Florida, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Modeling, CYP2D6, inhibitor, mutation

Objective: The role of individual active site residues of CYP2D6 for ligand binding is unclear. In this study, we explored the binding mode of various inhibitors to CYP2D6 using modeling approaches.

Methods: Discovery Studio was used in our docking and modeling studies. During docking studies, the binding modes of CYP2D6 inhibitors were compared between wild-type and virtually mutated CYP2D6.

Results: We developed and validated a pharmacophore model for CYP2D6 inhibitors, which consisted of two hydrophobic features and one hydrogen bond acceptor feature. We also constructed and validated a QSAR model for CYP2D6 inhibitors which gave a poor to moderate prediction accuracy. Finally, a panel of CYP2D6 inhibitors were subject to molecular docking into the active site of wild-type and mutated CYP2D6 enzyme. We demonstrated that 8 residues in the active site (Leu213, Glu216, Ser217, Gln244, Asp301, Ser304, Ala305, and Phe483) played an important role in the binding to the inhibitors via hydrogen bond formation and/or pi-pi stacking interaction. All the four inhibitors tested could not be docked into the active site in CYP2D6 with the mutation of Thr309Val, while Ala305Asp failed to dock pimozone, quinidine, and halofantrine. The Ala300Glu, Leu121Trp, Leu248Asp, Phe120Ala, Phe483Ala, Ser304Ala, and Val119Met mutations eliminated the hydrogen bond formation of bufuralol with Ser217. Leu248Asp and Ser304Ala completely abolished the hydrogen-bond forming capacity with halofantrine. Apparent changes in the binding modes of the inhibitors have been observed with Phe120Ile, Glu216Asp, Asp301Glu mutations in CYP2D6.

Conclusion: Our study has provided insights into the molecular mechanisms of interaction of compounds with human CYP2D6.

High Throughput Screening to Investigate the Effect of a Library of Kinase Inhibitors on Clinically Important Cytochrome P450s: An Efficient Tool to Identify Drug-Drug Interactions

Zhi-Xin Wang ⁽¹⁾, Jiazhi Sun ^(1,2), Jun Liang ⁽¹⁾, Kevin B. Sneed ⁽³⁾, and Shufeng Zhou ⁽¹⁾ ⁽¹⁾ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL 33612 ⁽²⁾ Department of Molecular Medicine, College of Medicine, University of South Florida, Tampa, FL 33612 ⁽³⁾ Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida, Tampa, FL, University of South Florida, College of Pharmacy Dept. of Pharmaceutical Science

Keywords: CYP, tyrosine kinase inhibitor, high throughput screening, drug drug interaction

Objective: Tyrosine kinase inhibitors (TKIs) used in targeted cancer treatment are often metabolized by multiple cytochrome P450s (CYPs) and show remarkable inhibitory effects on various CYPs, raising the potential of TKI-drug interactions. This study investigated the effect of a library of KIs (n = 80) on human CYP1A2, 2D6, 2C9 and 3A4 and the structure-inhibitory activity relationship (SAR).

Methods: The inhibitory effect of KIs on human CYPs was examined using high throughput screening kits with fluorescent probes as the model substrates. Selective inhibitors such as furafylline and quinidine were used as the positive controls. The SAR was studied using AutoDock and Discovery Studio software.

Results: The KIs exhibited differential inhibitory effect on CYP1A2, 2D6, 2C9 and 3A4, while some KIs showed activating effect on CYP2C9 and 3A4. For example, SP 600125 was a potent inhibitor for CYP1A2 with an IC₅₀ of <1 μ M, but enhanced the activity of CYP2C9 4-fold. Similar results were observed for GW 5074 and KN-62. Among all the 80 KIs, about 15% showed significant inhibition (IC₅₀ \leq 1 μ M) to CYPs; other KIs exhibited moderate to minor or negligible inhibitory effects to CYPs. About 3% of the KIs inhibited two CYPs, e.g. KN-93 inhibited CYP 2D6 (IC₅₀ \leq 1 μ M) and 3A4 (IC₅₀ = 1 μ M); apigenin inhibited CYP1A2 (IC₅₀ = 1 μ M) and 3A4 (IC₅₀ = 1 μ M). Our docking studies demonstrated the tight binding of these inhibitors to respective CYPs.

Conclusion: The findings can be used to predict important drug interactions between KIs and other drugs that are extensively metabolized by CYPs.

Creating Stable Cell Lines in BE(2)-M17 Cells for Various Mutations of Alpha-Synuclein

Clement G.Y. Yang, Umesh K. Jinwal, Daniel C. Lee (Department of Pharmaceutical Science, College of Pharmacy, USF Byrd Alzheimer's Institute, University of South Florida)

Keywords: alpha-synuclein, Parkinson's disease, in vitro, stable expression, BE(2)-M17

Objective: Parkinson's disease (PD) is a progressive neurodegenerative disorder. PD patients suffer from selective loss of dopaminergic neurons in the substantia nigra (a part of mid brain). The neurons of PD patients develop Lewy bodies, caused by abnormal aggregation of alpha-synuclein (a-syn) proteins. In addition, duplication and triplication of wild type and several mutations in a-syn promote disease pathology. Despite intense research efforts, successful therapeutics targeting a-syn pathways remain less well defined. In this study, we created stable cell lines over-expressing various forms of a-syn in dopaminergic neurons. We endeavored to identify if viable and stably expressed forms of a-syn would promote aggregation in vitro.

Methods: Wild-type and various mutations (A30P, E46K and A53T) of a-syn genes were stably transfected into dopaminergic human neuroblastoma BE(2)-M17 cells. Stable cells were selected and maintained using G418.

Results: The over-expression level of a-syn was quantified by western blot analysis. The aggregation phenotype of wild type and mutant clones were characterized with the ProteoStat Protein Aggregation Assay® which monitors protein and peptide aggregation. Furthermore, immunocytochemistry double labeling experiments showed the presence of a-syn and positive aggregation profiles.

Conclusion: Finally, we aim to identify molecular mechanisms between the various forms of a-syn and protein aggregation in vitro. Future studies will also employ these cells for drug screening and therapeutic reduction of a-syn in dopaminergic neurons.

Research supported by: USF New Researcher Grant

Novel Targeted Cyclodextrin Based Nanoparticle Delivery Systems for Cancer Chemotherapy

Juan-Juan Yin⁽¹⁾ and Shu-Feng Zhou⁽¹⁾ ¹ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, Florida

Keywords: nanoparticle, drug delivery, nanodrug complex, doxorubicin

Objective: Tumor resistance and drug toxicity are two major limitations for cancer chemotherapy. A possible approach for overcoming drug resistance and the toxicity due to drug resistance is the application of targeted nanoparticles covalently linked to (or encapsulating) cytotoxic drugs, improving drug delivery.

Methods: A novel, self-assembling targeting supramolecular nanodrug complex was synthesized from small molecules, such as folic acid, integrin ligand grafted cyclodextrins (CyDs), and doxorubicin for tumor therapy.

Results: The resulting targeting supramolecular drug complex uses through host-guest interaction between targeting β -cyclodextrin and adamantane modified doxorubicin. β -cyclodextrin, conjugated with the tripeptide RGD (Arg-Gly-Asp) or folic acid, allows for specific binding to tumor cells over-expressing integrin $\alpha v \beta 3$ or folate receptors. The reaction of mono-6-deoxy-6-amino- β -cyclodextrin derived from β -cyclodextrin and the carboxyl-terminal of the oligopeptides or folic acid resulted in formation of the host moiety, while the guest molecule was a cytotoxic prodrug obtained by the reaction of adamantyl chloride and doxorubicin hydrochloride, in which the adamantyl group serves as a perfect candidate for the host-guest interaction with CyDs. Synthesis of this supramolecular nanodrug delivery system was confirmed by structural analysis using HRMS and NMR.

Conclusion: The successful synthesis of this nanodrug complex bodes well for the development of targeted drug treatments for chemotherapeutic agents. Further in vivo testing will be done to test the efficacy, safety, pharmacokinetics, and pharmacodynamics of this modality of treatment.

Therapeutic Effect of Transplanting Magnetically Labeled Bone Marrow Stromal Stem Cells in a Liver Injury Rat Model with 70%-Hepatectomy

Xiao-Wu Chen ⁽¹⁾, Jun Liang ⁽²⁾, Kevin B. Sneed ⁽³⁾ and Shufeng Zhou ⁽²⁾ ⁽¹⁾ The First People's Hospital of Shunde affiliated to Southern Medical University, Shunde, Guangdong 528300, China ⁽²⁾ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL, University of South Florida, College of Pharmacy, Dept. of Pharmaceutical Science

Keywords: Liver injury, bone marrow stromal stem cell, transplant, rat

Objective: There are a number of studies on the application of bone marrow stromal stem cells (BMSCs) for the treatment of chronic liver diseases, but only few reports about the use of BMSCs for the treatment of traumatic liver injury. This study aimed to study the therapeutic effect of fluorescence-labeled bone marrow stromal stem cells administered to male SD rats subject to traumatic liver injury.

Methods: Male SD rats with a 70% resection of the liver were injected with feridex-labeled BMSCs which could be induced to functional hepatocytes in vitro. Liver function was assayed and the liver scanned by 1.5-T MRI at 12 hrs and on days 1, 3, 5, 7, and 14 post-operation. The pathological changes of liver sections were monitored.

Results: The serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), direct bilirubin (DBIL), and total bilirubin (TB) in the transplantation group were significantly lower than the control group. The MRI showed rats of the transplantation group had an oval low signal area at 12 hr after operation; the low signal range gradually expanded and the signal intensity gradually decreased over 14 days after operation. The low signal range in the control group disappeared 12 hr after the operation. After Prussian blue staining, rats of the transplantation group contained blue granules with no significant hypertrophy or edema in hepatocytes, while the control group showed no blue granules with significant hypertrophy and edema. The BMSCs transplanted into the injured rat liver gradually migrate to the surrounding liver tissue and partially repair the liver surgical injury in rats.

Conclusion: BMSCs may represent an effective therapeutic approach for acute liver injury.

Variation in Patterns of Angiogenesis-Associated Gene Expression Among Different Sunitinib-Resistant Brain Tumor Models

Qingyu Zhou ⁽¹⁾, James Gallo ⁽²⁾. ⁽¹⁾ Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL ⁽²⁾ Department of Pharmacology and Systems Therapeutics, Mount Sinai School of Medicine, New York, NY

Keywords: Antiangiogenic therapy, acquired drug resistance, brain tumor, sunitinib.

Objective: The development of acquired drug resistance is a major factor in the failure of sunitinib (SU) treatment for solid tumors. This study was focused on the establishment of SU-resistant brain tumor models that can be used to illustrate how tumor cells and their microenvironment modulate their expression profiles in response to the antiangiogenic therapy and to explore the potential escape pathways.

Methods: SU-resistant tumors were developed in three different human U87MG glioma models: the subcutaneous tumor model, and the autologous-transfer and heterologous-transfer orthotopic tumor models. Tumor-bearing mice were given oral once-daily dosing of 40 mg/kg of SU. The phenotypic sensitivity and resistance of individual animals to the SU treatment were defined by the fold-change of tumor volume relative to the initial volume and the survival time for the subcutaneous and orthotopic tumor models, respectively. The quantitative real-time PCR array was used to determine the expression levels of angiogenesis-associated genes in the control and SU-treated tumors.

Results: The differences between the expression levels of several angiogenesis-associated genes in the SU-treated tumors and those in the control tumors were significant, whereas no difference was found between the SU-sensitive and -resistant tumors, irrespective of the tumor model in which the experiment was conducted.

Conclusion: The variation in the expression profiles of angiogenesis-associated genes is attributable to tumor location and treatment duration. Although none of the models can precisely recapitulate all aspects of the acquired human brain tumor resistance to the SU treatment, the individual models can be of considerable use to test strategies that may reverse the drug resistance.

Improving Women's Health Care through a Collaborative Process: Learning a Common Language across Medicine and Public Health

Erica Anstey, MA, CLC; Angela Dimaggio, BA; Rosa Ore, BA; Lauren Young, BA; Lynne Klasko, BA; Nadine Connor, MSN, ARNP-c; Laurie Woodard, MD; Ellen Daley, PhD University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Women's health interdisciplinary co-learning

Objective: Community health clinics (CHC) provide primary care to uninsured women in the US and are often training programs for health sciences students. Communication proficiency is an important part of professional training; cross-disciplinary discourse may improve these skills. The purpose of this study is to understand the benefits of co-learning for public health and medical students in a collaborative clinical setting and analyze public health students' perceptions of collaboration and patient care.

Methods: Public health students participating in a women's health training program at a CHC kept detailed journals documenting patient interactions with providers and students, interdisciplinary observations, and personal insights. A student and an independent coder analyzed six journals using a priori and emergent codes in NVivo.

Results: Public health students identified interdisciplinary teams as important. Common themes included positive impact on health behaviors, understanding patient needs and improved health maintenance. Varying degrees of receptivity to interdisciplinary communication and an increased awareness of the difficulties in communication among health professionals were noted themes. Students also identified a greater awareness and appreciation for the institutional challenges faced by clinicians working with underserved populations.

Conclusion: Addressing complex health issues among women who have been marginalized due to economic, cultural, and linguistic factors can be challenging. Co-learning experiences provide valuable opportunities for students in health disciplines to learn best practices for patients at individual and population levels, broaden students' perspectives, and encourage improved communication across healthcare disciplines.

Developing a Network of Community Research Councils to Promote and Facilitate Clinical Prevention Trial Participation in Medically Underserved Populations

Atalie A. Ashley, BA¹, Kevin B. Sneed, PharmD², Julie Baldwin, PhD³, Maisha Standifer, MPH⁴. (1) College of Public Health, University of South Florida, Tampa, FL (2) USF School of Pharmacy/USF Health, University of South Florida, Tampa, FL (3) Department of Community and Family Health, College of Public Health, University of South Florida, Tampa, FL (4) Department of Community and Family Health, College of Public Health, University of South Florida, Tampa, FL, University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Clinical Trial, Medically Underserved, Center for Equal Health

Objective: The Community Research Council (CRC) was established to advocate for and oversee clinical and translational research activities in the Tampa Bay region. This governing body serves to: 1) Strengthen the relationship of the research institutions with the community; 2) Provide oversight, protection, and advocacy of community participants involved in clinical and translational research activities performed by academic and clinical institutions; 3) Create and enhance clinical trial opportunities for underrepresented communities; 4) Empower underrepresented communities with decision-making opportunities concerning research activities that involve their members; and 5) Enhance and expand trust between academic and clinical institutions and the communities that they serve.

Methods: Once clinical trials are created or identified in the region, we will develop a plan to monitor minority participation in these trials over time. Long term goals of the CRC include lobbying pharmaceutical companies and private investors to provide more clinical research opportunities in the defined region (i.e., the Florida Counties of Hillsborough, Pasco, and Pinellas).

Results: We expect to see self-reported increases in clinical research knowledge within one year of CRC implementation in the region.

Conclusion: We believe that when clinical practitioners, research institutions, members of the community, and pharmaceutical companies are provided with a central organization that provides education, ethical guidelines, and an opportunity for networking, the long term result will be an increase in minority participation in clinical trials.

Research supported by: Center for Equal Health at the University of South Florida, and the Moffitt Cancer Center

Confusion Regarding Cervical Cancer Screening: Pap Smear Knowledge Among Three High-Risk Populations of Women

Elizabeth Baker, MPH, CPH, Natalie Hernandez, MPH, Judith Syfrett, MPH, Erica Anstey, MA, CLC, Stephanie Kolar, MSPH, Cheryl Vamos, PhD, Ellen Daley, PhD. University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Pap smear, human papillomavirus, health education, women's health

Objective: To explore women's Pap smear knowledge among three high-risk populations over time.

Methods: Three groups of high-risk women completed identical surveys assessing Pap smear knowledge: 154 HPV+ women (pre-vaccine era population in 2005-2006), 276 college women (post-vaccine era population in 2008), and 693 minority college women (post-vaccine era population in 2011). Frequencies were employed to compare differences.

Results: Although the majority of women in all three studies (75%-84%) correctly reported that the Pap smear is a test for cervical cancer, a considerable proportion of women from each population incorrectly believed that the Pap smear tests for pregnancy (17%-38%), herpes, (53%-80), gonorrhea (55%-81%), HPV (83%-91%), HIV/AIDS (22%-59), yeast infections (65%-86%), and vaginal infections (76%-92%).

Conclusion: While Pap smear rates among U.S. women are encouraging, it is disconcerting that women are engaging in this screening behavior without adequate knowledge of its purpose, as this may result in women foregoing other appropriate testing. Furthermore, cervical cancer screening guidelines have recently changed, which may add to women's confusion and present even more missed opportunities for primary and secondary prevention. Identifying potentially harmful misconceptions about Pap smears may help researchers design appropriate methods to educate high-risk women about the purpose and guidelines for cervical cancer screening and other appropriate STI testing.

Research supported by: Department of Community & Family Health Student Research Award (COPH) & CDC S1676-21/23

Assessing the Psychometric Properties of a Positive Youth Development/Teen Pregnancy Prevention Program Evaluation Instrument

Heather D. Blunt ⁽¹⁾, Charlotte A. Noble ^(1,2), Natalie Klinkenberger ⁽¹⁾, Sarah Maness ⁽¹⁾, Kara E. McGinnis ^(1,2), Rita D. DeBate ⁽¹⁾, Karen M. Perrin ⁽¹⁾, Ellen Daley ⁽¹⁾, Stephanie L. Marhefka ⁽¹⁾, Wei Wang ⁽³⁾, Eric R. Buhi ⁽¹⁾. ⁽¹⁾ Department of Community and Family Health, College of Public Health, USF ⁽²⁾ Department of Anthropology, College of Arts and Sciences, USF ⁽³⁾ Department of Epidemiology and Biostatistics, College of Public Health, USF, University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Adolescents, Teen Pregnancy Prevention, Reliability, Validity, Surveys

Objective: The purpose of this cross-sectional study was to pilot test a survey instrument developed to evaluate a federally-funded teen pregnancy prevention project. This analysis reports the psychometric characteristics of 4 scales used in this study.

Methods: A pilot survey was administered during five class periods (1 day) in June 2011 in a rural Florida high school. The survey included measures of Positive Youth Development (PYD), with subscales assessing character, caring, connection and confidence; self-regulation (SR), with subscales assessing emotion, cognitions, and behaviors; expectations/aspirations; and community service (CS). Surveys were analyzed in SPSS 20.0. Analyses include Cronbach's alpha and confirmatory factor analysis with Varimax rotation.

Results: Of the 72 youth completing the survey, 58 report answering questions honestly. Reliability and validity statistics were calculated for the scaled items. Results show the scaled data are sufficiently reliable (Cronbach's alpha: Character=.877, Caring=.774, Connection=.908, Confidence=.819, CS=.970, Expectations/Aspirations=.860). Only SR (Cronbach's alpha=.641) resulted in debatable score reliability. Confirmatory factor analysis found theoretically sound results that reflect previous research findings. Validity statistics are acceptable with percent variance explained ranging from 54% (emotions subscale of SR) to 79% (CS).

Conclusion: Detecting meaningful effects depends on reliable and valid data/scores. Despite a small sample size, the data in this pilot study appear to be reliable and valid. Assessing the psychometric characteristics of survey data is an important first step to explain the influence of measurement error on results.

Research supported by: A grant from the Office of Adolescent Health, USDHHS.

Creating Connections Between Adolescent Health and Adult Medicine: Transitions for Undergraduate Students with Health Challenges

Dr. Karen M. Perrin¹, Dr. Alan J. Kent², Nicole Johnson³, Jarrett N. Brunny¹, Terrill Curtis¹, Coralia Vázquez-Otero¹, ¹College of Public Health, ²Student Affairs, ³Bringing Science Home. University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: chronic health challenge, adolescent health, transitions, university services, qualitative

Objective: Identify the unmet needs of undergraduate students at the University of South Florida that are living with chronic health conditions and negotiating transitions from adolescent health to adult medicine. Determine the strengths and weaknesses of current campus services that serve undergraduate students living with a health challenge.

Methods: Twenty-four semi-structured interviews were conducted over a one year period with students living with a chronic physical or mental health challenge. Principles of grounded theory and the constant comparative method were used for analysis. A second data collection phase consisting of triangulation through mixed method surveys is currently ongoing.

Results: Foundations of transitions from adolescent health to adult medicine in undergraduate students living with a chronic health challenge include establishing independence; adoption of medical and lifestyle management behaviors; perceptions about the health care and insurance environment; availability and use of health care services; and degrees of positive psychosocial support. Unmet needs of undergraduate students living with a health challenge appear when foundations of the transition are out of balance.

Conclusion: Health transitions are critical points of student development, and the ability to successfully negotiate the transition from adolescent health to adult medicine is further complicated by the presence of a chronic health challenge. University based medical, psychological, social and educational service providers are key players in the transition. This research confirms that a formative, collaborative effort between University service providers and their student clientele is an important step to ensuring successful health transitions.

Research supported by: Bringing Science Home

Violence in the Workplace in Nursing Home Settings: A Preliminary Analysis

Vanessa Chee, Dr. Carla VandeWeerd, Dr. Martha Coulter, College of Public Health, Department of Community and Family Health, University of South Florida

Keywords: Nursing homes, workplace violence

Objectives : The CPH Harrell Center Study of *Job Experiences in Nursing Homes*, funded by the Sunshine Education and Research Center (ERC), is a pilot study seeking to explore the extent to which physical, psychological, or sexual aggression takes place against nursing home staff by residents or co-workers, and to describe the context of these incidents. The goals of this study are: to identify the context of aggression towards staff and its perpetrators; to identify the impact of negative interactions between staff and residents; and to explore on the job experiences of nursing home staff. Findings will be used to develop recommendations for nursing home facility administration for both reducing negative interactions against staff by residents and co-workers, and reducing the impact of these negative incidents.

Methods: Semi-structured interviews will be conducted with staff from nursing homes throughout the United States. Of particular interest is the extent to which co-worker aggression occurs within the context of personal relationships, and the identification of the contextual factors that contribute to these incidents and their outcomes.

Results: Thus far 10 participants have been interviewed. Interviewees have been of various ethnic backgrounds and job descriptions such as: Certified Nursing Assistant, RN Weekend Supervisor, Receptionist, Assistant Director of Nursing, Housekeeping, and MDS Coordinator. Preliminary results suggest that workplace violence that includes physical assault (for example, getting punched, hit, or kicked) and verbal abuse is a common occurrence in nursing home settings, although staff who experience this may not define these incidents as violence. Counseling, training and safety measures offered to staff vary considerably across facilities. Further analysis will identify common conceptual themes in participant responses regarding the context of negative interpersonal experiences, adverse consequences, and personal feelings about these incidents. Analysis will investigate differences in these outcomes depending on whether perpetrators are residents or co-workers.

Conclusions: Recommendations will be generated regarding prevention and intervention based on participant responses.

The Fagerström Nicotine Dependence Scale: How do USF student smokers weigh in?

Pamela C. Guevara, MPH, Elisabeth A. Franzen, Eric R. Buhi, MPH, PhD, Department of Community and Family Health, College of Public Health, University of South Florida, Mary P. Martinasek, PhD, MPH, CHES, Department of Health Science and Human Performance, College of Natural and Health Sciences, University of Tampa, Department of Community and Family Health, College of Public Health, University of South Florida.

Keywords: Nicotine Dependence, Smoking Cessation, Young Adult, Student Health Services.

Objective: To assess nicotine dependence by using the Fagerström Scale among USF college smokers and how dependence correlates with readiness and confidence to quit.

Methods: A pilot, longitudinal randomized controlled trial was implemented in 3 phases with USF students seeking smoking cessation services (SCS). Each participant was prompted to complete a baseline survey and 2 follow-up web-based surveys (at 3 and 6 weeks post-quit date). Inferential statistics were conducted using SPSS 19 to assess students' nicotine dependence based on the Fagerström Scale. The scale is divided into 2 levels: 1) Low to moderate dependence or 2) Significant dependence of nicotine. Pearson Correlations were conducted to assess relationships between students' level of dependence and readiness to quit, confidence that they can quit, and number of times that they have tried to quit smoking.

Results: From December 2010 to January 2011, 47 USF students were recruited into this study. Of the recruited students, 25 (53.2%) were of low to moderate dependence on the Fagerström Scale, and 22 (46.8%) were significantly dependent on nicotine. From conducting the Pearson Correlation between the Fagerström Scale and the continuous variables listed above, only the variable that asked, "During the past 12 months, how many times have you tried to quit smoking for at least 1 day?" was statistically significant ($r=.303$, $p<.05$, $n=46$).

Conclusion: Our results indicate that the more dependent a person is on the Fagerström Scale, the more times they have tried to quit smoking. It may be useful for campus health practitioners to focus on assessing dependence when smokers present for SCS and, based on the student's level of dependence on nicotine, more appropriate and tailored SCS can be provided.

Research supported by: USF AHEC.

Beyond The Condom: A Text and Mobile Video Pilot Project Promoting Long-Acting, Reversible Contraception Methods to College-Age Women.

Harsch, K. L., Ogunrinde, A. C., Rella, N. C., Helmy, H. L., Pravetz, C., & Buhi, E. R. University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: health promotion; innovation; mobile video; long-acting reversible contraception; contraceptive education

Objective: Beyond the Condom (BtC) is a text and mobile video intervention pilot project promoting the use of long-acting, reversible contraceptives (LARCs) among college students. BtC was developed utilizing a university-community advisory board (UCAB) comprised of students and sexual health professionals. The goals of BtC are to promote awareness, dispel myths/misconceptions, increase use intention, and link students with providers.

Methods: BtC was developed in 5 phases with continuous feedback from the UCAB. Phase 1 involved creating a LARC Friendly Provider Database, enabling users to locate providers. Phase 2 involved developing text messages and mobile videos. Phase 3 included testing and revision of text messages and videos, and Phase 4 involved usability and acceptability testing through focus groups of USF undergraduate students. Phase 5 included a campus-wide marketing campaign for broader acceptability and outcome assessments.

Results: Within 45 days, 769 participants texted into BtC, 679 loaded the mobile landing page, 253 navigated to the video page, and 108 accessed the provider directory. 59% of respondents ($N=80$) searched for additional information regarding LARCs on the internet and 40% reported intention to use LARCs. Half rated BtC as "much better" than contraception information received elsewhere. Over 95% reported recommending BtC to friends.

Conclusion: To date, no interventions utilizing mobile video to promote behavior change have been identified in the peer-reviewed literature. Findings from the BtC campaign suggest that a text and mobile video intervention is evaluated positively among college students and promotes information through a widely used and accepted modality.

Research supported by: The National Campaign to Prevent Teen & Unplanned Pregnancy

Attitudes about Medical Mistrust and HPV Vaccination among Young Women of Color

Hernandez, N., Daley, E., COPH, Community and Family Health Kolar, S., Young, L., COPH, Epidemiology and Biostatistics, Romero-Daza, N., College of Arts and Sciences, Department of Anthropology, Chandler, R. College of Nursing, Linda Nguyen, College of Arts and Sciences, Dept. of Chemistry

Keywords: HPV vaccination, minority health, medical mistrust

Objective: To examine differences among racial/ethnic minority women on medical mistrust and HPV vaccination.

Methods: Women at a southeastern university completed a web-based survey assessing HPV vaccine uptake and mistrust of the health care system (n=693). The 12 mistrust items were summed to create a Medical Mistrust Scale (theoretical range 0-48) with higher scores indicating higher mistrust. Wilcoxon tests were employed to compare differences among participants.

Results: The mean score on the Medical Mistrust Scale was 14.4 (SD=7.8; range 0 to 40). Self-identified Black women scored significantly higher ($p<0.01$) on the mistrust scale (mean=18.3) compared to Hispanic (mean=13.7), Asian (mean=13.6), or White (mean=10.6) women. Black women who reported receiving at least one dose of the HPV vaccine had significantly lower mistrust scores compared to Black women who had not received the vaccine ($p=0.02$).

Conclusion: More prevalent mistrust beliefs among Black women may explain low HPV vaccine uptake among this population. These findings suggest that unique educational strategies need to be developed, based on the needs and perceptions of the targeted audience, in order to achieve higher HPV vaccine uptake.

Research supported by: Department of Community and Family Health

High School Football Injuries among Athletes in West-Central Florida Siwon Jang*, MA, Karen D. Liller*, Ph.D., Jeff Konin**, Ph.D., Barbara Morris**, DHSc., Siew Wong*, MPH *USF College of Public Health **USF Morsani College of Medicine, University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Sports injury, Football, High school, Registry

Objective: The purpose of this study was to describe the incidence and risk factor information related to football injuries using a sports injury surveillance system developed by the Sports Medicine and Athletic Related Trauma (SMART) Institute of the University of South Florida.

Methods: Football injury data were collected from high school athletes enrolled in five public high schools in west-central Florida from August 9 - December 12, 2010 utilizing professional sports injury surveillance software. The surveillance system captured exposure and risk factor information of the athletes. Five certified athletic trainers (ATCs) were hired by the SMART Institute of the University of South Florida to collect the data. The ATCs exported the information to the university once a week for analysis.

Results: Overall, 96 football injuries were reported by the ATCs. The injuries took place during practices (single-sessions) (55.2%) and competitions (41.7%). The majority of all injuries was new (86.5%) and the most common mechanism of football injuries was contact with another player (20.8%). The leading player positions of athletes suffering an injury included linebacker (12.5%) and offensive guard (12.5%). The most common physiologic injury reported was sprain (34.2%) followed by concussion (18.9%). The leading body parts injured were the head (19.8%) and right ankle (11.7%).

Conclusion: These data show the incidence and risk factor information related to football injuries among this group of high school athletes. These data will serve to inform future research and practice to prevent football injuries. The ultimate goal is the development, implementation, and evaluation of targeted interventions that will decrease football injuries among high school athletes.

Diabetes Distress in Parents of Children with Type 1 Diabetes Nicole Johnson, MPH, MA, Stephanie Melton, MA, MPH University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: diabetes, family functioning, diabetes distress, coping

Objective: Type 1 diabetes management requires adherence to daily treatment regimes, which can result in challenges and stressors for families impacted by the disease. This qualitative study assessed parents' perceptions of how diabetes affects their family dynamics and social relationships.

Methods: This research was conducted using focus groups and interviews with parents of children young adults with Type 1 diabetes.

Results: The results of this study indicate that parents face many challenges around diabetes, and multiple factors combine to create a high level of distress in parents who respond with coping strategies that may indirectly increase distress. In these families increased stress and poor coping responses negatively affect the child's diabetes outcomes. For parents of youth with Type 1 diabetes, the demands of care giving create parental needs that often go unaddressed resulting in chronic diabetes distress.

Conclusion: This research highlights the unmet needs of parents and the potential role of health care providers in identifying diabetes-related distress and providing support tools for families affected by diabetes.

Research supported by: A gift from The Patterson Foundation

Postpartum Depression Screening: Are Pediatricians on Board? Courtney Judd, MD - University of South Florida, Sharon Dabrow, MD - University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: postpartum depression, screening, pediatric

Objective: The purpose of this study is to determine the prevalence of postpartum depression (PPD) screening among outpatient pediatric primary care providers in Florida.

Methods: A 15 item multiple choice survey was sent by electronic mail to Florida AAP members and Florida pediatric residency programs. Eligible respondents were primary care physicians who provide outpatient care for infants 6 months of age or younger. Survey questions elicited information about the frequency and style of PPD screening, appointment types during which screening occurs, action taken for concerning screening results, and provider awareness of suggested PPD screening practices.

Results: Out of 71 total respondents, 65 were eligible to complete the survey. Of those, 92.1% reported ever discussing PPD with parents. Only 47.6% of providers have ever used a formal PPD screening scale, with 63.3% of them reporting use of the Edinburgh Postnatal Depression Scale and 30% reporting use of the Postpartum Depression Screening Scale. The highest use of PPD screening scales occurs during the 1-2 week (70%), 1 month (60%), and 2 month (63.3%) well visits. Use of PPD screening tools drops after 2 months, with 16.7% of physicians using them at 4 month visits and 10% at 6 month visits. Less than half (42.9%) of providers are aware of any AAP suggestions regarding PPD screening.

Conclusion: This study of Florida pediatric providers reveals that less than half of physicians are consistently using a PPD screening tool, and few are screening mothers after the infant's 2 month check-up. Awareness and knowledge regarding AAP recommendations are low. Future efforts directed at improving pediatric provider knowledge may help to promote routine PPD screening and thus ensure healthy environments for children.

Evaluation of Urinary Pesticide Biomarkers Among Children and Adolescents

A. LeBeau, G. Johnson, J. McCluskey, and R. Harbison University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Biomonitoring, Biomarker, Urine, Organophosphate, Pyrethroid

Objective: The current research investigates the relationship between the detection of non-persistent pesticide urinary biomarkers of exposure and differences in height and weight of children age 6-11 from the 2001-2002 NHANES dataset. Three biomarkers were detected in more than 50% of the sample (n=3152): 3,5,6-trichloropyridinol (TCPY); paranitrophenol (PNP); and 3-phenoxybenzoic acid (3PBA).

Methods: Mean values for weight and height were determined for each age group of children with detectable biomarker in the urine sample and compared to the equivalent mean of children that did not have a detectable level of biomarker in the same group.

Results: In most age groups, t-test comparisons did not indicate significant differences between children with a recorded biomarker detect compared with those with a non-detect. Significant differences of note: PNP recorded significant height difference for children age 8 with detect mean height= 130.9 cm (n=49) and non-detect mean height=134.3 cm (n=38), p=0.046. PNP also had a significant height finding for children age 11 with a detect mean height at 153.7 cm (n=63) and non-detect mean height at 149.9 cm (n=37), p=0.022. Children age 7 in the 3-PBA analysis recorded a significant difference in weight with the detect mean weight=28.6 Kg (n=76) and a non-detect mean weight= 25.6 (n=27), p=0.009.

Conclusion: In most age groups, t-test comparisons did not indicate significant differences between children with a recorded biomarker detect compared with those with a non-detect. Of the 36 comparisons made between detectable levels and non-detectable levels of the biomarker, 33 did not have any significant findings at the p< 0.05 level.

Women living with HIV: Experience and feelings in a video-group intervention.

Lynn, V⁽¹⁾., Marhefka, S⁽¹⁾., Fuhrmann, H⁽¹⁾., Benton, A⁽¹⁾., Lopez, B⁽¹⁾., Eldridge Q⁽¹⁾., Joseph, A⁽¹⁾., Glueckauf, R⁽²⁾., & Baldwin, J⁽¹⁾. University of South Florida⁽¹⁾, Florida State University⁽²⁾ University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Women, HIV, video-group, intervention, cohesion

Objective: To explore whether women living with HIV can feel connected during a video-group intervention.

Methods: WLH (n=28) were recruited from 4 different counties in Florida. Groups consisted of 3-7 participants. Each group met via video-phone twice a week for three weeks. Participants completed a computerized post-intervention survey immediately following the sixth session.

Results: Group participants (M age = 42.15; SD = 8.076; 57% African-American/Black; 29% Caucasian; 14% Hispanic) reported being mostly satisfied or very satisfied (95.14%) with their overall experience with the intervention. Participants reported that group members respected the agreement of confidentiality (92.9%), there was a positive relationship among the group members (96.5%) and they felt comfortable expressing disagreements within the group (92.9%). Participants also reported there was a feeling of unity and togetherness among group members 96.4%) and they felt free to share information (96.4%). Open-ended responses also indicated high group cohesiveness and comfort level within the groups.

Conclusion: While video-group interventions do not allow for physical reassurance and affirmation, preliminary findings indicate women felt connected and felt comfortable in a video-group intervention. Video-groups are promising strategy for delivering behavioral interventions for WLH.

Research supported by: R34 grant from the National Institute of Mental Health

Sexual and Reproductive Health Behaviors of Ninth Grade Youth: Findings from a Pilot Study in a Rural Florida High School

Sarah Maness⁽¹⁾, Heather Blunt⁽¹⁾, Charlotte Noble⁽¹⁾, Natalie Klinkenberger⁽¹⁾, Kara McGinnis⁽¹⁾, Rita DeBate⁽¹⁾, Kay Perrin⁽¹⁾, Ellen Daley⁽¹⁾, Stephanie Marhefka⁽¹⁾, Wei Wang⁽²⁾, Eric R. Buhi^{(1), (1)} Department of Community and Family Health, College of Public Health,⁽²⁾ Department of Epidemiology and Biostatistics, College of Public Health, University of South Florida

Keywords: Adolescents, School Health, Sexual Health, Risk Behaviors

Objective: The purpose of this cross-sectional study was to pilot test a youth survey instrument, developed as an evaluation tool for a federally-funded teen pregnancy prevention project. The aim of the current analysis is to describe the sexual and reproductive health (SRH) behaviors reported by 9th grade youth attending a rural Florida high school.

Methods: After IRB review/approval, we administered a pilot youth survey in a high school in rural central Florida. The survey was given in five class periods during a one day period in June 2011, and asked questions related to youth goals, self-esteem, participation in school activities, SRH behaviors, and views on and involvement in community service. Surveys were scanned with TeleForm and analyzed using SPSS 20.0.

Results: Of the 72 youth responding, 58 reported answering questions honestly. Of these 58 respondents, the average reported age was 14.98 years. The majority reported never having had sexual intercourse (67.2%), yet 3.4% reported ever having been pregnant or caused a pregnancy. Of all respondents, 15.5% reported having had sexual intercourse within the past three months and nearly half of these youth (44.4%) reported not using any effective form of birth control at least once.

Conclusion: Results of this pilot study indicate that although slightly lower than the national average, a majority of high school 9th graders surveyed have not had sexual intercourse. Among students recently engaging in sexual activity, nearly half reported not using an effective contraceptive method. These findings support the utility of implementing adolescent pregnancy prevention programs among 9th graders to facilitate positive decision making before students become sexually active.

Research supported by: Office of Adolescent Health, USDHHS

A Patchwork Quilt:***Services & Supports for Infants and Toddlers with Down Syndrome and their Families***

Jennifer Marshall, Jean Paul Tanner, Ashleigh L. Simon, Yekaterina Kozyr, Russell S. Kirby University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Down Syndrome, Access to Services

Objective: The purpose of this project was to describe the system of care for infants and families affected by Down syndrome to better understand experiences with and barriers to services in Hillsborough County and statewide.

Methods: This qualitative, exploratory study utilized focus groups with 13 English or Spanish-speaking parents and 37 community providers recruited through local agencies and support groups to better understand experiences in accessing Down syndrome-related perinatal, infant, and early childhood services and supports. Recordings were transcribed and analyzed with Atlas.ti utilizing grounded theory to identify 33 codes, organized into a taxonomy developed to explain relationships and factors influencing families' experiences across the time span from the prenatal period through school age.

Results: The study identified important key experiences, transitions, and influences impacting the experiences of parents of a child with Down syndrome regarding prenatal diagnosis and perinatal care; medical and developmental services, care coordination and service systems, and social and community support. Findings guided the development of factsheets, a resource guide, research summaries, and a statewide survey to examine access to and satisfaction with various services.

Conclusion: The family, community, and system-level interactions across the event span greatly impact the timeliness and quality of services a family receives. Formal systems of care are not adequately prepared to provide appropriate supports to individuals with Down syndrome and their families. Individuals with disabilities require varying levels of formal and informal support to be successful in meeting their goals and to achieve and maintain a high quality of life.

Research supported by: Dr. Kirby

Evaluation Protocol for an Adolescent Pregnancy Prevention Program in Non-metropolitan Florida High Schools Kara E. McGinnis (^{1, 2}), Heather D. Blunt (¹), Natalie R. Klinkenberger (¹), Sarah Maness (¹), Charlotte A. Noble (^{1, 2}), Ellen M. Daley (¹), Karen M. Perrin (¹), Rita D. DeBate (¹), Stephanie L. Marhefka (¹), Wei Wang (³), and Eric R Buhi (¹) (¹) Department of Community and Family Health, College of Public Health, USF (²) Department of Anthropology, College of Arts and Sciences, USF (³) Department of Epidemiology and Biostatistics, College of Public Health, University of South Florida

Keywords: Protocol, Evaluation, School Health, Positive Youth Development, Adolescent Pregnancy

Objective: To describe how the RE-AIM framework guides the replication evaluation of the Teen Outreach Program (TOP), a positive youth development (PYD) program. The purpose is to longitudinally evaluate TOP and assess how the 5 Cs (Character, Competence, Caring, Connection, Confidence) of PYD may be mediating mechanisms for the prevention of teen pregnancy.

Methods: The study involves 27 schools in 11 Florida non-metropolitan counties and uses a delayed intervention/cohort sequential design. Participating schools are randomized into TOP or control. In years 1 and 2, TOP and control schools will remain the same; in year 3 all schools will receive TOP. Youth will be surveyed at baseline, post-intervention, and 1- and 2-year post-intervention.

Results: Results will assess outcomes regarding teen pregnancy, school suspension/drop-out, course failure, and the 5 Cs. Instrument development is guided by the RE-AIM framework. REACH is determined using class level attendance sheets and county participation rates. EFFICACY is assessed by youth surveys, focus groups, and school personnel interviews. ADOPTION is analyzed by school personnel interviews. IMPLEMENTATION fidelity is monitored by facilitator logs, a community service learning record, and the Youth Program Quality Assessment Tool. MAINTENANCE is assessed through long-term impact focus groups and interviews and the RE-AIM Impact calculator.

Conclusion: This poster is an overview of the project and the RE-AIM framework. No current evaluation of TOP has examined long-term impacts of program participation on participants. The rigorous design of this study, based on the RE-AIM framework, suggests that it could be a model for conducting future longitudinal school-based evaluations.

Research supported by: Office of Adolescent Health, USDHHS

Do The Parents of Children Diagnosed with Autism Spectrum Disorders Experience Issues Related to Access to Child Care? Laura K. Merrell, MPH CPH, Pamela C. Guevara, MPH, Department of Community and Family Health, College of Public Health, University of South Florida, Samuel Matos, MD, MPH, CPH, Department of Global Health, College of Public Health, University of South Florida.

Keywords: Autism Spectrum Disorders, Child Care, Child Health

Objective: In the US, 71% of women with children are in the workforce, and of children aged 0 to 5, 54% are enrolled in child care. Parents of children with disabilities face issues in finding care that can accommodate their child. Autism spectrum disorders (ASD) are characterized by symptoms such as developmental delays, restricted interpersonal interactions, and ritualized behaviors. ASD presents in early childhood when children are most likely to utilize non-familial child care. Does a diagnosis of autism interfere with a family's ability in obtaining child care? If so, does severity of disorder matter?

Methods: The National Survey of Children's Health (NSCH), a national telephone survey (n=91,642) was analyzed using chi-square analyses of answers relating to both a child's ASD and parents' access to child care. Families asked both sets of questions regarding their children aged 2 to 5 were included in this study (n=17,944).

Results: 0.7% of this study population was currently diagnosed with ASD. Of those, 56.22% self-reported their condition as mild; 35.61% as moderate, and 8.17% as severe. Significant differences were found among those currently diagnosed with ASD, those ever told, but not currently diagnosed, and those without ASD in terms of their work being affected, problems with child care, and ability to access child care because of children's behavior and health status. However, the level of severity of ASD was not significant when looking at these issues.

Conclusion: ASD interferes with the family accessing outside care for the child, uncovering an important area of unmet need among this population. As with other areas such as medical and therapeutic needs, access to child care is an important area for policy makers and service providers to consider.

Health Disparities and Science: Bridging the Gap Among Underrepresented and Disadvantaged Youth in the Tampa Bay Community Mezelle Moore, ABJ, Kevin Sneed, PharmD, Maisha Kamboon, MPH, Julie Baldwin, PhD, B. Lee Green, PhD, MEd University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Adolescents, community-based partnership, health disparities

Objective: To increase opportunities for disadvantaged and underrepresented adolescents in the Tampa Bay Community to be exposed to careers in science and health.

Methods: The University of South Florida and H. Lee Moffitt Cancer Center have created the USF/Moffitt Science Tour program. An evaluation form was administered at the end of each tour to obtain feedback from the students, chaperones, and presenters.

Results: Since 2009 there have been 5 tours, with 95 students, 22 staff members, and 15 chaperones. Students who responded to the survey identified themselves as African-American/Black (56%), Caucasian/White (9%), Hispanic/Latino (7%), Asian (5%), Multiracial (18%) and other (5%). Student ages ranged from 9-19 years old, and grade levels ranged from 4th-12th grade. Students expressed interest in hands-on activities including microscopy laboratory exploration and cancer risks and treatment. 58% of science presenters reported accomplishing the main objectives of their presentations. Over 60% of students were exposed to their first research lab during the program. After visiting pharmacology, microscopy, molecular medicine and simulation laboratories, 25% of students reported experiencing a career interest in at least one of these fields. When asked, 30% of students chose the microscopy laboratory of the H. Lee Moffitt Cancer Center was the preferred laboratory of the program.

Conclusion: The tour program not only promoted health career exploration among underserved teens, but also served as a primary introduction to health research.

Research supported by: The University of South Florida and H. Lee Moffitt Cancer Center. The Community Engagement and Outreach Core (CEOC) of The Center for Equal Health, funding from the National Center on Minority Health and Health Disparities.

Online Dating Among Older Women: An Exploratory Study of the Risks and Benefits Associated with Online Relationship Seeking

Jaime L. Myers MPH, Carla VandeWeerd PhD, Jaime Corvin PhD, Martha Coulter PhD, Robin Telford MA
University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: elder mistreatment, intimate partner violence, online, technology, aging

Objective: Though recent research has focused on the risks and benefits of meeting people online, the research largely focuses on younger populations. Little is known about online relationship seeking among older adults. This exploratory study examines the risks and benefits of online relationship seeking among older women.

Methods: Women over 50 years old who indicated they were looking for relationships in their publically available Myspace profiles were recruited to participate in a 23 item online questionnaire. A systematic, random, quota sampling technique of women within a 25 mile radius of Tampa Bay resulted in the recruitment of 45 participants (15 White, 15 Black, 15 Hispanic).

Results: Most women reported having more than one online account. Facebook (75.6%), match.com (71%), and eharmony (58%) were the most frequently reported. The majority (84%) of participants had developed a relationship with someone they had met online. Adverse events experienced through meeting people online included financial exploitation (40%), threats (55%), and physical harm (38%). However, only 2% of women indicated feeling threatened via their Myspace account by someone they originally met in person. Among women who experienced some form of abuse from a relationship started online, only 17% reported these negative events to others. Despite many women reporting negative experiences, 89% of women felt that the information provided by others on the internet was truthful.

Conclusion: Preliminary findings indicate that many women seeking relationships online experience negative outcomes and are unlikely to report negative events to law enforcement. Future studies should examine the protective and risk factors associated with online dating to develop an online dating toolkit.

Preliminary End User Evaluation Of An Educational Brochure To Increase Awareness Of Hereditary Ovarian And Breast Cancer Alison Nelson, USF College of Public Health, Dept. of Maternal Child Health/Epidemiology

Keywords: African American, educational materials, HBOC awareness, cancer history

Objective: Low uptake of genetic counseling (GC) and testing services among African Americans (AA) may be, partly, due to low levels of awareness and knowledge of hereditary ovarian and breast cancer (HBOC) and GC as well as lack of family communication about cancer. Our study team and community advisory panel co-designed a culturally-targeted brochure to promote awareness of HBOC. The purpose of the current study is to evaluate the utility of the brochure among those who received it and compare responses based on cancer diagnosis.

Methods: Brochures were disseminated through distribution by individuals and community organizations. Each brochure included a survey evaluating recipients' perceptions of brochure utility and intentions to share or discuss brochure information. SPSS was used to obtain descriptive statistics and compare participant responses based on cancer diagnosis.

Results: A total of 156 completed surveys were analyzed. Of recipients who reported a breast and/or ovarian cancer diagnosis (n = 48), 35.1% reported they were "very likely" to discuss their personal and/or family history of cancer with their healthcare provider after reading the brochure, compared to 64.9% of participants without a cancer diagnosis (n = 108). Participants who reported they were "very likely" to share information with others about HBOC after reading the booklet was 34.8% and 65.2% for those with and without a breast or ovarian cancer diagnosis, respectively. Relative to participants with a breast or ovarian cancer diagnosis, more participants without a breast diagnosis reported the brochure was "very useful" in terms of increasing understanding about familial cancer (29.3% vs. 70.7%, respectively).

Conclusion: Compared to the respondents with a breast and/or ovarian cancer diagnosis, those who have never been diagnosed may be more likely to utilize this brochure. Results suggest a need for developing materials specific to cancer survivors about HBOC. Additional research is needed to examine reasons for differences in perceptions about the brochure among those with and without a breast or ovarian cancer diagnosis.

Research Supported by: Florida Breast Cancer Foundation, Komen for the Cure Foundation

Conserved and Variant Epitopes of Plasmodium vivax Duffy Binding Protein as Targets of Inhibitory Monoclonal Antibodies

Francis B. Ntumngia¹, Jesse Schloegel¹§, Samantha J. Barnes¹, Amy M. McHenry¹†, Sanjay Singh⁴ Christopher L. King^{2, 3}, and John H. Adams^{1*} ¹Department of Global Health, University of South Florida, Tampa, FL, United States ²Case Western Reserve University, Cleveland, OH, United States ³Veterans Affairs Medical Center, Cleveland, OH, United States ⁴Genova Biopharmaceuticals Ltd, Pune, India

Keywords: Plasmodium vivax, Monoclonal antibodies, Malaria

Objective: To develop high titer-inhibitory monoclonal antibodies to Plasmodium vivax Duffy binding protein region II (PvDBPII), broadly reactive against diverse Plasmodium vivax strains.

Methods: We generate a set of monoclonal antibodies against PvDBPII and functionally analyzed them for reactivity to a panel of allelic variants. The monoclonal antibodies were also evaluated for ability to inhibit DBPII-erythrocyte binding using a standard in vitro erythrocyte-binding inhibition assay.

Results: Quantitative analysis by ELISA determined that some monoclonal antibodies reacted strongly with epitopes conserved on all DBP variants tested, while reactivity of others was allele-specific. Qualitative analysis characterized by anti-DBP functional inhibition, using an in vitro erythrocyte-binding inhibition assay indicated that there was no consistent correlation between the end point titers and functional inhibition. Some monoclonal antibodies were broadly inhibitory while inhibition of others varied significantly by target allele.

Conclusion: Our data demonstrate a potential for vaccine-elicited immunization to target conserved epitopes and leads to a better understanding of the specificity needed for a protective immune response against the DBP and designing an effective vaccine against diverse vivax strains.

Research supported by: This work is supported by NIH Grant: R01 AI064478 (to JHA)

Utilization of Well Child Care and Effective Care Coordination: An Analysis of Data from the 2007 National Survey of Children's Health

Adejoke Ogunrinde, College of Public Health, University of South Florida, University of South Florida College of Public Health, Dept. of Community & Family Health

Keywords: Well-child care, Care coordination, Utilization, Poverty level, Insurance coverage

Objective: The need for an improved delivery of primary care services is increasingly being noted as important in efforts towards improving access to health care and having a primary care provider who coordinates and assures this quality care for children have also been identified as a key factor in health care. Research shows that guidance given during a well-child care (WCC) visit can change parenting practices and affect choice to breastfeed. This study sought to determine if there is an association between utilization of WCC and care coordination and to understand the effect of other factors on utilization of WCC

Methods: Data used was collected by telephone interview on 60,845 children 0-10 years using parental reports from the National Survey of Children's Health 2007. Chi-square analyses was used to describe the relationship between care coordination and utilization of WCC. Logistic Regression was performed to examine the association between the utilization of WCC visits, coordination of care and other control variables

Results: Having all components of care coordination is associated with utilization of WCC visits; Black non-Hispanics, Hispanics were 49%, 17% of time respectively more likely to utilize WCC visits in the US. The poorer the family, the less likely to get WCC, those with private health insurance are 3 times more likely to attend WCC than the uninsured, odd ratio (OR) for those with public 3.9 (CI 3.0, 5.0) and private insurance OR 2.9 (CI 2.3, 3.6)

Conclusion: There is significant association between effective care coordination and WCC visits and additional research needs to be conducted to understand other factors that may influence utilization such as poverty levels and insurance coverage

Research supported by: Initially conducted as a class project in PHC 6197, Fall 2011

Exploration of Mobile Technology and Social Media Use to Enhance Adolescent Self-Management of Asthma

Anthony D. Panzera¹, Tali Schneider¹, Mary Martinasek¹, James Lindenberger¹, Carol Bryant¹, Marisa Couluris²,

¹Social Marketing Group – FPRC, ²Division of Pulmonology, USF Department of Pediatrics. University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: social media technology, social marketing, qualitative, asthma, teens

Objective: Adolescents with asthma are the least compliant age group for disease self-management. Considering the increased popularity of mobile technology and social media use, the researchers explored the potential for such platforms to deliver asthma education, to monitor current asthma clinical status and to strengthen self-management.

Methods: The social marketing framework guided qualitative research methods to explore adolescent and caregiver perceptions on asthma management, and attitudes toward the use of social media and mobile technologies in asthma care. 18 in-depth interviews were conducted with adolescents and their caregivers. Interview guides reflected the marketing mix that would later inform the construction of technological tools and a marketing plan to address teen asthma monitoring and self-management.

Results: Teens and caregivers are willing to participate in an database system, whereby patients send measures to the database and receive tailored feedback in response via mobile devices. Suggested message content includes medication, peak flow reading reminders and pollen counts. Participants reported interest in receiving alerts when their asthma status worsens, including recommended treatment strategies. Participants varied in their willingness to participate in asthma related social networking.

Conclusion: More exploration on the relevance of social networking sites as a platform for skill-building asthma education is needed among teen asthmatics. Mobile devices constitute a viable platform to assist adolescents with monitoring their asthma and have the potential to lead to improved asthma self-management.

Research supported by: USF College of Medicine

Identifying Mothers' Perceptions and Expectations of Paternal Involvement: Perspectives of Black Women in Hillsborough County

Natalie Rella, College of Public Health Erica Coates, College of Arts and Sciences Adejoke Ogunrinde, College of Public Health Jamila Seaton, College of Public Health Robert Lucio, FMHI University of South Florida College of Public Health, Dept. of Community & Family Health

Keywords: Paternal involvement, infant mortality, perceptions

Objective: Gaining a linguistic understanding of how Black mothers perceive paternal involvement is an important element when developing culturally sensitive interventions. We seek to obtain adequate knowledge regarding mothers' perceptions and expectations of paternal involvement for the purpose of both informing the literature and encouraging the implementation of interventions relevant to the population studied.

Methods: Objectives will be achieved by conducting focus groups among Black men women over the age of 18 who have had one child within 12 months of focus groups

Results: Preliminary results include linguistic definition of paternal involvement revealed in the following themes; support, barriers, responsibility, and relationships.

Conclusion: Conclusions are contingent upon data analysis; however, preliminary results point to the fact that perceptions of father involvement relate to the behaviors of Black mothers.

Research supported by: The Graduate School and The Heart of East Tampa Front Porch Council, Inc.

Evaluating a Community-Based Cervical Cancer Patient Navigator Program: Outcomes from the TBCCN-CCPNP

Maria I. Rivera, USF; Kristen J. Wells, H. Lee Moffitt Cancer Center, USF; Sara K. Proctor, Catholic Mobile Medical Services; Gloria Arroyo, H. Lee Moffitt Cancer Center; Gwendolyn P. Quinn, H. Lee Moffitt Cancer Center, USF, Marlene Rivera, Catholic Mobile Medical Services; Cathy D. Meade, H. Lee Moffitt Cancer Center, University of South Florida, College of Public Health Dept. of Community & Family Health

Keywords: patient navigation, cervical cancer, farmworker, pilot study

Objective: Patient navigation (PN) aims to increase the number of patients who receive recommended cancer-related services. The Tampa Bay Community Cancer Network (TBCCN) Cervical Cancer Patient Navigator Program (CCPNP) was developed to address needs reported by Catholic Mobile Medical Services (CMMS). CMMS provides free health care to a population of primarily Spanish-speaking Hispanic farmworker families. The PN program at CMMS aims to improve the provision of timely cervical cancer screening and follow-up for abnormal Pap tests.

Methods: Using a pre-post design, the TBCCN CCPNP was evaluated using data collected from medical records at CMMS before and during PN intervention. The outcome evaluation tested for differences in the provision of care between women who received services with and without PN. We examined if women who received PN were more likely to: receive their Pap results; receive their results in less time; adhere to follow-up after an abnormal Pap test; obtain follow-up in less time; and adhere to a surveillance Pap test after an abnormal Pap.

Results: Data from 192 patients who received care before PN intervention (99% Hispanic, mean age= 39.6; mean years of education= 8) indicate that 6.1% had an abnormal Pap. Data from 348 patients who received care during PN intervention (99% Hispanic, mean age= 37.9; mean years of education= 8) indicate that 11.2% had an abnormal Pap. Women who received PN were more likely to receive their Pap results ($P<0.0001$) and in less days ($P<0.0001$), and obtained follow-up care more often after an abnormal Pap ($P=0.01$) than women seen without PN.

Conclusion: A PN program implemented in a Hispanic farmworker population is effective in reducing barriers to follow up care for abnormal cervical cancer screening results.

Health in Late Life: The Villages is Not God's Waiting Room

Rosen, D.^{1,2}, Curry, E.², Rella, N.¹, Rodriguez, M.¹, Tyler, S.^{1,2}, Fishleder, S.^{2,3}, VandeWeerd, C.¹, Sharkey, S.⁴, Corvin, J.⁵, Williams, A.⁶, ¹Department of Community and Family Health, College of Public Health, ²Department of Applied Anthropology, College of Arts and Sciences, ³Department of Epidemiology, College of Public Health, ⁴College of Public Health, ⁵Department of Global Health, College of Public Health, ⁶Department of Health Policy and Management, College of Public Health. University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Successful Aging, Health, Aging, Quality of life, QOL

Objective: The number of seniors in the US is rapidly rising. To better understand perceptions of healthy aging, USF Health has partnered with The Villages, a 55+ active adult community located in Florida. Objectives include: 1) identifying residents' definition of health within the framework of the theory of Successful Aging; 2) assessing residents' perceptions regarding the importance of good health; and 3) identifying the resources available to residents that enhance quality of life.

Methods: 59 focus groups (FGs) were conducted in a convenience sample of residents (n=451) from October to December 2011. FGs were stratified by age, gender, and health status. FGs were designed to assess perceptions across the following domains: 1) Definition of health; 2) importance of good health; and 3) mechanisms for facilitating good health in The Villages. FGs were executed in 3 phases: general inquiry, clarifying themes, and member validation. Sessions were taped, transcribed and entered into NVivo9 for analysis. Content analysis was conducted to identify relevant themes across research questions.

Results: Resident's definition of good health was consistent with the Theory of Successful Aging and was defined as the ability to conduct daily activities, physical fitness, and mental acuity. Good health was reported to be of primary importance. Key factors included avoiding disease and disability, maintaining high cognitive and physical functioning, and being fully engaged with life through activity and social connection. Positive engagement in the community was identified as a key resource in enhancing quality of life.

Conclusion: Implications for policy and practice will be discussed in terms of enhancing the quality of life of seniors to further understanding of successful aging.

Social Capital and Social Cohesion in an Adult Retirement Community: Perceptions of Benefits to Health and Quality of Life

Solomon, M., Department of Community and Family Health, College of Public Health; Siegel, K., Department of Environmental & Occupational Health, College of Public Health; Radwan, C., Department of Anthropology, College of Arts and Sciences; McNab, P., Department of Anthropology, College of Arts and Sciences & Department of Community and Family Health, College of Public Health; Rose, M., Department of Health Policy and Management, College of Public Health; Fishleder, S., Department of Epidemiology, College of Public Health; VandeWeerd, C., Department of Community and Family, College of Public Health; Corvin, J., Department of Global Health, College of Public Health; Sharkey, S., College of Public Health; Williams, A., Department of Health Policy and Management, College of Public Health, University of South Florida

Keywords: Healthy aging, social networks, Quality of Life, QOL

Objective: The literature has documented the benefit of strong social networks to health and quality of life. Increased social connectedness has been linked to reduced rates of depressive symptoms and improved health status, especially in late life. The purpose of the project is to conduct a formative assessment to explore perceptions of social capital and cohesion among residents of The Villages, an active adult retirement community in Florida. Objectives include: 1) Assess resident's definitions of social support and social cohesion in The Villages; 2) Identify the mechanisms by which social support networks are developed and expanded; and 3) Identify residents' perceptions of the impact of social support on health.

Methods: Collaborative efforts between key stakeholders from The Villages and the University of South Florida guided the iterative formative assessment process. Focus groups were conducted in a convenience sample of elderly residents (≥ 55 yrs) stratified by gender, age, and health status. Groups were conducted using a three phase process of first, broad questions; second, clarification; and third, validation. NVivo 9 was used to identify salient themes.

Results: Fifty-nine groups (n=451) were convened between October and December 2011. Residents shared insights into relationships between social cohesion and mental, physical, and spiritual health. Residents report their community encourages interaction with neighbors, development of friendships, referrals from fellow Villagers, and stewardship of neighbors.

Conclusion: Implications of the findings will be discussed in terms of the practice of public health for an aging population. Findings will contribute to healthy aging.

Severe Asthma Triggers

Sara Spowart, MPA, PhD Student USF Health University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: severe asthma, triggers, interventions, children, young adults

Objective: This study assessed root causes of severe child asthma symptoms as seen from literature reviews and data derived from the 2007 National Survey of Children's Health (NSCH). The objective was to identify major triggers of severe asthma.

Methods: The hypothesis based on literature reviews was that children ages 3-17 years with severe asthma are more likely to be from metropolitan settings, male, of non-white origin, and at a higher poverty level. The dependent variable was asthma severity. The independent variables were poverty measured through the Federal Poverty Line (FPL), race measured through the four categories of White, Black, Hispanic and Other, sex through either male or female, age of child through age groups 3-7 years, 8-11 years and 12-17 years, and living or not living in a metropolitan setting. Multivariate analysis along with logistic regression were used in the investigation through SAS programming.

Results: The outcomes demonstrated significance in all areas except living in a metropolitan setting, and significance was approached for age of child. Overall race, poverty at 100% FPL, being in the age group 3-7 or 8-11 years and sex of the child were associated with severe symptoms.

Conclusion: These results have important public health policy implications for interventions to reduce severe asthma. According to this study, interventions targeting male children ages 3-7 and 8-11 in Black, Hispanic, and Other groups at 100% FPL would likely be effective.

Does Childhood Obesity Influence Parental Aggravation?

Allison Vander Molen, B.S., Russell Kirby, PhD, University of South Florida, University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Parental aggravation; Childhood obesity; Obesity; Parent-Child relations

Objective: To examine the relationship between child obesity status and reported parental aggravation (PA) and to identify the demographic and family characteristics which increase the likelihood of PA.

Methods: Using data from the National Survey of Children's Health, the sample of 45,897 children aged 10 to 17 years old and their parents were surveyed. Child obesity was defined as BMI ≥ 95 th percentile. Parental aggravation (PA) was defined as feeling the child was harder to care for than other children. PA was assessed based on three questions: feeling the child was harder to care for, the child made more demands on the parent, and the child's actions were a source of frustration. Respondents with obese children (BMI ≥ 95 th%) were compared with non-obese children (BMI < 95th%) to assess if there were any differences in reports of PA. Weighted estimates are presented.

Results: There was no significant association between child obesity status and parent reported PA. However, parents with less than 12 years of education (aOR 1.73, 95% CI 1.36-2.21); being poor, below the Federal Poverty Level (FPL) (aOR 2.07, 95% CI 1.39-3.08) or 100-199% above the FPL (aOR 1.67 95% CI 1.17-2.38); having children of Hispanic (aOR 2.19, 95% CI 1.61-2.96) or Black ethnicity (aOR 2.08, 95% CI 1.62-2.68); and having an older child (aOR 1.5, 95% CI 1.2-1.91) were positively associated with increased likelihood of reporting PA.

Conclusion: Parenting an obese child is not associated with an increased risk of PA, but certain demographic and family characteristics can increase the likelihood of reporting PA.

Smoking Among HIV Positive Youth: The Intersection between Behavioral Health and Chronic Diseases

Todd Wells University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Behavioral Health, HIV, Smoking, Adolescents

Objective: 1. Describe health complications associated with being HIV positive and smoking. 2. Describe the prevalence and intensity of smoking among HIV positive youth and adolescents. 3. Provide results from study investigating relationship between HIV positive youth and smoking.

Methods: This study investigated the prevalence and intensity of smoking among HIV positive youth and tested the hypothesis that there is no relationship between age and tobacco usage among HIV infected persons in America will be tested using data from the 2009 National Survey on Drug Use & Health. Target Population- Participants of the 2009 Health and Behavior Survey Sampling Frame- Participants of the 2009 Health and Behavior Survey who are HIV positive Data Collection- Secondary data analysis Data Analysis- Descriptive statistics were used to analyze the gender distribution and number of cigarettes smoked while a Chi Square analysis was used to look at the relationship between age and smoking.

Results: N = 63 Sex Female-29 Male- 34 Smoking Status Smoker- 46 Non smoker- 17 The critical value 11.070 is less than the obtained value of 12.232 ($p=.032$), suggesting that there is a relationship between age and smoking among HIV infected persons.

Conclusion: Almost half of the sample began smoking before age 23 and the data indicates that an earlier onset of smoking is associated with greater smoking intensity. The results further suggest differences between age groups when HIV infected persons begin smoking.

Abstract #: 260

Presented by: Stephen Harbison, MPH, Graduate Student

Pulmonary Function Testing in Utility Workers

S.C. Harbison, G.T. Johnson, J. McCluskey, P. Xu, J. White, S. Mohammed, J. Wolfson, and R.D. Harbison. University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: Pulmonary Function; Utility Worker; Healthy Worker Effect

Objective: This investigation used occupational health monitoring examination data to characterize pulmonary function (PF) in a population currently employed as utility workers in the state of Florida.

Methods: PF tests for male workers ($n=227$) who required health examinations to ensure fitness for continued respirator use were compared to NHANES III Raw Spirometry subjects ($n=4,958$) to determine if decreased PF was associated with employment as a utility worker. Mean FVC and FEV1 values were determined and multivariate regression was used to evaluate the impact of utility worker status on PF after adjusting for confounders.

Results: Workers produced a higher mean FVC of 4.84L (95%CI 4.72-4.96) compared to a mean NHANES III subject value of 4.70L (95%CI 4.68-4.73). No significant difference was detected between the worker FEV1 mean of 3.81L (95%CI 3.72-3.90) and the mean NHANES III subject value of 3.71L (95%CI 3.69-3.73). No significant differences were found between mean pulmonary function test values of workers and NHANES III study subjects when stratified by age, height, and smoking status except among older utility workers, who demonstrated modest PF increases compared to their NHANES III counterparts. Multivariate regression analysis demonstrated that significant predictors of FEV1 included age, height, pack-years of smoking, and utility worker status. Significant predictors of FVC also included age, height, pack-years of smoking, and utility worker status.

Conclusion: The direction of effect for utility worker status was beneficial for lung function. The modest increase in PF observed in utility workers in multivariate analysis is likely due to a combination of effective exposure controls in the workplace and the healthy worker effect among aging workers.

Local Health Impact Assessment Method for Formaldehyde

Shabnam Mehra, Haofei Yu, Thomas J. Mason, Ph.D., Amy L. Stuart, Ph.D., College of Public Health; Daniel Santiago, Ashley Mullen, Department of Chemistry; University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: Formaldehyde, CR-function, HIA, local health impact assessment

Objective: The main objective of this research is to develop a method which can estimate impact on asthma emergency department visit due to change in local formaldehyde. The primary focus is to develop concentration response (CR) functions and background asthma incidence rates necessary for performing local formaldehyde HIA.

Methods: Detailed review of published literature on health effects of Formaldehyde and health impact assessment HIA was performed. Using published literature CR functions were developed. Dispersion model for local formaldehyde was developed. Asthma ED data 05-06 from the State agencies (FL-AHCA) were obtained. Data was managed and analyzed using SAS® and SQL. For local formaldehyde levels incidence of asthma ED was calculated using HIA formulae.

Results: Incidence of asthma for emergency department visit is seasonal and is higher for males at younger ages. The local formaldehyde concentration for Hillsborough county ranged from 0.61-6.1 µg/m³. The Asthma ED cases attributed to Formaldehyde concentrations in the area were highest in the more densely populated areas of the age group and the variation is more pronounced in males between the ages of 5-12 than in females of the same age group or males between the ages of 13-17.

Conclusion: Formaldehyde exposure is associated with increase in Asthma ED visit. The Asthma ED rates for male decrease as age increases, for females they increase slightly. Formaldehyde concentration is highest near downtown while Asthma ED rates are highest in densely populated areas. HIA method used in this research can be modified for other pollutants.

Research supported by: Graduate School 2011 Student Challenge Grant. The material from H. Yu is based upon work supported by the National Science Foundation under Grant No. 0846342.

The Public Health Implications of Marina Pollution on Recreational Beaches

Jill Sears, author Dr. Amy Stuart, University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: Marinas, Pollution, Fecal Contamination

Objective: Beaches provide access to waters in the United States used by people of all ages for swimming and recreation. Maintaining beach health and water quality is essential to ensuring the public's safety. This work seeks to determine how pollution from marinas may impact the water quality of nearby recreational beaches.

Methods: Bacteriological quality of Florida beaches was investigated quantitatively by performing a descriptive statistical analysis of Florida Department of Health beach water quality data. A qualitative survey of beach and marina locations was used to identify characteristics which may impact the transport or accumulation of pollutants.

Results: Results suggest that contamination from fecal waste, boat maintenance, and engine fuel may impair the health of nearby beaches, but is not being monitored. Locations with poor water circulation and low volumes of tidal exchange are most vulnerable to accumulating pollutants in high enough concentrations to cause gastrointestinal sickness and chronic disease. Results from a review of federal and state initiatives aimed at reducing marina pollution suggest that federal efforts to control the problem have not been adequately designed, and states lack the political will and resources needed to implement mandatory programs addressing the issue.

Conclusion: Efforts to monitor pollutants specific to boating activities will be required to understand the scope of public health impacts of marina pollution. Greater attention and firmer direction from state and local agencies will be necessary to address the issue of marina pollution in order to protect the health of recreational beach users.

Characterization of Veteran's Poisonings in the State of Florida

J. White, G.T. Johnson, C. Younger, R.D. Harbison University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: Veteran, Poisoning, Hospital

Objective: The objective of this study was to characterize patterns associated with poisonings in veterans presenting to VA hospital emergency rooms.

Methods: The Florida Poison Information Centers provide emergency department consultation for suspected poisoning cases presenting to hospital emergency rooms, including Veterans Administration (VA) hospitals. The exposures, case demographics, treatments, and clinical outcomes are recorded for all reported cases.

Results: A total of 601 poisoning cases from 6 VA hospitals in the state of Florida occurring between the years 2005 and 2009 were evaluated. The population was predominately male (88.1%) with a mean age of 51.5 years (STD 13.7 years). Nearly half (46.2%) of all cases were classified as intentional suspected suicide and 87.6% of poisonings occurred in the patient's residence. Though death was a rare event (2 cases), 37.7% of cases resulted in clinical outcomes that were considered 'major' or 'moderate'. More than 50% of cases reported a medication as one of the substances implicated in the poisoning.

Conclusion: Future research into poisoning interventions among veterans may focus on patient suicide risk, medication monitoring, and medication safety education.

Pharmaceuticals and the Environment: A case study of disposal techniques at hospice facilities in Alachua County, Florida

Hillary Wolf University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: Pharmaceuticals

Objective: More information should be gathered regarding disposal of pharmaceuticals at hospice organizations because hospice nurses work in a variety of medical facilities, including both hospitals and long-term care facilities. In addition, hospice nurses deal with terminally ill patients and are responsible for handling their medications and disposing of them after death. The objectives of this study were to gain information on current disposal practices at hospice organizations within Alachua County in order to safely regulate pharmaceutical disposal and to determine the benefits of local government hazardous waste generator compliance assistance visits.

Methods: To fulfill these tasks an interview was conducted at each of the two hospice organizations in Alachua County and results were analyzed.

Results: Data suggests that differences in disposal methods in these organizations stem from where the disposal policies originate. There was no solid evidence which linked improvements to the local government hazardous waste generator compliance assistance visits, although the possibility should not be ruled out.

Conclusion: Through this project, I found that university research is the best method to gain insight into disposal practices because they do not pose a threat to medical facilities. Specifically in the state of Florida, I recommend that companies which provide Universal Pharmaceutical Waste Bins (UPW) help educate Florida based facilities on the Universal Waste rule. Further research is needed, with a larger study group, to investigate if there is truly a statistically significant correlation between disposal practices and the level at which the organization originates.

Associations of Stress and Sleep with Prevalence of HPV: Preliminary Results from a Study of HPV in Men Stephanie Kolar, MSPH¹, Aurora Sanchez-Anguiano, MD, Ph D¹, Kathleen O'Rourke, Ph D¹, Anna Giuliano, Ph D², Ellen Daley, Ph D³, Skai Schwartz, Ph D¹, and Wei Wang, Ph D¹ ¹University of South Florida, College of Public Health, Department of Epidemiology and Biostatistics ²H. Lee Moffitt Cancer Center and Research Institute ³University of South Florida, College of Public Health, Department of Community and Family Health

Keywords: HPV, men, psychosocial, stress, sleep

Objective: Anogenital HPV infection, the most common STI, is associated with genital warts and anogenital cancer. Behavioral and psychosocial factors are associated with immune function and could impact HPV infection through moderation of immune responses. The purpose of this analysis is to examine associations between perceived stress, sleep quality and HPV prevalence among men.

Methods: Participants were tested for HPV and completed self-report items on stress and sleep quality at a baseline visit (n=399). Stress scores were dichotomized into high (4th quartile) and low stress (1st-3rd quartiles; reference group). Sleep quality scores were categorized into low (1st quartile), moderate (2nd& 3rd quartiles; reference group), and high sleep problems (4th quartile). Age, smoking, and lifetime number of sex partners were associated with the exposures and HPV prevalence and were included in multivariate analyses.

Results: In univariate analyses, men with high stress were more likely to test positive compared to men with low stress (OR=1.77, 95% CI:1.10-2.84) and men with high sleep problems were more likely to test positive compared to men with moderate sleep problems (OR=1.68, 95% CI:1.03-2.76). Associations were attenuated in multivariate logistic regression (stress OR=1.52, 95% CI:0.86-2.68, sleep OR=1.12, 95% CI:0.63-2.00).

Conclusion: Stress and sleep quality were associated with HPV prevalence in this analysis, though significance was not maintained in multivariate analyses. Results suggest that age, smoking status, and lifetime number of sex partners could modify or confound associations between stress and sleep quality with HPV prevalence. Further research is needed to understand relationships between stress, sleep quality, other factors and HPV infection.

Research supported by: NIH

A Multifaceted Study of Distance from Liver Transplant Center Affecting Outcomes Post-Transplantation Alexia Makris MS¹, Angel E. Alsina MD², Nyingi Kemmer MD³. ¹Department of Epidemiology and Biostatistics, College of Public Health, University of South Florida, Tampa, FL, United States, ²Transplant Surgery, Tampa General Hospital, Tampa, FL, United States. University of South Florida College of Public Health, Dept. of Epidemiology & Biostatistics

Keywords: Liver Transplantation, survival, distance, Accelerated Failure Time, Cox Proportional Hazards, Logistic Regression.

Objective: It is hypothesized that further distance of the patient's residence from the LTx center results in inferior post-transplant outcomes. The aim is to determine if a relationship between distance and survival post LTx can be established and if such factors can be predictive of morbidity and mortality outcomes.

Methods: 627 patients were identified, all of whom had undergone LTx at Tampa General Hospital (TGH) between Jan. 1, 1996 and Dec. 31, 2009. The population is multi-ethnic and multi-gender; those with acute liver failure were excluded. Models were developed using logistic regression, Cox Proportional Hazards model and accelerated failure time models as called for by the distribution of the data.

Results: 214 patients died before the end of the study and 413 were alive. Hepatitis C (Likelihood Ratio (LR) p-value<0.0001) and compliance (LR p-value 0.0086) were clearly significant factors affecting survival and were adjusted for in the models. Logistic regression 1 year post LTx showed that at the 240 mile cut off the odds ratio was 3.357 (p-value=0.0364) and results were similar with the Accelerated Failure Time (AFT) models using the exponential distribution. Cox was in close agreement with a hazard ratio of 2.1 (p-value=0.0392).

Conclusion: After adjusting for HCV and compliance, patients living more than 240 miles/4 hours from the LTx center have decreased survival rates; this being especially pronounced in the first year post LTx. Different statistical models were employed but the results regarding the effects of distance from LTx on patient survival remain unanimous.

Geospatial Distribution of Fresh Produce Availability in Low-Rural Communities: Florida Case-Study

Emanny Sanchez^{1,2}, Mathieu Poirier², Curtis Devetter², Jaime Corvin, PhD², ¹University of South Florida, College of Public Health, Department of Epidemiology and Biostatistics, Tampa, Florida, USA, ² University of South Florida, College of Public Health, Department of Global Health, Tampa, Florida, USA. University of South Florida, College of Public Health, Dept. of Epidemiology & Biostatistics

Keywords: Case-study, geospatial mapping, food desert, food environment

Objective: Discussion and research involving food deserts is of paramount importance. Areas viewed as “food desert” compound problems surrounding nutrition—often propagating unhealthy life styles. A prime characteristic of food deserts and a well-known barrier to nutritious food consumption is the distance between populations and healthy food vendors. In this case-study we assessed and evaluated the food environment among a local community in Tampa, Florida to determine whether a ‘food desert exist’.

Methods: A geographical area, encompassing the greater University of South Florida area, was surveyed to identify all food stores within the community. A geographic information system was utilized to measure and geospatially map all food stores found to offer fresh produce. Household distance between these foods stores within five contiguous census tracts was evaluated.

Results: Seventy-five fast food restaurants, 42 restaurants, 29 convenience stores, 21 grocery stores, 3 Supermarkets, 4 liquor stores, and 7 general stores in a 7.5 km² area to the west of the University of South Florida were identified. Though the distribution was fairly heterogeneous, clusters of fast food restaurants are seen to surround the block groups with the highest unemployment rates and lowest per capita incomes, whereas areas with higher percentages of white residents have fewer fast food restaurants nearby.

Conclusion: Our results indicate a complex distribution of food outlets which may result in unequal access to healthy food. Evidence of a ‘food desert’ within this area suggest the residence inability to obtain fresh food produce.

Limited Understanding of Cervical Cancer Screening among a Racially Diverse Sample

¹ Young, L., ¹ Daley, E., ¹ Hernandez, N., ¹ Vamos, C., ¹ Kolar, S., ² Romero-Daza, N., ³ Chandler, R., ⁴ Chong, W., ¹ University of South Florida, College of Public Health ² University of South Florida, College of Arts and Sciences ³ University of South Florida, College of Nursing ⁴ University of South Florida, Morsani College of Medicine

Keywords: understanding cervical cancer diverse sample

Objective: To explore differences between white and minority women’s understanding of the Pap test.

Methods: Findings from a web-based Study (Study 2, 2011) assessing Pap smear knowledge among minority college women (n=693) were compared to similar results from mostly white college women (n=276) surveyed prior to the current Pap test guidelines (Study 1, 2009). Frequencies and chi-squares were employed to compare differences between studies.

Results: Most women in Study 1 were white (73%) with a mean age of 19 years; most women in Study 2 were Hispanic (46%) or black (25%), mean age=23. Knowledge of the purpose of Pap smear testing was low overall. Although women in both studies reported that the Pap smear tested for cervical cancer (75% and 82% for Study 1 and Study 2 respectively), women also thought it tested for HIV/AIDS (29% and 14%), Herpes (51% and 30%), Gonorrhea (54% and 31%), HPV (73% and 64%), yeast infections (66% and 49%), and vaginal infections (74% and 59%). After stratifying by age, women in Study 2 were significantly more likely to correctly report that the Pap smear did not test for HIV/AIDS, Herpes, Gonorrhea, HPV, yeast infections, and vaginal infections.

Conclusion: Although minority women had a better understanding of Pap testing, these studies reveal that there is still confusion among college women about the purpose of cervical cancer screening tests. Results from this study indicate the need for intensive patient education among women undergoing annual exams, Pap smear testing, and STI testing.

Research supported by: University of South Florida, College of Public Health, Department of Community and Family Health

Evaluating Florida's Trauma Triage Criteria Against Trauma Center Need

Benjamin Abes, University of South Florida, College of Public Health, Dept. of Global Health

Keywords: pre-hospital, emergency medical services, trauma, triage

Objective: Accurate triage to trauma care, especially in the most seriously injured patients, can result in decreased morbidity and mortality. While there is evidence to both support and refute the ability of paramedics to judge injury severity and trauma center need in the field, the specific efficacy of the four-step methodology used in Florida has not been studied.

Methods: Data for 2,944 patients was retrieved from the trauma registry at a Level II Trauma Center, and 2,868 records were included in the study. Indicators of trauma center need and resource utilization were derived. Positive predictive values were calculated for nearly all measures. Calculations for two recently used definitions of trauma center need were also developed.

Results: Patients enrolled under scorecard and Glasgow Coma criteria required trauma center resources more frequently. Two calculations of trauma center need showed positive predictive values of .541 and .518. Blue scorecard criteria showed more consistent performance against measures of resource utilization than others. Patients enrolled under paramedic discretion criterion died before discharge just 3% of the time, compared to a range of 13 to 15% for other criteria.

Conclusion: Florida's pre-hospital trauma triage criteria fared well in this specific setting, meeting established standards for overtriage. More research is necessary to identify if these results can be reproduced in other areas. Additionally, there may be specific anatomic indicators, co-morbidities, and mechanisms of injury that can be isolated as candidates for future scorecard criteria.

Blood Feeding Patterns of Aedes aegypti and Aedes mediovittatus in Puerto Rico

Andrea M. Bingham¹, Hassan K. Hassan¹, Thomas R. Unnasch¹, Manuel Amador², Roberto Barrera^{2 1}

University of South Florida, Tampa, FL, United States² Centers for Disease Control and Prevention Dengue Branch, San Juan, PR, United States, University of South Florida, College of Public Health, Dept. of Global Health

Keywords: mosquitoes, blood meal, dengue virus, PCR

Objective: Aedes (Stegomyia) aegypti (L.), the main vector of dengue viruses (DENV) worldwide, co-occurs with Ae. (Gymnometopa) mediovittatus (Coquillett), the Caribbean treehole mosquito. This mosquito overlaps with Ae. aegypti in urban, suburban, and rural areas with tall vegetation and it has been shown to be a highly competent vector of DENV, with one of the highest rates of vertical transmission in the laboratory. This study investigated if Ae. mediovittatus actually feeds on people and compared its feeding patterns with those of co-occurring Ae. aegypti in two rural communities in Puerto Rico.

Methods: Adult specimens of mosquitoes were captured every week for three consecutive days using BG-Sentinel™ traps with skin lure that were placed in the front of houses in both communities from July 2009 to May 2010. Three methods were used to identify the 756 blood meals that were obtained in this study: a multiplex PCR for humans, dogs, and cattle targeting cytochrome b, a PCR targeting the 16S rRNA, and a nested PCR targeting cytochrome b.

Results: Aedes mediovittatus fed mostly on humans (45-52%) and dogs (28-32%), but also on cats, cows, horses, rats, pigs, goats, sheep, and chicken. Aedes aegypti mostly fed on humans (76-79%) and dogs (18-21%), as well as on cats, horses, and chickens.

Conclusion: Our results showed that Ae. mediovittatus does have a relatively high rate of vector-human contact that might facilitate virus transmission or harborage in this rural area of Puerto Rico.

Research supported by: Centers for Disease Control and Prevention Dengue Branch, San Juan, Puerto Rico

A Method and Composition Using a Putative Pseudophosphatase of Plasmodium Falciparum as an Antimalarial Drug Target

Christopher O. Campbell, USF Department of Global Health Bharath Balu, SRI International Steven P. Maher, USF Department of Global Health Roman Manetsch, USF Department of Chemistry John H. Adams, USF Department of Global Health, University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Malaria, Plasmodium, signal transduction, drug discovery, phosphatase

Objective: Genomic analysis of Plasmodium has revealed vital information about the parasite biology and pathogenesis, however much of the encoded proteins remain uncharacterized. PF13_0027 is a conserved protein phosphatase expressed in all stages of development.

Methods: A null PF13_0027 parasite revealed an altered cell cycle resulting in an attenuated growth phenotype. Genetic complementation rescued the wild-type phenotype and revealed that PF13_0027 is important for asexual development.

Results: Further analysis has uncovered that it may not participate in signal transduction but in a role characteristic of a pseudophosphatase. The conserved substitution of one of the catalytic residues suggests that it may retain substrate-trapping ability without dephosphorylation.

Conclusion: Currently there is an urgent need for new antimalarials because of increasing resistance to common drugs and the absence of an effective vaccine. Blocking the expression of PF13_0027 to create a null parasite reduces the malaria parasite's ability to survive thus providing a novel drug target or an attenuated blood stage parasite vaccine.

Research supported by: F31 AI 83053-01 R01 AI33656

Fruit and Vegetable Access in Low-Income Rural Communities: Florida Case-Study

Curtis DeVetter¹, Emanny Sanchez², Mathieu Poirier¹, Jaime Corvin¹, ¹University of South Florida, College of Public Health, Department of Global Health, ²University of South Florida, Department of Epidemiology and Biostatistics. University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Case Study, Fruits and vegetables, Thrifty Food Plan, Price, Accessibility

Objective: The purpose of this study was to evaluate the disparities in access to fresh produce in the Tampa metropolitan area by assessing and comparing the availability, variability, quality and price of fruits and vegetables (F/V) in food stores in one Tampa area.

Methods: A geographic area west of the University of South Florida was surveyed to identify all food stores within the community. Data was gathered to inventory F/V and each food store was evaluated. Availability was indicated by the presence or absence of F/V items at a given food store while variety was determined on whether the store carried different varieties of F/V as well as varying kinds of a particular food item. F/V were assigned a quality indicator of Excellent, Good, or Poor rating based on apparent bruising and ripeness. Cost was assessed based on price per pound or price per item. Food stores were evaluated on availability and price of F/V in order to assess the fulfillment of the US Department of Agriculture Thrifty Food Plan (TFP) guidelines and TFP basket.

Results: Twenty-four food stores were surveyed and 310 different F/V item were identified across the study area. The quality of produce was found to be more consistent in grocery stores than convenience stores, however a correlation between quality and price was not significant. Lower costs of F/V were observed among grocery stores and supermarkets. Conversely, convenience stores exhibited higher prices on F/V items. Less than half of all the stores surveyed were able to fill a TFP basket.

Conclusion: The absence of quality and affordable foods presents a barrier to access to F/V and healthy diets. Eliminating these barriers forms an integral part in achieving the objectives set forth in Healthy People 2020.

Apicomplexa-Specific Kinase is Tightly Cell-Cycle Regulated

Jesse Diasparra, Carrie Butler, Elena Suvorova and Michael White University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Apicomplexans, Toxoplasma gondii, Kinase

Objective: Toxoplasma gondii is an obligate intracellular pathogen from the phylum Apicomplexa. Diseases caused by these infectious microorganisms are the result of increased parasite burden and the accompanying host tissue cell lysis.

Methods: The recent completion of the genome sequence and the cell cycle transcriptome for several Apicomplexa has allowed the identification of regulatory genes that may be essential for parasite growth. Within the core group of cell division cycling (CDC) genes shared by the Apicomplexa are 16 novel protein kinases with distributed timing across the replication cycle. Epitope tagging of these kinases has allowed for subcellular localization to be pinpointed, and with antibody co-markers the precise cell cycle expression determined.

Results: The 16 CDC kinases unique to Apicomplexa pathogens are conserved at several levels; protein primary and secondary structure organization and cell cycle peak timing, mRNA abundance and dynamic change during parasite division. One kinase termed K14 was endogenously tagged at the C-terminus by homologous recombination. Immunofluorescent analysis of transgenic clones revealed exclusive nuclear localization with tight cell cycle expression. Maximum protein expression was associated with the G1 phase of the cell cycle into early S phase.

Conclusion: Because of their conservative nature within the Apicomplexa family and unique structure compared to the animal host, protein kinases are an attractive target for therapeutic intervention. Kinase 14 has been localized within the parasite nucleus and may play a role in the steps preceding DNA replication in S-phase that are associated with the START checkpoint. Future studies will focus on the specific role this kinase serves in cell cycle progression.

Research supported by: NIH

A Liver Sinusoid Device for Studying Plasmodium Exoerythrocytic Forms and Antimalarial Therapeutics

Steven P. Maher (USF), Anilkumar H. Achyuta (Draper Lab), Amy J. Taylor, Alla A. Epshteyn, Emilee C. Bannister, Wajeeh M. Saadi Joesph D. Cuiffi (Draper Lab), Naresh Singh, John H. Adams, Dennis E. Kyle, University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Malaria, Microfluidics, Liver

Objective: Novel antimalarial vaccines and drugs need to target malaria liver forms but current in vitro models do not recapitulate the microenvironment of the liver. To improve upon current models used to study human Plasmodium liver invasion and development, and as a prototype drug-screening platform, we engineered a microfluidic device incorporating key features of a liver sinusoid. Our hypothesis is that these features, including cell co-cultures, 3D cell orientation, extracellular matrix, media perfusion, and nutrient diffusion are essential to obtain in vivo-like hepatocytes and parasites within an in vitro model.

Methods: The device consists of two channels formed in thin layers of PDMS sandwiching a polycarbonate membrane mimetic of the basal lamina and space of Disse of a liver sinusoid. Media is perfused through the sinusoid-like channel while hepatocytes are cultured under static conditions in the second channel across the membrane. The membrane includes 10 µm holes permitting nutrient diffusion and sporozoite invasion from the sinusoidal to parenchymal chambers.

Results: Hepatocytes survive for several days in the parenchymal chamber of the device with the sinusoid channel under flow. After initial hepatocyte culture, P. berghei sporozoites injected into the flowing sinusoid channel successfully traversed the membrane into the parenchymal chamber, invade hepatocytes, and develop into liver forms while under observation with high resolution time lapse imaging.

Conclusion: The microfluidic device is suitable for hepatocyte culture and support malaria liver stages. Future studies will include sporozoite invasion, biology of liver stage development, and the effect of novel antimalarial therapeutics.

Research supported by: Bill and Melinda Gates Foundation

Drug-Sensitivity Phenotyping of Piggybac Mutants to Validate And Prioritize Plasmodium Falciparum Targets

Brian Martens* Dr. Anupam Pradhan* Dr. Dennis Kyle* Dr. John Adams* Dr. Bharath Balu* Dr. Naresh Singh*

*University of South Florida, College of Public Health, Department of Global Health 3720 Spectrum Blvd Suite 304 Tampa, FL 33612 University of South Florida College of Public Health Global Health

Keywords: Malaria Drug Discovery Plasmodium falciparum**Objective:** The rapid emergence of drug resistance in Plasmodium falciparum requires the discovery of new drug targets. Given that most of the malaria genome is comprised of genes of unknown function and relatively few targets have been validated, we adopted a forward genetics approach coupled with high-throughput phenotypic analysis to identify novel drug discovery targets.**Methods:** Using piggyBac insertional mutagenesis, a panel of unique mutant P. falciparum (NF54) clones was created with single defective genetic loci. More than 50 genetic loci were successfully screened in a high-throughput drug susceptibility assay against a set of >50 known and unknown chemotypes to different biochemical pathways of P. falciparum.**Results:** As expected, most mutants did not differ significantly in susceptibility to the parent line and mutants with human DHFR served as positive controls. Validation of this approach for finding genotype:phenotype associations was observed with differential responses to cyclosporin A of mutants for the hypothetical cyclophilin genes PF08_0086 and PF13_0318. These mutant lines were resistant to CSA, but not to FK-506 demonstrating a possible defect in calcineurin-mediated signal transduction in the mutant parasite. We also observed significant resistance (>10 fold growth change) with existing antimalarials like artemisinin and 4-aminiquinolines with many of the piggyBac mutants.**Conclusion:** These data validate a forward genetics approach for identifying new drug discovery targets and possible functions of genes in the malaria parasite. Furthermore, these data demonstrate the potential utility of developing a full panel of mutants as an important resource for validating new drug discovery targets in vulnerable pathways important for drug discovery.**Research supported by:*****Sharps Usage Patterns and Hazards Among Firefighters and Emergency Medical Services Personnel at a Suburban Fire Department***McGuire-Wolfe, Christine^{1,2}, Haiduven, Donna¹, C. Duncan Hitchcock²(retired), ¹USF-COPH, Global Health, ²Pasco County Fire Rescue. University of South Florida, College of Public Health, Dept. of Global Health**Keywords:** Firefighters, Needles, Recapping, IV stylet, Sharps safety**Objective:** To identify trends in sharps usage that impact the risk of needlestick injury among firefighters and emergency medical services workers at Pasco County Fire Rescue, Florida.**Methods:** Discarded sharps from 11 fire stations were collected during two one-week periods in 2010. Sharps boxes were opened under controlled conditions and sharps were classified by type of device and desired/undesired behaviors. Total counts and frequencies were calculated to identify common practices. Chi-square tests were calculated using EpiInfo 6.0 for comparisons of sharps practices and additional variables.**Results:** 2473 sharps were classified. Undesirable behaviors included altering the safety device on IV stylets (5.58% of 1882 IV stylets), adding a needle and recapping an added needle with pre-filled syringes (7.05% and 1.28% of 468 pre-filled syringes), and recapping traditional needles (36.90% of 84 traditional needles). Desirable/undesirable behaviors were analyzed by call volume and location without any statistically significant associations. There were statistically significant associations between desirable/undesirable behaviors with pre-filled syringes and traditional needles and type of medication [code/urgent vs. all other/less urgent](p<0.00000). Additional unanticipated sharps hazards were identified.**Conclusion:** Undesirable behaviors occurred in noteworthy frequencies and appear to be influenced by call urgency. Efforts should be made to disseminate information about newly identified hazards, such as intra-osseous needles, patient's own syringes, broken glass vials, and razor blades.**Research supported by:** Student Research Award from the COPH's Interdisciplinary Research Innovation & Creativity Committee and the Samuel P. Bell III Endowed Scholarship.

Characterization of Drug Resistant Malaria in Southeast Asia Lindsay Morton, Amanda Hott, Kansas Sparks, Dennis Kyle, University of South Florida; Francois Nosten, Shoklo Malaria Research Unit: University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Malaria, Artemisinin derivatives, Drug resistance, Southeast Asia,

Objective: Malaria remains a devastating infectious disease worldwide. Drug resistant *Plasmodium falciparum* historically originated in Southeast Asia and swept across malaria endemic regions leaving conventional monotherapy treatment ineffective. Currently, the last and most effective combination of antimalarials includes artemisinin derivatives. Thus, the characterization of artemisinin-resistant malaria in Southeast Asia is imperative for malaria treatment and control worldwide.

Methods: We conducted drug susceptibility assays with artemisinin derivatives and other antimalarials to screen clinically resistant patient isolates. Hypoxanthine was used as an indicator of parasitic growth to determine the half maximal inhibitory concentration (IC50) to measure the effectiveness of each compound on the patient blood samples containing *Plasmodium falciparum*. Genetic analysis was conducted to compare laboratory produced artemisinin-resistant strains and clinically resistance isolates clones from Southeast Asia.

Results: Some isolates with reduced parasite clearance rates in vivo showed a shift in IC50 values suggesting a resistant phenotype; these data were confirmed in clones. Genetic analysis identified increased copy number of *pfmdr1* in resistant strains compared to wild-type.

Conclusion: We have isolated the first culture adapted *P. falciparum* isolates and clones with stable artemisinin resistance phenotypes from Asia. These reagents will be critical in the search for the elusive artemisinin resistance mechanism.

Research supported by: Bill & Melinda Gates Foundation, WHO, NIAID

Re-emergence of Cholera in the Americas: Risks, Susceptibility & Ecology

Mathieu Poirier, USF College of Public Health, Ricardo Izurieta, USF College of Public Health, Sharad Malavade, USF College of Public Health, Michael D. McDonald, University of Maryland School of Public Health, University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Cholera, Americas, Haiti, Ecology, Risks, Epidemic

Objective: The reemergence of cholera in Haiti has established a new reservoir for the seventh cholera pandemic which threatens to spread to other countries in the Americas. Analysis of the risks which may facilitate the spread of disease and susceptibility to these risks can help us prevent further epidemics.

Methods: Statistics from this new epidemic are compared to the 1991 Peru epidemic, which demonstrated the speed and complexity with which this disease can spread from country to country.

Results: Environmental factors implicated in the spread of *Vibrio cholerae* such as ocean currents and temperatures along with biotic factors from zooplankton to waterfowl pose a risk for many countries in the Americas. The movement of people and goods from Hispaniola are mostly destined for North America, but occur to some degree throughout the Americas. These modes of transmission, and the probability of uncontrolled community spread beyond Hispaniola, however, are completely dependent upon risk factors within these countries such as water quality and availability of sanitation. While North America has excellent coverage of these deterrents to the spread of infectious gastrointestinal diseases, many countries throughout Latin America and the Caribbean lack these basic services and infrastructures.

Conclusion: In order to curb the immediate spread of cholera in Hispaniola, treatment availability should be expanded to all parts of the island and phase II epidemic management initiatives must be developed.

A Socio-Ecological Approach to Assessing the Delivery of Culturally Competent Care to Uninsured Women

Ashley Richards MPH, Erica Anstey MA, Megan McLaughlin MPH, Alyssa Schmidt, Laurie Woodard MD, Ellen Daley PhD, MPH University of South Florida, College of Public Health, Dept. of Global Health

Keywords: socio-ecological model, cultural competence, barriers

Objective: Addressing cultural competence has been identified as a priority for providing better healthcare in the U.S. Incorporating cultural competence to reduce health disparities requires identification of the complex health needs among ethnically diverse communities. The purpose of this study is to evaluate barriers to providing culturally competent care to women across levels of the socio-ecological model.

Methods: Semi-structured journals were completed by Women's Health Project student participants. A priori and emergent codes based on the socio-ecological framework were used to assess barriers to culturally-competent care across these levels. Data were analyzed in NVivo to achieve appropriate inter-rater reliability.

Results: Content analysis of the student journals revealed consensus on several themes across all levels of the socio-ecological framework. General themes included language and health literacy, variations between providers and patients' perceptions of the causes and significance of various diseases, lack of acknowledgement of cultural and linguistic differences among Latina subgroups as well as the need for translators to address sensitive topics, and the limited availability of auxiliary services. Themes concerning insurance coverage and eligibility were also identified.

Conclusion: The students identified several barriers to best practices in culturally-competent patient care at this particular clinic. Using the socio-ecological framework affords both future clinicians and public health practitioners a perspective on barriers and stressors for uninsured women and an increased understanding of maximizing health services utilization for this population.

Research supported by: MCH Training Grant

Analysis of MDR Acinetobacter baumannii in the Healthcare Setting: Risk Factors and Predominant Genotypes Associated with Infection

Lylah Seaton, MT(ASCP), Dept. of Global Health, College of Public Health; Megan Gumke, MPH; Dr. Azliyat Azizan, PhD., Department of Global Health, USF College of Public Health; Jacqueline Whitaker, RN, MS, LHCRM, CIC, Director Infection Control, Florida Hospital Tampa; Christen L. Mayer, MLS(ASCP), MPH, CPH, CIC, Infection Control, Florida Hospital Tampa; Victor Ohaya, MD; Colton Faza, University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Acinetobacter, multi-drug resistant organisms, infections

Objective: Identify patient risk factors associated with development of infection with multi-drug resistant (MDR) Acinetobacter baumannii in a local hospital and long-term care facility.

Methods: A descriptive study was conducted over a 24-month period. Patients with multi-drug resistant organisms on admission to the health care facility were identified. Respiratory specimens were collected and cultured on MacConkey plates. Pulse-field gel electrophoresis (PFGE) was performed on all positive MDR Acinetobacter isolates. Medical records from Florida Hospital Tampa and its long term acute care facility at Connerton were reviewed. Information abstracted included (and not limited to): use of antibiotics, length of stay and invasive devices.

Results: A total of 69 isolates were collected and three prevalent genotypes were identified: Type O (31%), Type J (23%) and Type A (15%). 38% of the patients with MDR A. baumannii infection were age 60 – 74 and 29% were in the ≥75 year old group. 58% of the infected patients were female and 42% were male. 58% of the infected patients were transferred from other facilities. Length of stay was evaluated with a resultant Z-score of 6.593 ($p=0.05$). The average length of stay for MDR A. baumannii patients at the Florida Hospital Tampa campus was 25.63 ($p=0.05$) and for the general population was 5.5 days.

Conclusion: The analysis demonstrated that age and gender was a risk factor and length of stay was impacted by development of MDR Acinetobacter baumannii infection. Inpatients with positive cultures were older than those in the general population and had a longer length of stay than those in the general population at the Florida Hospital campuses.

Research supported by: Infection Control Department, Florida Hospital Tampa

The Phenotypic Characterization of the Plasmodium falciparum Gene Knockout Not1 (PF11_0049)

Phaedra J. Thomas, Anatoli Naumov, John H. Adams - USF Global Health Department, Bharath Balu - SRI International Biosciences

Keywords: malaria, CCR4-Not complex, gene expression, immunofluorescence, phenotype

Objective: The objective of this work is to characterize PF11_0049 and validate the phenotype of the Not1 mutant. The Not1 gene is apart of a larger gene regulatory system in eukaryotes known as the CCR4-NOT complex, which is involved in the initiation of mRNA degradation. According to studies in yeast, the protein acts as a scaffold for the other proteins in the complex and participates in translational repression. Our research focuses on understanding what happens during the asexual stages of the wild-type malaria parasite and mutant, by which we will determine the localization and expression profile of Not1.

Methods: Through bioinformatics analysis, the Not1 domain and its relationship with other NOT family proteins in Plasmodium falciparum was examined along with its homolog in other species. From these sequences, primers were designed for RNA expression analysis, which will be used to identify any changes in the developmental cycle as it pertains to six time points. The localization of Not1 will be determined by immunofluorescence assays (IFA).

Results: The P. falciparum Not1 gene shows a constitutive expression pattern with possible variation in asexual stage expression. The Not1 mutant shows a 50% fold change in expression as compared to the wild type. The preliminary immunofluorescence data for the Not1 mutant shows patterns similar to that of the wild type when using the antibodies (Gap45 and EBA-175).

Conclusion: Validation of the Not1 mutant phenotype results in slow growth and delayed invasion, which will be visualized by microscopy. Currently, microarray data is being analyzed and RNA expression analysis is being conducted to confirm these results.

Research supported by: NIH/NIAID award #R01AI033656 and the Florida Education Fund's McKnight Doctoral Fellowship Program

Analysis of Field Trapping Methodology for Aedes Aegypti and Aedes Albopictus Species in Hillsborough County

Brian Trang, MPH, CPH¹; Jose Hasemann, MPH, MA¹; Dr. Azliyati Azizan, PhD¹; Dr. Carlos Fernandes²; Steven Sullivan²; Leonard Burns²; Ron Kolson²; Charmont Bonner²; Andrea Bingham, MSPH, CPH, PhD¹; Bridget Leivan, MPH¹ ¹Department of Global Health, University of South Florida College of Public Health Community & Family Health; ²Hillsborough County Mosquito and Aquatic Weed Control Hillsborough County

Keywords: Aedes albopictus aegypti Dengue Hillsborough

Objective: Dengue causes problems in Florida with reports of local transmission since 2009. Ae. aegypti is globally accepted as the primary vector for dengue virus, while Ae. albopictus is the implicated secondary vector. The efficacy of ovitraps was tested and compared to the current mosquito trapping methodology to determine Aedes mosquito distribution in Hillsborough County.

Methods: After an analysis of historical data, 8 ovitrap locations were chosen. Each trap was assigned a geographic coordinate and associated with predetermined parameters (percent vegetation, percent visual shade, estimated distance to nearest home). At each trap location, one experimental (clear) cup was paired with our standard (black cup) ovitrap. Mosquito eggs were collected every 7 days for 3 weeks and counted independently per trap by two researchers. Statistical analyses were performed using SPSS 18.

Results: The egg counts in the experimental cups were significantly different by treatment. Furthermore, visual shade percentage moderately affected egg counts that could be collected, and estimated distance from the nearest home had the most significant impact on egg count. Additionally, spatial temporal maps of the areas were created to further correlate the trap sites and collection results with relevant environmental parameters.

Conclusion: The historical data did not significantly correlate to the data produced in this study, but we were able to statistically identify the months with the highest density of adult mosquitoes in the traps, and the best months for egg collection. Overall, our methodology forms the basis for field sampling design for our microsatellite analysis to genotype Ae. albopictus in several Florida Counties.

Research supported by: USF COPH & Hillsborough County Mosquito Control

Novel Quinolones: Transmission-Blocking and Radical Curative Anti-Malaria Drugs against Plasmodium falciparum and Plasmodium berghei Parasites

Kenneth Udenze¹, Alexis N. LaCrue¹, Fabian Saenz¹, R. Matthew Cross², Jordany Maignan, Roman Manetsch², Dennis E. Kyle^{1*} ¹ Department of Global Health, University of South Florida, Tampa, FL, ² Department of Chemistry, University of South Florida, Tampa, FL

Keywords: Plasmodium falciparum, Plasmodium berghei, transmission blocking, drug resistance

Objective: Malaria affects millions of people throughout the world and new drugs to treat and prevent malaria are urgently needed. In particular new classes of compounds are required that block transmission and eradicate the persistent liver stages of relapsing malaria. In this study we assessed how quickly resistance can develop to ICI56, 780 a 7-(2-Phenoxyethoxy)-4-(IH) quinolones (PEQ) that has previously being shown to have curative activity against P. cynomolgi and P. berghei liver stage parasites

Methods: To assess how quickly resistance develops to ICI 56,780, both in vitro and in vivo studies were performed. In vitro P. falciparum (W2) was subjected to increasing drug pressure and changes in susceptibility were evaluated. For in vivo studies Balb/c mice infected with P. berghei; were treated subcutaneously with 12.5mg/kg, 25mg/kg, 50mg/kg and 100mg/kg of ICI56,780 and observed for recrudescence. For the transmission-blocking assay P. berghei infected mice were treated with ICI 56, 780 and then exposed to non-infected female Anopheles stephensi mosquitoes. Ten days post-exposure mosquito midguts were evaluated for the presence of oocysts.

Results: For the in vitro assay, there appears to be a difference in clearance times following two rounds of drug selection with ICI 56, 780. Additionally, in vivo studies revealed that following one round of drug selection, parasites were much less susceptible to treatment with ICI 56,780.

Conclusion: Our studies suggest that decreased susceptibility to ICI 56,780 develops rapidly in vivo. Additional rounds of drug selection are underway to determine how quickly resistance develops in vitro. These PEQ resistant lines will allow future studies on cross-resistance with other mitochondrial inhibitors.

Research supported by: NIH:(1R01GM097118-01).

Habitat Associations of Eastern Equine Encephalitis Transmission in Walton County Florida

Patrick T. Vander Kelen¹, Joni A. Downs¹, Christy L. Ottendorfer¹, Kevin Hill¹, Brenda Hunt³, Steve Sickerman⁴, Lillian M. Stark^{1,2}, Thomas R. Unnasch¹ University of South Florida¹, Florida Department of Health, Bureau of Laboratories-Tampa², North Walton County Mosquito Control District³, South Walton County Mosquito Control District⁴, University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Equine Encephalitis Virus, Habitat, arbovirus, GIS, transmission

Objective: Eastern Equine Encephalitis virus (EEEV; family Togaviridae, genus Alphavirus) is a pathogenic arbovirus with a high fatality rate. The ecology of EEEV in Florida is more diverse than in other parts of the USA. Geographical Information Sciences(GIS)was used in conjunction with sentinel chicken EEEV seroconversion rate data as a means to examine landscape features associated with EEEV transmission in Walton County, Florida.

Methods: Sentinel sites were categorized as enzootic, periodically enzootic, and negative based on the number of chicken seroconversions to EEEV from 2005-2009. EEEV transmission was then categorized by land cover usage using Arc GIS 9.3. The land classification data was analyzed using the Kruskal-Wallis test for each land use class to determine which habitats may be associated with virus transmission as measured by sentinel chicken seroconversion rates.

Results: The habitat class found to be most significantly associated with EEEV transmission was tree plantations. The ecological factor most commonly associated with reduced levels of EEEV transmission was vegetated non-forest wetlands. Culiseta melanura, the species generally considered to be the major enzootic EEEV vector, was relatively evenly distributed across all habitat classes, while Aedes vexans and Anopheles crucians were most commonly associated with tree plantation habitats.

Conclusion: Targeting tree plantations for surveillance could improve the protection of both human and horse populations in the Panhandle region of Florida by providing earlier warnings of transmission activity and more effective opportunities for resource management and prevention measures.

Research supported by: National Institute of Allergy and Infectious Diseases and United States Department of Defense

Induction of Miltefosine Resistance in Leishmania donovani.

Brian Vesely and Dennis Kyle, University of South Florida, College of Public Health, Dept. of Global Health

Keywords: Leishmania, Drug Resistance, Miltefosine

Objective: Miltefosine is the only drug for visceral leishmaniasis that has not generated clinical resistance; however, the drug has a long half-life that raises concerns resistance will emerge. Our objectives were to use a novel axenic amastigote line to assess the potential for generation of drug resistance in *L. donovani* and to characterize the resistance phenotypes generated in vitro and in vivo.

Methods: We used discontinuous step-wise drug pressure in vitro to generate a stable miltefosine resistance phenotype. Importantly we used a novel axenic amastigote line of *L. donovani* so that resistance would be selected in the relevant mammalian infectious stage of the parasite. The resultant miltefosine resistant parasite (Milt-R) and its sensitive parent (Milt-S) were studied for sensitivity to standard anti-leishmanial drugs in vitro and in vivo.

Results: A stable Milt-R parasite line was generated with an IC50 of 150 μ M as compared to 3 μ M for the parental line. The resistance phenotype was observed in both the infected macrophage and in the infected hamster models of disease. When exposed to 5 days of drug pressure in vivo at 30 and 50 mg/kg of miltefosine, Milt-S parasite burden was reduced 85 and 95%, respectively. Conversely 30 mg/kg drug had no effect on Milt-R and 50 mg/kg reduced parasite burden only 40%. Interestingly, bisbenzimidazole was more effective against Milt-R than Milt-S in vitro.

Conclusion: We generated a stable miltefosine drug resistant *L. donovani* that expressed a stable high level resistance phenotype in vitro and in vivo. The Milt-R line will be an invaluable reagent to characterize resistance before it emerges in the field.

Does The Tip and Grain of a Bullet Affect Post Impact Expansion?

Matthew Ball, Douglas Reeb University of South Florida

Keywords: Physics & Astronomy

Objective: To determine if the tip & grain affects PIE (post impact expansion)

Methods: 1. Purchase Knox gelatin, fruit pectin, water, non-stick cooking spray, & large containers to make ballistic gel molds. 2. Make ballistic gel molds per recipe and allow ample time for each mold to set. 3. Purchase ammunition having all firearms are cleaned and ready to fire. (.22, .7mm, 30-06, & 50 cal.) 4. Measure distances at 50m, 100m, and 150m in front of concrete safety ammunition barrier. 5. Place ballistic gel downrange allowing time for shooter and any bystanders to apply ear plugs and NRA approved shooting glasses on appropriately. 6. Position gun sled at 50m mark in preparation for firing rotation. 7. Beginning with initial firearm to be used, double check all safety equipment and firearms. 8. Load ammunition, have shooter position self in safe firing position behind gun sled. 9. Ensure bystanders are positioned behind the shooter. 10. Shooter is to take aim and fire initial round while photographer photographs events. 11. After initial firing, place safety on gun and expel discarded bullets. 12. Bystander will collect measurements and record data. 13. Replace ballistic gel target with new target and repeat steps 5-12. 14. Change caliber of firearm and repeat steps 5-13 until all chosen firearms have been tested. 15. Reposition gun sled at 100m mark in preparation for firing rotation. 16. Repeat steps 5-14. 17. Reposition gun sled at 150m mark in preparation for firing rotation. 18. Repeat steps 5-14. 19. Collect all data, interpret, analyze, and form conclusion.

Results: Grain & tip affects PIE

Conclusion: Hypothesis was proven correct that PIE is affected by tip & grain.

Research supported by: Personal interview with gunsmith Riley Smith.

Abstract #: 287

Presented by: Jamie Casteel, High School Student

Can Saltwater Hermit Crabs Adapt to Living in Freshwater

Jamie Casteel University of South Florida N/A

Keywords: Hermit Crabs, Scallops, Feather Dusters, Anemone

Objective: The purpose of doing this project was to see if saltwater hermit crabs could adapt to life in freshwater. This scientist predicted that the hermit crabs could adapt to freshwater, because other organisms adapt to new environments.

Methods: In order to conduct this experiment, first 5 hermit crabs were collected from the Gulf of Mexico. In addition, 4 scallops, 3 marine feather dusters, and 1 anemone were gathered. Next all crustaceans were placed into a 29 gallon Bio Cube fish tank. The salinity of the water started out at 32ppt. Then, the salinity was decreased every seven days to see if saltwater hermit crabs could adapt to life in freshwater. Every week the scientist also observed the hermit crab's actions and behavior.

Results: The results of this project were that, on week six one of the hermit crabs died, and on week ten, (the last week) three hermit crabs died, and so only one hermit crab is still alive. This crab was the smallest of them all.

Conclusion: In conclusion it is very hard for saltwater hermit crabs to adapt to complete fresh water, and it may be easier for them to adapt to complete freshwater if they are smaller. Also, they can tolerate a very low salinity (6ppt.) brackish water. Similar results were seen for some of the other organisms.

Abstract #: 288

Presented by: Madison Coffey, High School Student

Can A Home-Made Tesla Coil Wirelessly Transmit electricity to light lamps?

Madison Coffey University of South Florida N/A

Keywords: Can Tesla Coil Light Lamps?

Objective: The purpose of this project was to build a working Tesla Coil.

Methods: In order to build the device, technical skills such as soldering, wire termination, drilling, sanding, and painting were learned.

Results: The results of this project produced a miniature working replica of the original Tesla Coil which emitted electrical streamers from the 12 inch torrent.

Conclusion: This scientist has proven that a Tesla Coil can be built to transmit electricity wirelessly to light a lamp.

Does Facebook Affect the Face-to-Face Communication of Teenagers?Emily Crawford, Delaney Davey University of South Florida N/A**Keywords:** Facebook**Objective:** The purpose of this project is to see if Facebook has any correlation with the degrading of teenagers being able to communicate face-to-face, and if active use of Facebook can be addicting to teenagers.**Methods:** In order to test this, first gather a number of 11th grade high school teenagers for test subjects. Then hand out the Facebook Surveys and the Human Consent Forms. Next, gather the completed forms. Then, create data tables and charts for the gathered information. Observe the subjects at lunch for the next week to see if they use Facebook and how they interact with surrounding people.**Results:** After analyzing our data, we found that students who have Facebooks log on anywhere from one to six times per day, averaging two times per day. Students log on anywhere from one time to one hundred times per week, averaging thirteen times per day. At night students are active on Facebook from twenty minutes to five hours, averaging one and a half hours per night. In the cafeteria, students would not communicate with others, and instead were on Facebook.**Conclusion:** Based on the data and results of the experiment, the hypothesis is supported in that Facebook does indeed effects to the face-to-face communication of high school teenagers. It decreases the natural ability of students being able to communicate effectively face-to-face. By using such technology so young, there will be a lack of natural communication. Students also claim that they are not addicted to the sites. However, after studying the data students in fact show signs of addiction by spending up to five hours on Facebook every night. By stopping the use of this website, students could learn how to communicate again and in doing so expelling the addiction to the website.***Can Red Worms Consume a Biosolid and Create Vermicompost?***Elizabeth Fairchild University of South Florida N/A**Keywords:** Biosolid, Vermicompost**Objective:** The purpose of this experiment was to determine if ordinary red worms could consume a bio-sludge and create healthy vermicompost. This scientist predicted that the red worms would consume the bio-sludge when mixed with newspaper, peanut shells, eggshells, cow manure and peat moss to create beneficial vermicompost.**Methods:** In order to conduct this experiment, this scientist had to create an environment for the red worms that would allow them to consume the bio-sludge over a two month period. By using organic materials that could easily be repeated on a larger scale, I was able to create a habitat that included some of the worm's favorite foods. This was to combat the worm's natural aversion to the bio-sludge. Then, this scientist had to collect 2.5 ounces of vermicompost from each of the three 2011 containers for a total of half a cup, and 2.5 ounces of vermicompost from each of the three 2010 containers for a total of half a cup when the two month period was over. Afterwards, this scientist sifted through the vermicompost and poured both samples into the two separate Solvita test jars. After putting the vermicompost in Solivita test jars, this scientist put in the carbon dioxide level probe and the soil/grain test probes into each jar. This scientist waited four hours to collect the results and then another twenty-four hours to collect the final results.**Results:** The result of this project was that the red worms were able to consume the bio-sludge and create vermicompost.**Conclusion:** In conclusion under the right conditions and mixed with the right organic material red worms will consume this bio-sludge. While the process has to be tweaked, it has been submitted for a provisional patent due to the fact that it has never been done before.

Are You Exposed to Potentially Dangerous EMF/ELF Fields?

Chance Frisch University of South Florida N/A

Keywords: EMF ELF Fields Radiation

Objective: Extra low frequency (ELF) and electromagnetic (EMF) are radioactive. They are produced by electrical wiring, electric devices, and power lines. The student's hypothesis is that a middle class home will not be at a potentially dangerous level EMF/ELF.

Methods: The experiment is being done to determine how radioactive a middle class home is and to make people aware of the dangers of EMF/ELF radiation. The student will measure appliances in the home by room and total all of the measurements to the room's average. After all averages have been found, they will be added together to determine the home's average as a whole.

Results: Results go on to show that the appliances exceeding the limit of 16 mG were the laptop and 8-plug outlet. Appliances that exceeded or came close to the limit of 12 mG were the alarm clock, microwave, drying machine, and the house phones.

Conclusion: The total for the house was a measurement of 41.3 mG. The student's hypothesis was not supported due to the fact that the safest level of EMF/ELF is 16 mG (12 mG for pregnant women), and the house's level exceeded that limit.

MMSE Vs. mCDR; Tools in Detecting Alzheimer's Disease

University of South Florida N/A

Keywords: Alzheimer's Disease

Objective: The purpose of this science fair experiment is to determine if the Mini Mental State Examination (MMSE) is more sensitive than the Modified Clinical Dementia Rating (mCDR) in detecting Alzheimer's disease in patients of 65 years or older. In determining this, this researcher hopes to provide physicians and testing sites with up to date statistical proof as to which of these tests are the best and most efficient to use. This researcher predicts that the MMSE will be more sensitive to Alzheimer's.

Methods: To conduct this experiment, first data was collected. After receiving data, scores on each test were graphed against age, diagnosis, and gender. Analysis was made through t tests and correlations for each graph to determine significance. Record data and draw conclusions.

Results: The results of this experiment showed that the graphs comparing the scores for both tests vs. age had slopes of zero. The results of all the graphs showed that neither tests were biased by age or gender. The t tests for Score vs. Diagnosis graphs for both tests showed that the test scores could predict with 95% confidence the diagnosis for MCI and AD within two standard deviations of the mean.

Conclusion: In conclusion, this project showed that both the MMSE and mCDR are significant in detecting Alzheimer's disease in patients of 65 years or older.

The Effects of Firing Different Types of Glass Together

Lauren Nieves, Denise Gibson: Glass Fusion Expert University of South Florida

Keywords: Glass Fusion

Objective: The purpose of this project is to show the importance of not firing incompatible glass together, because of the stress within the glass. The hypothesis for this project is that when different glasses are fired with another type of glass, the glass will fracture either in the kiln or later due to the stress that is created from the glass expanding at different rates, due to their coefficients of expansion.

Methods: The procedure for this project is as follows. First all the pieces of glass need to be cut. Four three by three inch pieces of 96 COE, 90 COE, float, and stained glass, and four one and a half by one and a half inch pieces of the previously listed glass each need to be cut. The pieces then need to be measured, cleaned, and put into the kiln, one one and a half by one and a half inch piece put on each type of the three by three inch bases, and fired at a temperature up to 1500 degrees Fahrenheit. After the firing the kiln shelves and glass needs to be cleaned, the glass measured and all changes observed.

Results: All of the four types of glass were fired to the other types as well as the same type. Out of all of the pieces of glass that were fired together, only two of them ended up fracturing, these were the float and stained glass with 96 COE on top. Every other piece had stress, except for the stained and float pairs. The ones with stress should eventually fracture though.

Conclusion: The hypothesis of the experiment was not supported, not every combination of incompatible glass had stress, and only two of the pieces fractured. The glass that has stress has it because of the differing coefficients of expansion, and those pieces that don't change as much or their coefficients of expansion do match up, won't have stress.

Does Food Packaging Influence Children's Ability to make Healthy Choices?

Ugwumsinachi Nwaubani

Keywords: Packaging, Children's Behavior, Foods

Objectives: This scientist's purpose for this experiment was to conclude whether or not food packaging influences children's ability to make healthy choices. This scientist hypothesized that the children will always go for the decorated packaging and the sugary foods rather than the healthy foods.

Methods: This scientist conducted this experiment with the following procedure; the experiment will be done in two days. On day one there will be two classes participating one kindergarten class and one first grade class. There should be double the number of bags as there are children for each class, and half the bags should be decorated bags and the other half should be plain bags. On day one the children will pick any bag they want without being told anything, after that take pictures and record the observations. On day two do everything exactly the same but label the bags with what is inside them.

Results: The results of the experiment showed that the majority of the children picked the decorated bags over the plain bags and sugary over healthy. On day one with both the classes, the majority all together picked decorated bags blinded. On day two with both classes the majority picked decorated bags with the sugary snacks inside them knowing what was inside them.

Conclusion: In conclusion food packaging does influence children's ability to make healthy choices. On day one the boys picked plain and the girls picked decorated because of the feminine colors. This led this scientist to conclude that packaging influences children's ability to make choices and has accepted her hypothesis.

Research Supported by: N/A

Does Rooting Affect the Quality of a Plant? Does Temperature Affect Plant's Growth?

Rachel Russell and Kimberly Guice University of South Florida N/A

Keywords: Case Study

Objective: The purpose of this project was to see if rooting a flowering plant such as the desert rose, will result in the same quality of the mother plant, or the plant that it is rooted from. These scientists also would like to determine which temperature or condition is better suited for the plant after it is rooted, the spring or summer condition. These scientists hypothesized that the spring condition will be best when rooting and also that the quality of the plant will not be affected by grafting during either condition.

Methods: First, mix potting soil and sand into a large plastic container. Take tablespoon and measure soil in tablespoon and place into egg containers. Repeat until container is full. Next place small hole within soil that is about an inch deep. Determine which plant you will be grafting from and cut a small growth from the top or sides of the plant. Cut stem in a diagonal angle and dip small cut into root growth. Only dip about three fourths of an inch into formula. Place each small plant into holes within the soil. Place clear containers over each egg container, you should have two. These represent the different conditions of growth. Place one container in 75 degrees home and another in 65 degrees home. Check plants once a day and spray 64 degrees dome once a day with 1 Tb of water, and only spray 75 degree plants 3 times a week with 1 Tb of water each time and record data each week.

Results: In the summer condition, the desert rose grew 0.1 inches and in the spring condition, the flower grew about 1.4 inches.

Conclusion: The quality of the plant rooted was in affected, but by the conditions in which it grows. The data clearly shows that the spring conditions were much better suited for the desert rose but these can vary with the plant.

How Fresh is Your Milk? Is Standard Plate Bacteria (SPC) Count Higher in Organic or Non-organic Milk?

Hayden Fox Siverson University of South Florida N/A

Keywords: Bacteria, Organic, Non-organic, Milk

Objective: The purpose of this experiment was to see whether organic milk or non-organic milk had a higher standard plate bacteria count after set amounts of time. Standard plate bacteria (SPC) count is a total count of all bacteria types found in the sample. My hypothesis was that the organic milk would have a lower SPC due to the fact that organic milk is pasteurized at a much higher temperature, which allows most bacteria in the milk to be eliminated.

Methods: To begin this experiment, both organic and non-organic milk samples were purchased from local stores. The milk samples were taken to Southeast Milk Inc. Quality Control Lab where the SPC was measured. All surfaces were sanitized with isopropyl alcohol. Samples were drawn from both the organic and non-organic milk using a pipette and mixed with predetermined amounts of water. A sample was also taken from water that was to be used as a control. Samples were placed on a Petri film and then samples were placed in an incubator. SPC bacteria were measured after 1, 2, 4, 22, 28, and 45 hours. Several samples from the same mixtures were sampled at the same time.

Results: After 28 hours, the organic sample diluted at 1:100 had a colony count of 520 (too high to count so the 1:1000 count was used) and at 1:1000 the count was 49. The organic sample diluted at 1:100 had a count of 320 (too high to count so the 1:1000 count was used) and at 1:1000 the count was 47.

Conclusion: After completing this experiment, it was found that both the organic and non-organic milk had very similar bacteria growth rates. I found that the organic milk would only stay fresh longer if it has no contact with air. Once the milk is opened, its shelf life is very similar to that of non-organic milk.

How does airfoil design affect the efficiency of a rotor at different wind speeds?

Hunter Stafford, University of South Florida N/A

Keywords: Airfoil

Objective: The purpose of this experiment is to determine if there is a more efficient alternative to the standard three-foil design that is used in today's wind generators. By testing three separate airfoil designs at different wind speeds the hope is to either confirm that our wind turbines are currently as efficient as possible or to discover a more efficient design.

Methods: 1. Place standard two-foil rotor in wind tunnel set at 5 mph (440 fpm) 2. Extinguish all fluorescent lighting and turn on the digital tachometer 3. Wait 30 seconds to insure the rotor is rotating at its peak rpm 4. Record the RPM ten times, once every 10 seconds and average 5. Repeat steps 2-3 for 10, 15, 20, 25, 30, 35, 40 and 45 mph 6. Repeat steps 1-5 with three and four-foil rotors 10. Compile data and acknowledge any trends.

Results: The results show that in wind speeds up to 15 mph (1320 fpm) the standard three-foil design was more efficient than the standard two-foil as predicted. The two-foil design was more efficient in wind speeds of 20 mph (1760 fpm) and greater. The four-foil design exhibited greater revolutions per minute at all wind speeds and was the most efficient design tested.

Conclusion: It was hypothesized that out of the three airfoil designs tested, the three-foil design would be most efficient in slower wind speeds, the two-foil design would be more efficient at higher wind speeds and the offset four-foil design would be as efficient, if not more efficient than the 2 and 3-foil designs. This hypothesis was proven correct; in wind speeds of 15 mph and below the three-foil out preformed the two-foil, but as predicted the two-foil had the advantage at higher speeds. The four-foil design was the most efficient design tested in all wind speeds.

Local Medical Practices: A Source of Pathogenic Bacteria?

Ana S. Torres University of South Florida N/A

Keywords: Microbiology research

Objective: It is a common belief that local medical practices present a risk for harboring pathogenic bacteria. However, few studies exist that support this notion. The goal of this study was to collect samples of inanimate objects from medical practices and determine if they are a source of pathogens. If medical practices follow OSHA guidelines from aseptic and general cleanliness technique, there should be no evidence of pathogenic bacteria in the waiting room, restroom, or exam of the facilities.

Methods: Permission to anonymously utilize eight medical practices in the Lake and Sumter county area was obtained. Nine samples were collected from objects in the waiting room, restroom, and exam room totaling 72 samples. Samples were cultured on renal blood agar plates and incubated at 37°C for at least 24 hours. Resulting cultures demonstrated a variety of normal flora growth including staphylococcus, bacillus, streptococcus, micrococcus, and corynebacterium species. Gram staining, catalase, and coagulase testing was performed on colonies displaying pathogenic characteristics. Two colonies on plate 2W3 were identified as oxacillin susceptible *S. aureus*, the remaining suspicious cultures were *S. epidermidis*, which is generally non-pathogenic.

Results: Ultimately, the hypothesis was supported. Only 1.4% of samples taken contained pathogenic growth, therefore medical practices are not a substantial source of pathogenic contagion.

Conclusion: Samples taken represent a variety of medical disciplines including internists, pediatricians, dermatologists, and plastic surgeons. These results should reassure the public that visiting their local physician, no matter the discipline, does not present a risk for contracting disease under standard conditions.

What is Growing in Your Makeup?Isabel Torres University of South Florida N/A**Keywords:** makeup, bacteria

Objective: The purpose of this experiment was to determine if there's a widespread bacterial contamination in foundation, and if so, determine if it's associated with daily use, owning it for a long period of time, sharing it, not storing it in a cool place, or not keeping it tightly closed when not in use. The hypothesis was that the more these behaviors were followed, the higher amount of contamination will be found.

Methods: The procedure started by selecting a study group in terms of age. Then, a questionnaire was given to the subjects assessing how they used their makeup and obtained samples of the subject's foundation for culture using a sterile swab. The sterile swab with the sample was placed in the transfer medium and taken to the laboratory. The blood agar plates were inoculated with the samples using the streaking for isolation method and incubated at 37C for 48 hours. The plates were then removed from the incubator, and the colonies were identified and counted. Bacteria data was analyzed and compared to the questionnaire information.

Results: One hundred percent of the samples where the user said to use their foundation only most days or occasionally, had only 1 colony grow or showed no growth. The samples of foundation that were used every day had 6 colonies or more grow, except for one.

Conclusion: This partially supported the hypothesis because bacteria growth was only found to be closely related to frequency of use. If it wasn't regularly used, bacteria growth was low or nonexistent.

Abstract #: 300**Presented by: Kunal Upadya, High School Student*****Which Type of Sugar Best Promotes the Growth of Yeast?***Kunal Upadya University of South Florida**Keywords:** sugar, yeast, bakers

Objective: The purpose of this project was to find out which type of sugar best promotes the growth of yeast. This scientist had predicted that powdered sugar would best grow yeast, because it is sucrose crushed up to make it easier for yeast to use.

Methods: When completing this experiment, first, each petri dish was labeled as a different sugar. Next the yeast was activated and added to the petri dishes. Second, 5mL of water was added to each petri dish. Third, a gram of respective sugar was added to each petri dish. Lastly, the yeast was allowed to sit for 48 hours. It was analyzed under a microscope at 12, 24, 36, and 48 hours.

Results: The results of this experiment were different from that of what this scientist thought. Aspartame Sweetener came in first with 29 cells in the sample; cane sugar had 27 cells in the sample; powdered sugar had 25 cells; sucrose and brown sugar had 24 cells; Splenda had 23 cells in the sample; and glucose and fructose both had 18 cells in the sample.

Conclusion: This scientist believes that the sweetness of the aspartame and the nitrogen-hydrogen chain of aspartame was what made it better promote growth. Aspartame did better than Splenda because Splenda is made by chlorinating sucrose.

Football The Underdog vs The Favorite

Ethan "Brock" Wiley University of South Florida N/A

Keywords: Statistics

Objective: The purpose of this project was to test one football season whether the underdog or the favorite wins the most. The scientist predicted that the underdog would win a majority of the time if the point spread was included.

Methods: 1. Create a EXCEL spreadsheet with the lines based upon a newspaper. 2. Watch as many football games as possible or get the newspaper with the lines and then again for the results. 3. Document the results on the spreadsheet. 4. Repeat steps 1-2-3 on a weekly bases. 5. Summarize the weekly results. 6. Calculate the season weeks 1 – 14 (up to science fair). 7. Form a conclusion to either prove or disprove the theory tested.

Results: The results of this project concluded that in the college season the underdog lost more games than the favorite but in the professional league the underdog won more than the favorite because the teams were more even than the college teams which most of the top-25 teams played much easier teams than themselves.

Conclusion: In conclusion the scientists hypothesis was partially correct because in professional football the underdog won more than the favorite but in college the underdog won less than the favorite did.

Occupational Asthma Associated with Sick Building Syndrome Risk Factors in United States and Puerto Rico

Julio O. Acevedo Matos, B.S. Industrial Hygiene Department, University of Puerto Rico, Rio Piedras, PR,
University of South Florida

Keywords: asthma, sick building syndrome, risk factor

Objective: Studies show a correlation between inappropriate air quality and occupational asthma, (" a disease characterized by variable airflow limitation, hyperresponsiveness, inflammation due to causes and conditions attributable to a particular occupational environment and not to stimuli encountered outside the workplace. Poor air quality has also been related to sick building syndrome, defined by World Health Organization (WHO, 2011) as a set of discomforts and associated diseases caused by force ventilation, inadequate temperature, ionic loads, and airborne, gases and vapors of chemical and/or biological origin in enclosed areas.

Methods: The aim of this study is to critically review and analyze studies associating sick building syndrome and occupational asthma, and compare studies performed in the United States with those in Puerto Rico.

Results: Reviewed studies identify biological agents, chemistry, material building, temperature, relative humidity, ventilation, odors, fibers and vapor as factors for asthma prevalence.

Conclusion: Sick buildings syndrome investigation and asthma research in Puerto Rico is predominantly epidemiological studies or biological agents association.

Incivility, Mobbing, Abusive Supervision and Undermining in the Workplace: A Qualitative Review

Josh Allen, John Wittgenstein, Mike Harari, Florida International University, USF SERC, University of South Florida

Keywords: Workplace Aggression, Qualitative Review

Objective: Recent research has called for a consolidation or reexamining of the various sub facets of workplace aggression research with focus on unifying workplace aggression sub fields by similarities. Workplace aggression research encompasses many different behaviors and is broadly defined by a range of topics including interpersonal conflict, mobbing, abusive supervision, incivility and social undermining. The different forms of workplace aggression all play significant roles as workplace stressors and are assessed here with an occupational stress outlook. The purpose of this project is to identify the antecedents, mediators and moderators of workplace aggression currently used by researchers in a qualitative manner.

Methods: Studies were included if (A) the location of the aggression experienced was from the workplace.(B) Aggression measured was the independent or predictor variable.(C) Study was conducted or translated into English.(D) Study was published in a scientific journal. The search terms used were social undermining, abusive supervision, incivility, and mobbing.

Results: The search produced 109 possible articles, with 50 studies meeting our inclusion criteria. Of the 50 articles there were 4 social undermining, 6 mobbing, 14 incivility, and 26 abusive supervision.

Conclusion: This literature review demonstrated that although the majority of studies in incivility and abusive supervision focused on moderators in their relationship to outcomes. Less than half of the studies measured a mediating variable and very few measured antecedents. Among other areas, we identified the overlap in scales used and outcomes measured. This literature review demonstrates the need for additional research examining and expanding the bounds of current information.

Comparing Visual vs. Microscopic Methods to Detect Blood Splatter from Intravascular Catheters (IVC) with Engineered Sharps Injury Protection (ESIP)

Aiysha R. Ansari, MD, USF-SERC, College of Public Health, Dept. of Environmental and Occupational Health, Donna J. Haiduven, PhD, CIC, USF-College of Public Health, Department of Global Health, Hamisu M. Salihu, MD, PhD, USF-SERC, University of South Florida College of Public Health, Community & Family Health, Padmaja Ramaiah MSBE, VA Research Center of Excellence, Lillian W. Collazo, MPH, MT (ASCP) CM, CPH, James A. Haley V.A. Hospital and University of South Florida, College of Public Health, Dept. of Environmental and Occupational Health.

Keywords: Blood splatter, Filter, Bloodborne pathogen, Chamber, Microscope, Intravascular, catheter

Objective: Retractable intravascular catheters (RIVCs) with ESIP have not been investigated for blood splatter potential. Research questions were: do RIVCs produce blood splatter, and does splatter frequency differ between visual methods vs. microscopy?

Methods: 100 RIVCs of the same brand were placed in a testing chamber with scientific filters labeled A, B & C, to capture blood spatter after activation in a simulated brachial venous system. Differences in filter mass, visual and microscopic analysis for blood were the units of analysis. Descriptive statistics, paired t-tests and kappa statistics were used for data analysis.

Results: The proportions of filters B and C with blood detected by the naked eye were 12% and 13% respectively. But for filter A, visual vs. microscopic methods detected blood 70% and 71% respectively. A statistically significant difference was observed in mean mass of filter A between pre- and post-activation confirmed visually ($t = -0.0013$, $p = 0.01400$) and microscopically ($t = -0.00014$, $p = 0.0092$). Kappa statistics indicated substantial agreement between methods for filters A, B and C. However, in 6 instances (6%), blood was detected by microscopy and not by the naked eye.

Conclusion: A potential for bloodborne pathogen exposure with use of a specific RIVC was detected. Scientific filters captured blood splatter that was not noticeable by the naked eye but was detected by microscopy in 6% of the instances. Therefore, healthcare workers (HCW) may not be able to detect blood splatter when it occurs and may not report a splash to mucous membranes or non-intact skin. This study reinforces the need for HCWs to wear personal protective equipment (e.g., masks, face shields, goggles) when using RIVCs.

Research supported by: USF-COPH-SERC

A Longitudinal Investigation of Emotions and Counterproductive Work Behaviors

Jeremy A. Bauer, Paul E. Spector, Psychology Program, University of South Florida, College of Arts and Sciences

Keywords: Emotions, Counterproductive Behavior, Aggression, Longitudinal

Objective: Studies have established relationships between counterproductive work behaviors (CWB), behaviors that harm the organization, and negative emotions (e.g. Cohen-Charash & Mueller, 2007). Almost all CWB studies have been cross-sectional; the need for more longitudinal studies has been noted (e.g. Dalal et al, 2009). The goal of the current study was to investigate the relationships among specific negative emotions and specific types of CWB while using a longitudinal design.

Methods: Data were collected from 228 preschool teachers in Germany. The participants were instructed to complete two surveys, each completed after work on a Friday with a one-week time lag. The emotions of interest were hostility, fear, guilt, and sadness. The CWB facets of interest were production deviance, withdrawal, sabotage, theft, and abuse.

Results: Each time 2 CWB facet was regressed onto each time 1 emotion while controlling for the corresponding time 1 CWB facet. Then, each time 2 emotion was regressed onto time 1 CWB facet individually while controlling for the corresponding time 1 emotion. All emotions predicted an increase in future reports of production deviance and abuse. However, CWB facets did not predict future reports of negative emotions.

Conclusion: The results provide evidence that emotions from a previous week can predict displays of CWB during the next work week. However, previous displays of CWB did not appear to predict emotions over the following work week. These results are congruent with models that identify negative emotions as a precursor to CWB (i.e. Berkowitz, 1998), but they do not support the reverse. Both methodological and theoretical explanations for these findings are discussed.

Research supported by: The Sunshine ERC

Chronic Diseases in the Workplace

Bethany G Brown, University of South Florida, College of Nursing, Occupational Health Nurse Practitioner, University of South Florida, College of Nursing

Keywords: Literature Review Chronic Disease

Objective: To review literature and research on chronic diseases in the workplace and how they influence health care costs. To investigate if employers' efforts to provide education and programs for employees with chronic diseases influences health care claims.

Methods: This was a review of literature that analyzed different employers' efforts to decrease health care claims for chronic diseases.

Results: The companies that were the most successful provided an onsite service to their employees that incorporated assistance with behavior modification. Some companies utilized telephonic and online services for employees instead of an onsite program.

Conclusion: More research needs to be done to prove to company leaders that chronic disease education and programs will decrease health care costs. These programs are benefits to employees but not necessarily proven cost reducers.

Research supported by: SERC

Personal Characteristics of LGB Employees: Personality and Disclosure

Jacob Waldrup, Natasha Buxo, Valentina Bruk-Lee, Florida International University (USF SERC)_University of South Florida

Keywords: Disclosure, LGB, Personality, CSE, Stress

Objective: This study aimed to expand on the current LGB research by examining core self evaluations (CSE) and authenticity in relation to disclosure and stress. LGB friendly policies and other organizational factors such as perceived organizational support (POS) were also analyzed.

Methods: Participants were recruited via internet and completed a short online survey without compensation. The sample consisted of 146 LGB individuals of varying ethnicity working in different industries throughout the United States.

Results: An analysis of variance comparing disclosed and non-disclosed individuals found significantly lower levels of CSEs and higher levels of self-alienation, a subscale of authenticity, for the non-disclosed group. Also, stress was found to be both positively related to CSE and negatively related to self-alienation. Regression analyses showed a positive relationship between both LGB policies and POS to "level of disclosure." A negative relationship was found between POS and stress, but no significant relationship was identified between stress and LGB specific policies.

Conclusion: Fear may be a motivator for LGB individuals not to disclose at work, however other factors, such as CSEs and self-alienation, may be separate motivating forces for disclosing one's sexuality. Also, LGB friendly policies and POS may both be important factors in the decision to disclose, however stress was only related to POS, not LGB policies. This suggests that organizations should not rely solely on having LGB friendly policies and initiatives to neutralize LGB fears of discrimination. Many employees may not even be aware of such policies. Organizations should strive to create supportive working environments for LGB employees in order to reduce their levels of stress.

Interpersonal Conflict, Coping, and Control: Interactive Effects on Well-being

Erin M. Eatough, Department of Psychology, University of South Florida; Chu-Hsiang (Daisy) Chang, Department of Psychology, Michigan State University; Brent Lyons, Department of Psychology, Michigan State University
University of South Florida College of Arts and Sciences Psychology

Keywords: Interpersonal Conflict, Coping, Control, Employee Stress, Well-being

Objective: This study was conducted to examine the interactive effects of interpersonal conflict at work, perceived control specific to that conflict, and coping on employee well-being.

Methods: Multi-source survey data was collected from 438 employed adults and 206 matched significant others or close friends to examine the interaction between interpersonal conflict, perceptions of control over the conflict, and coping strategies in predicting employee psychological well-being.

Results: Overall, findings suggested that the success of coping efforts hinges on the combination of the nature and severity of the stressor, perceptions of control over that stressor, and coping strategy used (problem-focused or emotion-focused coping). Interestingly, only when coping and control were considered simultaneously, not separately, did they have an interacting effect with interpersonal conflict on well-being. Specifically, when problem-focused coping was high, high perceived control mitigated increases in depression and job frustration. Additionally, emotional expression coping was most effective for mitigating the detrimental effects of conflict on well-being when control was low rather than high.

Conclusion: These results suggest that when one perceives little control of the stressor, it is adaptive to manage internal states rather than external states. Further, control is unlikely to mitigate the detrimental association between conflict and job satisfaction if an employee does not adopt coping strategies that capitalize on the control (i.e., not taking action to manage the situation).

Research supported by: The University of South Florida Sunshine Education and Research Center

Critical Heat Stress Evaluation of Chemical Protective Clothing Ensembles with a Full-Face Negative Pressure Respirator

Ocila Michele Fletcher, MD, College of Public Health (COPH), OMR, Thomas E. Bernard, PhD, COPH, EOH, Candi D. Ashley, PhD, College of Education, Hamisu M. Salihu, MD, PhD, COPH, EPB, USF SERC, University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: heat stress, respirator, WBGT, protective clothing

Objective: Protective clothing ensembles restrict heat loss. The purpose of this study was to determine if there are differences in heat stress (critical wet bulb globe temperature - WBGT_{crit}) and heat strain (heart rate, core temperature, physiological strain index [PSI]) among four chemical protective ensembles (TAP apron [TAP], TAP with chemical barrier pants [TAP + P], chemical barrier coveralls [VB + CA], all with full-face negative pressure respirator, and chemical barrier coveralls without respirator [VB + CA noR]); all compared to work clothes (WC).

Methods: Four acclimatized adult males wore all five ensembles in a balanced design while walking at a metabolic rate of about 170 W m⁻² in a climatic chamber at 50% relative humidity. A progressive heat stress protocol was used to find WBGT_{crit}, the point at which there was loss of thermal regulatory control. Mixed effects ANOVA was used to assess ensemble effects. Tukey's test was used to determine where differences occurred.

Results: There were no differences among ensembles for core temperature, heart rate, or PSI, which meant that the physiological strain was the same regardless of clothing or respirator. Significantly different WBGT_{crit}'s were found between WC and TAP and for WC and TAP compared to other ensembles (TAP + P, VB + CA, VB + CA noR). No differences were noted with the presence and absence of a respirator.

Conclusion: Progressively increasing heat stress burden was seen when moving from TAP to TAP + P to VB + CA. The type of protective clothing ensemble worn is a major contributor to workplace heat risk, but a respirator is not likely to increase heat stress risk.

Research supported by: URS, U.S. Army, USF SERC

Review of Health Impacts of Sludge Incinerator Exposure and Issues of Waste Management Effect on Workers and General Public in Puerto Rico

Fuentes Cruz, Kristle M, Orta, Lida, Industrial Hygiene Program, Department of Environmental Health, Medical Sciences Campus of Puerto Rico, UPR. University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Risk Management Factors on Incinerators, Sludge Waste Incineration, Landfills, Incineration, Health Risks of Heavy Metal on Incineration

Objective: This literature review assesses health effects, exposure and public concerns of workers, due to sewage waste and sludge incineration. Heavy metals have serious health effects directly concerning workers of the incinerators and indirectly exposing the population living near.

Methods: In Puerto Rico the incineration of dried sludge has been used for years to reduce the substantial volume of waste, converting it to ash. Around 4,000,000 tons/year of solid waste are generated in PR. Landfills serves as PR only means of disposal. Revision of the EPA regulation 40 CFR part 60 and 503 and OSHA standard 29 CFR. 1915.1000 parameters of exposure in the work place were analyzed and compared with results from the incineration of waste water in Puerto Rico and assess the possible risks to workers health.

Results: It was observed that proper maintenance, management and design of modern incinerators have been showed to reduce up to 99.8% of particulate emission. It was noted that if properly conducted risk management plans and evaluation of different routes of exposure are used on the facilities rather than predicting, could discard every operational uncertainty on incinerations of the articles evaluated.

Conclusion: More concise employee exposure information of health risks and diseases should be evaluated. Some severe effects of heavy metals may include reduced growth and development, cancer, organ damage, nervous system damage, and in extreme cases, death.

OSHA's Beryllium OEL: Inadequacy and Urgent Need for a New Standard, The Case of Recycling Operations and Dental Technicians

Nycole García-Román University of South Florida

Keywords: OSHA, beryllium, recycling, dental technicians

Objective: Beryllium is a metal that is found in nature. Because of its hardness, high melting point and lightweight it is used mostly for military applications, but it's also commonly used in electronics, aircrafts, atomic energy applications, sporting goods, dental prosthetics, auto parts, x-ray equipment, ceramic manufacturing, alloys and other consumer products. For some of these applications there is no substitute for beryllium. This metal is extremely toxic, especially by inhalation. Evidence suggests that the current OSHA guideline is not protective enough for workers exposed to this metal, which are susceptible to developing chronic beryllium disease (CBD) and beryllium sensitization (BeS).

Methods: Critical literature review

Results: In Puerto Rico, although there are no beryllium processing plants, it represents an occupational risk in electronics recycling plants and in the dental prosthetics industry. Social and occupational determinants such as the small size of organizations at risk, lack of awareness to risk factors due to the lack of education and information available to workers are evident in the meta analysis performed of the literature.

Conclusion: Many of these workers are exposed and under risk, due to ineffective regulations to protect them.

Abstract #: 312**Presented by: Mike Harari, BS, Graduate Student*****Justice, Strain, and Work Family Conflict: The Role of Distributive Justice as an Organizational Stressor***

Mike Harari, John Wittgenstein, Josh Allen, Florida International University, University of South Florida

Keywords: Distributive Justice, Work to family conflict, Psychological Strain.

Objective: Contemporary occupational health psychology research has begun reexamining the role of distributive justice, conceptualizing it as an organizational stressor rather than a mediator in the procedural justice-strain relationship. In this study, we build on these findings by examining distributive justice's relationship with psychological strain and work to family conflict. We hypothesized a mediation model whereby distributive (in)justice influences work to family conflict through psychological strain.

Methods: Data was collected from the Professional Worker Career Experience Survey (PWCES).

Results: Using the Hayes & Preacher (2011) mediation technique to test our model, we assigned distributive justice as the IV, Work family conflict as the DV, and psychological strain as the mediating variable. Our bootstrapped mediation model ($F[6,544]=12.8, p<.05$) accounted for 12% of the variance ($R^2=.12$) and provided support for our hypotheses. We observed a significant main effect of distributive justice on psychological strain ($\beta = -0.05, p < .05$) and work-family conflict ($\beta = 0.36, p < .05$), strain on work-family conflict ($\beta = 2.8, p < .05$), and an indirect effect of distributive justice on work-family conflict through psychological strain ($IE = -.15, SE = .05, p < .05$ (99% CI: $L = -0.27; U = -0.06$)). These results support our proposed model.

Conclusion: The results of this study support our hypothesis that distributive justice is an organizational stressor, influencing work to family conflict through strain. This study adds to the literature by demonstrating the direct and indirect effects of distributive justice on negative outcomes and helps to further solidify distributive justice as a meaningful variable in the study of work stress.

Evaluation of Heat Stress Level as a Modifier for Injury and Incident Rates During A Industrial Construction Project

Brian Hauck, Dr. Thomas Bernard, USF College of Public Health, Dept. of Environmental Occupational Health

Keywords: Heat Stress Level, Occupational Safety and Health

Objective: The objective of this study was to explore relationships between outdoor environmental temperatures and the total reported incident and injury cases over a 20-month period (Phase 1a) of a large industrial construction project located in Tampa, FL.

Methods: The effects of heat stress levels were used as a modifier of incident and injury rates. The working hypothesis is that incidents and injury rates will show a marked increase with the changes in WBGT. Occupational health data consisting of incident, injury and illness records, total man hours was obtained from Walbridge.

Results: It was discovered that around a WBGT of 25°C the rate of incidences observed appears to increase ($p=0.08$). The findings of this study with a p -value = 0.08 were approaching statistical significance (p -value < 0.05).

Conclusion: Although the results of this study did not achieve statistical significance, the resultant apparent increase in incidences at a WBGT around 25°C, is consistent and within close proximity to Ramsey's and Morabito's findings. While heat stress prevention should be an on-going practice during construction activities, careful consideration and a heightened heat stress prevention awareness and policy program should be implemented as temperatures approach a WBGT of 25°C.

Noise Exposure in Medical Helicopter Flights

Melissa Hay University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: helicopter, noise, exposure, medical

Objective: The dual purpose of this study is to measure the noise exposure of pilots, nurses and paramedics in medical helicopter flights and assess the hearing protection that is currently used. If the measurements are found to be above the OSHA PEL we will recommend protective measures or additional protection to reduce the risks of hearing loss in the personnel.

Methods: We are hoping to use two types of noise monitoring: area and personal sampling as instructed in OSHA standard 1910.95. Area meters will be used to measure the cabin noise level of the helicopter and determine if the area samples exceed the thresholds for noise exposure. Traveling to the location of the patient, the rear of the helicopter will be measured, then, to preserve space, the investigator will move to the front of the helicopter for the return flight to the hospital. During the flight we will observe the usage of helmets, headphones and earplugs by the medical personnel. Monitoring the rear of the helicopter will also allow us to calculate the exposure to the patient to evaluate if they are in any danger of hearing losses, specifically neonates. We are not planning on attaching monitors to any patients, but possibly placing them in the general area to monitor the noise levels. We also will use Quest 300 Dosimetry meters for personal sampling devices for the pilot, nurse and paramedic during transit to evaluate their individual exposures. These personal monitors from the personnel will be clipped to the collar of the person's shirt and should not affect their work performance. We will place the monitor before boarding the helicopter and remove it after we are back in the hospital.

Results: TBD

Conclusion: TBD

Research supported by: NIOSH, COPH Department of Environmental and Occupational Health

Work-Family Conflict and Flexible Work Arrangements: Deconstructing Flexibility

Tammy D. Allen, Ph.D.¹, Ryan C. Johnson, M.A.¹, Kaitlin M. Kiburz¹, Kristen M. Shockley, Ph.D.^{2, 1} University of South Florida Sunshine Education and Research Center, ²Baruch College – City University of New York. University of South Florida, College of Arts and Sciences, Dept. of Psychology

Keywords: flexible work arrangements, telecommuting, work-family conflict, negative spillover, meta-analysis

Objective: The study meta-analytically investigates the relationship between work-family conflict (WFC) and flexible work arrangements (FWA). These relationships were explored in detail by examining flextime, flexplace, as well as availability and use of each, separately. Furthermore, WFC was broken down into work interfering with family (WIF) and family interfering with work (FIW).

Methods: Academic databases, conference programs, and existing meta-analyses and reviews were searched using keywords (e.g., flexibility, telecommuting, work-family conflict). 61 samples from 58 articles were included. Each study was coded by two study authors, and analyses were conducted using the Comprehensive Meta-Analysis software package using a random effects model.

Results: We found that the direction of work-family conflict (WIF vs. FIW) and the specific form of flexibility (flextime vs. flexplace; use vs. availability) make a difference in the effects found. We also found that sample characteristics (single vs. multiple organizations; within the U.S. vs. outside the U.S.) served as moderators. Overall, the significant effects were small in magnitude with effects associated with WIF being stronger than FIW.

Conclusion: Our results demonstrate that the relationship between FWA and WFC may be smaller than assumed, and influenced by several factors including type of flexibility (flextime vs. flexplace; use vs. availability), direction of conflict (WIF vs. FIW), and sample characteristics. These findings also indicate that flexibility is not a reliable way to help mitigate work-family conflict, and demonstrate the importance of disaggregating flexibility to clarify the relationship between FWA and WFC.

Research supported by: University of South Florida Sunshine Education and Research Center

Linking Nonwork Stressors to Work Outcomes via Negative Mood and Event Appraisals

Cristina K. Kawamoto, BA, Edward E. Levine, PhD, USF SERC, University of South Florida, College of Arts and Sciences, Dept. of Psychology

Keywords: Nonwork Stressors Mood Events Work

Objective: This study aims to investigate the relationship between non-work related stressors (e.g. marital and financial) and work outcomes as mediated by the individual's mood. Borrowing from concepts of the Affective Events Theory (Weiss & Cropanzano, 1996) and the Spillover Hypothesis (Edwards & Rothbard, 2000), it is suggested that negative mood at home (created by nonwork stressors) will transfer to the work domain where it will cause the employee to appraise various work events more negatively. These appraisal s will contribute to a negative mood experienced at work which in turn will influence job satisfaction and performance dimensions. Lastly, social support is hypothesized to moderate this model by reducing chance of negative mood from home spilling over into the work domain.

Methods: Data collection of married, working adults who are head or co-head of their own households is currently in progress. Those who choose to participate are asked to complete a survey consisting of nonwork stressors, mood at home and at work, appraisals of work events and various work outcomes. In addition, their immediate supervisors are asked to complete measures of the employee participants' job performance.

Results: Data has not yet been analyzed, but will be done through correlational analyses and structural equation modeling.

Conclusion: If hypotheses are supported, this research is expected to expand upon previous research linking the work and non-work domains (especially with regard to the effects of negative mood). Additionally, it could have implications for areas such as employee assistance programs at work that deal with stress monitoring and coping as well as financial management (Garman, Leach & Grable, 1996; Sulsky & Smith, 2005).

Research supported by: USF SERC

Abstract #: 317

Presented by: Kaitlin Kiburz, BA, Graduate Student

Dispositional Mindfulness as a Unique Predictor of Work-Family Conflict

Kaitlin M. Kiburz, University of South Florida SERC Tammy D. Allen, University of South Florida
University of South Florida, College of Arts and Sciences, Dept. of Psychology

Keywords: Work-Family Conflict, Mindfulness

Objective: Can being more mindful potentially help reduce work-family conflict? Past research has shown that both situational and dispositional variables predict work-family conflict. This study is the first to investigate the relationship between work-family conflict and mindfulness, the act of being aware and in the present moment.

Methods: Correlational research (survey)

Results: Findings show a negative correlation between mindfulness and both directions of work-family conflict. Additionally, mindfulness was found to explain unique variance in work-family conflict beyond that explained by number of children, work hours, and personality.

Conclusion: This study introduces mindfulness as a predictor of work-family conflict. Future research involving mindfulness training for work-family conflict is discussed.

Research supported by: University of South Florida SERC

Abstract #: 318

Presented by: Alexander Maldonado-Pagán, BS, Graduate Student

Evaluation of Safety Programs in Surface Mining Procedures of Puerto Rico

Alexander Maldonado Pagán, UPR-RCM Graduate School of Public Health, University of South Florida

Keywords: Safety Surface Mining literary review

Objective: The mining industry is a very hazardous trade in terms of occupational injuries. Therefore surface mining companies in Puerto Rico would benefit from a system that adequately evaluates their safety programs and occupational health outlooks.

Methods: The need of personalized safety programs can be deduced from inquiries of mining companies and the observation that they deal with personnel safety problems that cannot be assessed by the standard formula currently used in the United States. This literary review presents the important aspects of surface mining safety programs by comparing similar industries in other states and countries.

Results: Existing evaluation tools are included presenting the deficiencies that support the hypothesis.

Conclusion: The findings suggest that a more concerted study should be implemented that directly considers factors like: lost workdays, mining mechanization, use of contractors, mine company size, personal protective equipment use, awkward position frequency, operation surface stability, psychophysical perceptions, duration of tasks, participative actions and the administrations emphasis on health and safety.

Research supported by: Literary Review

Nanoparticle Generation and Size Characterization

Adam Marty, MSPH, Yehia Hammad, D.Sc., College of Public Health, USF Sunshine ERC, University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: nanoparticle, aerosol, generation, agglomeration

Objective: The generation of nanoparticles is a necessary component for determining health outcomes as they relate to exposure in animal models. Unfortunately, a bulk nanopowder cannot simply be aerosolized into nano-sized particles due to the agglomeration that nanoparticles undergo. The objectives of this research are two-fold; to generate and characterize three different kinds of nanoparticles including one from a bulk source.

Methods: This research attempts to generate nanoparticles using three different methods, namely, from a sodium chloride solution, a metal salt solution, and from a bulk nanopowder source. Test aerosols are characterized using three particle counters. Samples are concurrently collected for visual inspection using electron microscopy. Comparative data analysis of the three particle counters relative to visual inspection is performed.

Results: Since this research is a work in progress, only limited data has been generated. Preliminary results indicate that NaCl particles can be generated at a predetermined size. One trial produced an aerosol with a dominate particle size of 20 nm. A second trial produced an aerosol with a dominate particle size of 100 nm. Visual inspection of the aerosol has yet to be performed.

Conclusion: The generation of particles from salt solutions is not new or novel. For the purpose of this research, it is a necessary aspect as a demonstration of our ability to characterize an aerosol. However, the generation of a nano-aerosol from a bulk nano-powder would be significant. If this method proves successful, it could offer a means to do research on the exposure, dose, and effect of nanoparticles in an animal model.

Research supported by: NIOSH, USF Sunshine ERC

Filtration Performance of a NIOSH Approved N95 Filtering Facepiece Respirator with Stapled Head Straps

Daniel E. Medina, MSPH Yehia Y. Hammad, Sc.D. Thomas E. Bernard, Ph.D. Steven P. Mlynarek, Ph.D.
University of South Florida, College of Public Health, Dept. of Environmental and Occupational Health

Keywords: Disposable, Filter, Efficiency, Polystyrene Latex Spheres, Aerosol

Objective: Are there differences in filtration efficiencies of respirators with stapled head straps vs. no stapled head straps when challenged with 3 different particle sizes?

Methods: Monodisperse polystyrene latex (PSL) spheres 0.5, 1, and 2 micrometers (μm) in diameter, were used to challenge four N95 single use respirators of the same model and made by the same manufacturer. All respirators were sealed onto a custom built testing assembly and tested in a sealed chamber. Particles were generated using a Collison nebulizer and passed through a diffusion dryer and a Krypton-85 radioactive source prior to entering the test chamber. The test chamber was constructed from glass and had dimensions of 32 x 53 x 122 centimeters. The respirators were challenged as received from the manufacturer and the same testing procedure was repeated for each respirator after sealing the stapled areas of filter medium with silicon rubber. Testing was conducted at a flow rate of 85 liters per minute, similar to the procedure utilized by NIOSH in the respirator testing protocol. A laser particle counter was used to measure the concentration inside and outside of the respirator.

Results: The results showed unsealed efficiencies for particle sizes 0.5, 1, and 2 μm to be 96.68%, 99.72%, 99.88% and sealed efficiencies of 97.35%, 99.82%, 99.93% respectively. There were no differences for particle size or sealing at 1.0 and 2.0 μm . A statistically significant drop in efficiency was observed when testing with 0.5 μm spheres.

Conclusion: The drops in efficiency are not sufficient to reduce the integrity of the respirator for N95 certification. However, the leakages detected will have a cumulative effect when added to other sources of single use respirator leakage in the field.

Research supported by: NIOSH

Enhancement of the Performance Capabilities of the USF Inhalation Challenge Chamber

Laura F. Riley MSPH, Yehia Y. Hammad, Sc.D. University of South Florida, College of Public Health Dept. of Environmental & Occupational Health

Keywords: aerosol, chamber, inhalation, particles, thoracic

Objective: The purpose of this study is to enhance the capabilities of a whole-body human exposure chamber (HEC) and determine the largest particle size that can be consistently generated. Once this size is determined, the inhalable and thoracic fractions of the dust cloud will be determined.

Methods: . This chamber is located in the Breath Laboratory of the Sunshine Education and Research Center at the University of South Florida's (USF's) College of Public Health. Previous work has been conducted with this chamber to generate respirable fractions, but not larger sizes.

Results: (Results are forthcoming, as actual research has not yet been conducted)

Conclusion: By determining the largest particle size that can be consistently generated, future inhalation challenge studies using inhalable and thoracic-size particles may be possible with this chamber.

The Interactive Role of Gender in CWB and Workplace Aggression

Zhiqing Zhou, Paul Spector, Department of Psychology,USF SERC University of South Florida, College of Arts and Sciences, Dept. of Psychology

Keywords: gender, CWB, workplace aggression,job stressor, personality

Objective: The purpose of our study was to explore the potential moderating effect of gender in the relationships of job stressors (interpersonal conflict and organizational constraints) and personality variables (agreeableness, conscientiousness, emotional stability, hostile attribution bias, and trait anger) with CWB (CWB-O and CWB-P) and workplace aggression (physical and relational).

Methods: Self-report data was collected from 673 employed participants at a large public university. The mean age of all participants was 21.6 years (SD = 4.3), and 77% of the sample were female. All study variables were measured using published measures with good reliability.

Results: Men were found to engage significantly more in all four types of behaviors. Both job stressors and all personality variables were significantly related to all four types of behaviors. Except for the relationships of conscientiousness and emotional stability with CWB-O, gender was found to moderate the relationships of both job stressors and all personality variables with CWB-O, CWB-P, physical aggression and relational aggression: the differences between men and women were larger when at high levels of trait anger, HAB, interpersonal conflict and organizational constraints, and when at low levels of agreeableness, conscientiousness, and emotional stability.

Conclusion: Although men were found to engage more in all four types of behaviors, we found that at low levels of predictor variables, both external and internal, that facilitate harmful behaviors, men were no more likely to report CWB or workplace aggression than were women; although both genders likely respond negatively to stressful job conditions, it is men more than women who respond to such conditions aggressively or counterproductively.

Religiosity and Spirituality

Rachel Baumsteiger- University of South Florida Saint Petersburg, Tiffany Chenneville- University of South Florida Saint Petersburg, University of South Florida, College of Arts and Sciences, Dept. of Psychology

Keywords: Religiosity Spirituality

Objective: Based on current research concerning the relationship between religiosity and spirituality, the objectives of this study were to examine (a) participants' definitions of religiosity and spirituality, and (b) the correlation between participants' scores on religiosity and spirituality measures.

Methods: Participants included 1037 undergraduate students who completed an online survey containing the following: (a) demographic questions such as the participant's reported religiosity (yes/no), religious affiliation, reported spirituality (yes/no), the participant's definitions of religiosity and spirituality, and the participant's view on the relationship between religiosity and spirituality (e.g., are they the same, different, related?); (b) the Santa Clara Strength of Religious Faith Questionnaire; and (c) the Spiritual Intelligence Self-Report Inventory.

Results: Preliminary data analyses were conducted to determine general findings. Results showed that 51.2% of participants reported being religious, while 65.3% reported being spiritual. The majority of participants said that religiosity and spirituality are "two distinct concepts that overlap in some/many ways." These preliminary data analyses indicate a moderate correlation between religiosity and spirituality. Additional data analyses will include descriptive statistics and correlational statistics.

Conclusion: Results support previous findings that religiosity and spirituality are related but separate constructs. Increasing knowledge about these constructs and how they are related can help us better understand how these constructs influence people's self-concepts, goals, perceptions of others, moral decision-making, and behaviors.

Research supported by: Research not funded.

Modulation of Reelin Processing by Apolipoprotein E and Amyloid-Beta

Andrew Hallmark, Justin H. Trotter, Qingyou Li, and Edwin J. Weeber University of South Florida College of Arts and Sciences, Dept. of Chemistry

Keywords: Reelin, apolipoprotein E, amyloid beta, Alzheimer's Disease

Objective: Age-dependent accumulation of amyloid-beta in senile plaques underlies neurodegenerative processes and cognitive dysfunction associated with Alzheimer's disease (AD). Specific apolipoprotein E (apoE) genotypes modify disease risk with carriage of the apoE4 allele associated with significant acceleration of the pathological progression of AD. Recent data suggests that apoE and amyloid-beta both affect the integrity of lipoprotein receptor signaling. In this study, we have explored upstream mechanisms of this interference by focusing on the expression level and processing of the critical lipoprotein receptor agonist Reelin.

Methods: First, we evaluated the ability of apoE to affect Reelin processing in vitro and vivo using western blotting. We then measured the level of Reelin products (full-length and fragments) in the hippocampus of young apoE targeted-replacement mice, where Human apoE alleles are expressed under the control of the endogenous murine apoE promoter. The compound effect of apoE genotype and amyloid-beta accumulation was determined by measuring changes in Reelin products in hippocampal and cortical lysates from the 5X-FAD AD mouse model that had been crossed with the apoE-TR and apoE KO mice. Moreover, Reelin localization was evaluated in these mice using immunohistochemistry.

Results: Our data reveals that apoE and amyloid-beta both affect Reelin processing, suggesting that impairments in lipoprotein receptor signaling may at least partially have an upstream origin.

Conclusion: Future studies will explore potential in vivo mechanisms whereby apoE and amyloid-beta affect Reelin processing, which may yield novel therapeutic avenues for the treatment of AD.

Aquaporin 5 is Expressed in the Murine Placenta and Regulated by Placenta-specific 1 (Plac1)

Jayme Coyle¹, Xiaoyuan Kong², M.D. Suzanne Jackman, M.D.², Michael Fant, M.D.^{2,3,4} ¹Department of Environmental Science, Policy and Geography ²Department of Pediatrics, ³Obstetrics and Gynecology, ⁴Pathology and Cell Biology University of South Florida College of Arts and Sciences Geography, Environment and Planning

Keywords: placenta, aquaporin 5, Plac1

Objective: Aqp5 is a transmembrane, water-selective channel protein linked to osmotic transmembrane water transport. The objectives of this study were to examine the expression of Aquaporin 5 (Aqp5) in the murine placenta and confirm its regulation by placenta-specific 1 (Plac1). Plac1 is a placenta-restricted gene that is essential for normal placental development. Deletion of the Plac1 gene results in placentomegaly and intrauterine growth retardation. Differential gene microarray analysis of mutant placentae at e16.5 identified aquaporin 5 (Aqp5) as one of the genes most significantly down-regulated (15-fold) in Plac1 mutant mice.

Methods: Plac1 was deleted in murine ES cells and bred against a C57BL/6 background. Timed matings were established between wild type (WT) or hemizygous males and heterozygous (het) females. Placentae obtained at e16.5 were subjected to differential gene microarray analysis using the NIH 15k mouse embryo gene microarray. Aqp5 mRNA was measured by Q-RT-PCR. Aqp5 protein was localized by immunofluorescence microscopy.

Results: Aqp5 mRNA was significantly down-regulated (>95%) in placentae associated with Plac1-null and het embryos compared to WT placentae. Immunofluorescence analysis demonstrated Aqp5 immunoreactivity in the spongiotrophoblast as well as labyrinthine trophoblasts, where placental transport and maternal-fetal exchange occurs.

Conclusion: These data suggest that Aqp5 may play also a role in regulating water transport and homeostasis at the maternal-fetal interface. Furthermore, they demonstrate that Plac1 expression is a major determinant of Aqp5 expression.

Research supported by: March of Dimes #6-FY09-503

The Many Faces of KickButt Quitters: Characteristics of College Smokers Participating in a Text-Messaging Tobacco Cessation Pilot Study at USF.

Elisabeth A. Franzen¹, Pamela C. Guevara, MPH¹, Mary P. Martinasek, PhD, MPH, CHES, CPH², Eric R. Buhi, MPH, PhD¹, ¹Department of Community and Family Health, College of Public Health, University of South Florida, ²Department of Health Science and Human Performance, College of Natural and Health Sciences, University of Tampa. University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Smoking Cessation, Tobacco Smoking, Young Adult, Student Health Services, Text Messaging

Objective: Among college smokers participating in a text messaging tobacco cessation pilot study, we evaluated students' baseline survey data to understand who seeks smoking cessation services (SCS) and assessed students' smoking environments and triggers.

Methods: A longitudinal study design was employed in 3 phases with USF students seeking SCS at Student Health Services. Basic descriptive statistics were conducted using SPSS version 19. Baseline survey questions included gender, age, sexual orientation, relationship status, residence, cigarette craving/trigger/stressor specifics, and smoking environment.

Results: From December 2010 to January 2011, 47 student smokers were recruited, of which the majority (55%) were female and enrolled full time (89%). Participants' ages ranged from 18 to 38 years with 18 years being the most commonly reported age (13%). Most participants (83%) identified as heterosexual, 50% were in a relationship (not living with the person), and 66% were living off-campus. Participants identified school stress as a leading stressor influencing their smoking (94%). Over half of students reported smoking regular/full flavored cigarettes (51%), and students reported that they tend to smoke more when they are around other smokers (88%), feeling anxious/stressed (88%), drinking alcohol (85%), and prior to an exam (85%). Students also reported school as a trigger for smoking (85%), along with being in their car (81%) or at a bar/club (79%).

Conclusion: From our findings, it is evident most USF college smokers smoke because of school related stress. We suggest campus-based SCS integrate evidence-based cessation strategies with stress management skill building exercises to increase the likelihood of students staying smokefree.

Research supported by: USF AHEC.

Factors Influencing Participation in a Study of the Etiology of Breast Cancer in Black Women

Jennifer Garcia, Devon Bonner, Courtney Lewis, Alyssa Schmidt, Ana Garcia, Sharland Johnson, Susan Vadaparampil, Tuya Pal| University of South Florida, College of Behavioral & Community Sciences Communication Sciences & Disorders; H.G. Moffitt Cancer Center & Research Institute

Keywords: Cancer Epidemiology, Genetics Research, Recruitment

Objective: To describe factors which influenced participation in a study to investigate the etiology of breast cancer in a sample of young Black women with invasive breast cancer.

Methods: Potential participants for a cancer genetics research study were recruited through a state-wide cancer registry. Eligibility criteria included Black women diagnosed with invasive breast cancer at age 50 or below in 2009 and 2010. Recruitment was conducted initially through mail followed by phone to discuss interest in participation. For those who declined, information as to the reason for their decision was obtained through a written response form or over the phone. For those who were interested, a survey was administered to assess factors influencing their decision. Data collected from these surveys was analyzed using descriptive statistics.

Results: Of the 158 subjects with whom the study personnel established contact, 26.6%(n=43) declined and 73.4%(n=115) expressed interest in participating. Of those who declined, 23.8%(n=10), stated "lack of time" as the primary reason and 50.0%(n=21) indicated they were "simply not interested" in the study. Of those who expressed interest, 59.1%(n=68) completed the survey to assess factors influencing their decision. The most commonly reported factors included receipt of incentives in appreciation for their time (57.4%) and no requirement for in-person visits (57.4%). Forty-seven percent indicated "not being finished with treatment" would make them less likely to participate in cancer genetics research.

Conclusion: This analysis suggests Black women are more likely to participate in cancer genetics research when no in-person visits are required. The use of study incentives as appreciation for time also seems to enhance participation.

Research supported by: Moffitt

BRCA Mutation Status and Other Factors Influencing Prophylactic Mastectomies among Participants in the Inherited Cancer Registry (ICARE)

Sidorela Gllava; Courtney Lewis; Andrea Doty; Devon Bonner; Susan Vadaparampil; Tuya Pal; University of South Florida College of Arts and Sciences Cell Biology, Microbiology & Molecular Biology; H. Lee Moffitt Cancer Center and Research Institute

Keywords: BRCA mutations, HBOC, prophylactic mastectomy

Objective: To describe whether BRCA mutation status and other clinical and socioeconomic factors influence uptake of prophylactic mastectomy among participants with prior genetic testing in the Inherited Cancer Registry (ICARE) Initiative at the Moffitt Cancer Center.

Methods: Self-reported data was obtained from ICARE participants who returned their baseline questionnaire between June 2010 and November 2011. Individuals who failed to report prior genetic testing were excluded from this analysis. Data was stratified based on whether the participant elected to have a prophylactic mastectomy. Frequencies were calculated for BRCA mutation status and other factors such as marital status, parity, family history of cancer, level of knowledge about hereditary breast and ovarian cancer (HBOC) and the delivery of genetic testing services within the two groups.

Results: Of the 312 ICARE participants who reported a genetic test result on their baseline questionnaire, 37.8% (n=118) elected for a prophylactic mastectomy. Of those who chose to have a prophylactic mastectomy, 91.5% (n=108) reported having a deleterious BRCA mutation, 5.1% (n=6) reported a negative BRCA test result and 3.4% (n=4) reported having a variant of uncertain significance. Of the individuals who did not have a prophylactic mastectomy, 17.0% (n=33) presented with no family history of cancer as compared to the 5.1% (n=6) of the individuals who chose prophylactic mastectomy with no reported family history of cancer.

Conclusion: As expected, the proportion of women with a deleterious BRCA mutation who opt for a mastectomy is higher compared to a negative or VUS BRCA test result. This analysis also suggests that bilateral prophylactic mastectomy was associated with a positive family history of cancer.

Research supported by: Moffitt

Developmental Associations between Positive Illusory Bias and Life Satisfaction in Youth with ADHD

Leah E. Hacker, USF; Casey D. Calhoun, M.A., University of North Carolina-Chapel Hill; Mark Cavitt, M.D., All Children's Hospital Psychiatry; Jeffrey Alvaro, M.D., All Children's Hospital Psychiatry; Eric A. Storch, Ph.D., USF/All Children's Hospital, University of South Florida, College of Arts and Sciences, Dept. of Psychology

Keywords: ADHD, Developmental, Positive Illusory Bias

Objective: In a sample of children with ADHD and their parents, the current cross-sectional study examines the association of intra- and inter-rater reports of life satisfaction (i.e., a more subjective, introspective measure of quality of life) with ADHD symptom ratings.

Methods: Our sample included 23 children (ages 8-17) and their parents, recruited from a community mental health clinic after receiving a principal component analysis. All children had comorbid pervasive developmental disorder (autism spectrum disorder). Parent and child ratings of life satisfaction were evaluated using the 7-item Student Life Satisfaction Scale (SLSS; Huebner, 1991). ADHD symptom severity was measured using the 21-item Vanderbilt ADHD Diagnostic Rating Scale (Wolraich, 2003).

Results: First, parent- and self-reports of symptom severity were only significantly correlated for adolescents, as were parent- and self-reports of child's life satisfaction. Parent reports of child's life satisfaction were not correlated with parent reports of symptom severity for either children or adolescents. Self-reported life satisfaction was negatively correlated with self-reported symptom severity for adolescents only. Lastly, results showed that positively biased symptom severity ratings were related to higher self-reported life satisfaction for adolescents but not children.

Conclusion: Our findings suggest that among adolescents with ADHD, self-reports of symptom severity could be highly influenced, or even confused with, perceived life satisfaction. The significant correlation between parent- and self-reports of symptom severity and life satisfaction among adolescents aligns with previous theory suggesting improved accuracy with age (Milich, 1994).

The Uniformity of Informed Consent for Biobanking, A Systematic Review

Alexa Halburian, Undergraduate BMS major (University of South Florida), Janique Rice, BS (Florida State University) MS (University of South Florida), Gwendolyn Quinn Ph.D (USF College of Medicine), Clement Gwede Ph.D (USF College of Medicine), Cathy Meade Ph.D, RN (USF College of Medicine) University of South Florida College of Arts and Sciences, Morsani College of Medicine, Dept. of Oncologic Sciences

Keywords: "Informed Consent Biobanking," "Blanket Informed Consent," "Simplified Informed Consent," "Menu Informed Consent"

Objective: Compare the simplified consent form to blanket consent form utilized by biobanks Assess what is needed in a consent form to effectively uphold legal and bioethical obligations in order to protect biobanking participants

Methods: A systematic web-based search was conducted using PubMed database. The inclusionary criteria for obtaining the 31 articles used in the review consisted of (a) Performed a search using the four keyword terms (b) Specified date range for article publication from 1/1/2001-12/31/2011 (c) Subject Specification informed consent in relation to biobanking and biospecimen collection.

Results: After systematically reviewing 31 articles, broad consent and simplified menu consent were compared in order to determine which would be more acceptable to scientific research participants. 58.1% of studies analyzed were descriptive and 41.9% were interventional. The majority of both types of studies (64.5%) favored the use of a simplified menu consent form as opposed to broad consent. In accordance to the Belmont Report, informed consent should be revised to include elements concerning commercialization, the purpose for biospecimen collection, privacy of information, and time limits for biospecimen storage and use.

Conclusion: Following the systematic review, three conclusions were made: No Uniformity exists amongst informed consent formats, key elements or methods for developing a universal consent. Commercialization, Purpose for Biospecimen collection, Privacy of information & time limits on biospecimen need to be addressed in Biobanking. Current literature favors simplified menu consent over the currently used broad consent.

Research supported by: Gwendolyn P. Quinn Ph.D, University of South Florida College of Medicine/ Oncologic Sciences

Characterization of Tau Overexpression Using a Tetracycline-Regulatable Transgenic Mouse Model and a Tetregulatable Adeno-Associated Virus

Jerry B. Hunt, Guang Yu C. Yang, Kevin Nash, Marcia Gordon, Dave Morgan, Daniel C. Lee College of Pharmacy, Department of Pharmacological Sciences, USF Byrd Alzheimer's Institute, University of South Florida; University of South Florida College of Arts and Sciences Cell Biology, Microbiology & Molecular Biology

Keywords: AAV, Tau, tetracycline, doxycycline, brain, Alzheimer's, mouse, gene regulation, GFP

Objective: An increasing number of transgenic mouse models have been generated using the tetracycline regulatable system. In this system, one mouse expresses the transgene under control of a tetracycline (tet) promoter, where another mouse expresses the tetracycline activator protein (tTA) under control of a cell specific promoter. Crossbreeding leads to cell selective expression of the protein. We aim to create a novel, versatile, and regionally specific tau transgenic mouse using a mouse that expresses the tau transgene under control of the tet promoter and driving the expression of tTA using adeno-associated virus (AAV).

Methods: Our AAV construct utilizes a bistrionic plasmid that expresses tTA under the control of the CBA promoter and another gene (Green fluorescent protein; GFP) on a separate promoter under control of a doxycycline regulatable tet promoter (tTA-AAV-GFP). Our model uses the tetOff system, where tau expresses in the presence of tTA but is turned off in the presence of doxycycline (Dox). Tau mice were injected intracranially with tTA-AAV-GFP into the hippocampus.

Results: After 4 months, GFP expression was significantly increased compared to mice that received tTA-AAV-GFP and administered Dox. Tau expression was also significantly increased compared to both Dox treated mice and control tau transgenic mice. A similar profile for phospho-tau species was also seen. Furthermore, regionally specific expression was observed in the hippocampus.

Conclusion: Our model permits us to directly evaluate potential therapeutic genes in vivo in neurons that only overexpress the pathological gene tau and the target gene compared to global overexpression. This enables us to measure the phenotypic impact of tau pathology more closely.

Research supported by: USF New Researcher Grant

MicroRNA-206 Modulates Human Pulmonary Artery Smooth Muscle Cell Proliferation, Apoptosis, and Migration

Samuel Jalali, Gurukumar Kollongod Ramanathan, Prasanna Tamarapu Parthasarathy, Richard F Lockey and Narasaiah Kolliputi Division of Allergy and Immunology, Department of Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa, University of South Florida, Morsani College of Medicine, Dept. of Internal Medicine

Keywords: microRNA-206, Pulmonary Hypertension, NOTCH3

Objective: Preliminary in vivo studies from our laboratory in pulmonary hypertensive mice showed reduced expression of miR-206. We investigated the effects of miR-206 on human pulmonary artery smooth muscle cell proliferation, apoptosis and migration in vitro.

Methods: Human pulmonary artery smooth muscle cells (hPASMCs) were transfected with miR-206 expressing plasmid, control vector only, or antagomiR-206 (antimiR-206). Proliferation (MTS assay), Apoptosis (TUNEL staining) and Wound healing assays were performed to assess the effect of miR-206 on hPASMCs. Levels of NOTCH3, a known target of miR-206 and an important mediator of PAH were assessed by Western Blotting.

Results: We report that miR-206 over expression decreases proliferation and migration of hPASMCs, while increasing apoptosis. The opposite effects were observed when miR-206 levels were reduced by treating hPASMC with antimiR-206. Expression of NOTCH3 was found to be down regulated in hPASMCs over expressing miR-206, indicating that effects of miR-206 on hPASMCs are mediated through NOTCH3 signaling.

Conclusion: MiR-206 down regulation induces a PAH phenotype in hPASMC and treatment with miR-206 could be a potential treatment strategy for PAH.

Research supported by: National Institute of Health, American Heart Association, National Scientist Development Grant

Compulsive Hoarding in Community Environments

Lauren B. Kaercher, B.A.,¹ Joseph F. McGuire, B.A.,¹ Jennifer M. Park, M.A.,¹ and Eric A. Storch, Ph.D.^{1,2},

¹Department of Psychology, University of South Florida, ²Departments of Pediatrics and Psychiatry, University of South Florida, University of South Florida, College of Arts and Sciences, Dept. of Psychology

Keywords: Compulsive hoarding, community, prevalence, cost

Objective: Compulsive hoarding is a severe mental health condition that causes significant impairment to individuals and affects their communities. While the majority of previous research has focused on hoarding in aging samples or clinically referred patients, this study explored the frequency, characteristics and outcomes of hoarding situations encountered in community settings.

Methods: Prior to in-service training, 236 code enforcement officials and social service staff completed surveys about their experiences with hoarding cases.

Results: Analyses revealed responders encounter between 2-3 hoarding cases per year, yielding an annual prevalence rate of 33 per 100,000. As each hoarding case was projected to cost over \$3,700 in trash removal fees, hoarding is a costly concern. Detailed hoarding encounters for 197 respondents revealed that hoarders were most often between 46-75 years old, Caucasians, lived alone and had little to no insight into their hoarding problem. Hoarding situations were frequently identified as extremely cluttered and caused moderate to severe interference in functioning. Situations appeared to be difficult to resolve and often involved multiple agencies. Difficulty in resolution may stem from the fact that 83% of these professionals had received no prior training for addressing hoarding situations.

Conclusion: Overall, compulsive hoarding is costly and often hazardous for the hoarder and the community. Given that multiple agencies are involved in addressing hoarding cases, the development of an evidence-based inter-agency response protocol may facilitate situational resolutions and result in timely referrals to mental health professionals to improve outcomes for compulsive hoarders.

The Effects of Art Programs on the Self-Concept of Children

Francisco Fernandez, M.D., Hank Hine and the Dali Museum, Daniel Lattimore, Eric Rinehardt, Ph.D, Yilmarié Rosado, Sriram Velamuri University of South Florida, College of Arts and Sciences, Dept. of Chemistry

Keywords: self-concept, children, art programs

Objective: A variety of art programs exist across the country. Some are designed for educational purposes and others are designed for therapeutic purposes. There are few studies available that show the effect that art programs have on self-concept. The goal of this study is to analyze the self-concept of children before and after enrollment in an art program at the Dali Museum in St. Petersburg.

Methods: The subjects of the study included 128 children between the ages of 7 to 13. All 128 subjects were tested before and after their participation using the Tennessee Self-Concept Scale 2 (TSCS:2). All subjects were given the short form test and 24 subjects were also given the long form test. Paired samples T tests were used to compare the means and significance of the subjects' self-concept scores before and after enrollment.

Results: Scores on the short form post-test ($M = 58.0$, $SD = 10.04$) were 2.9 points higher than scores on the short form pre-test ($M = 55.1$, $SD = 9.93$), $t(127) = -4.7$, $p < .01$, $d = 0.29$. Total (TOT) scores on the long form post-test ($M = 64.1$, $SD = 12.70$), were 4.5 points higher than TOT scores on the long form pre-test ($M = 59.6$, $SD = 13.32$), $t(23) = -3.4$, $p < .01$, $d = 0.35$. Sub-tests for Academic work, behavior, satisfaction and others also showed significant increases.

Conclusion: Post-test scores for the short form TSCS:2 reveal that there was a modest improvement in the self-concept of children who participated in the art program. The long form revealed an even greater increase in self-concept compared to the short form. Improvement in specific areas, such as academic work, behavior and satisfaction were also apparent. These results indicate a positive effect of art programs on the self-concept of children.

Family Adversity and the Positive Illusory Bias: Further Support for the Self-Protection Hypothesis

Amanda Keene, University of South Florida Leah E. Hacker, University of South Florida Casey D. Calhoun, University of North Carolina-Chapel Hill Mark Cavitt, M.D., All Children's Hospital Psychiatry Jeffrey Alvaro, M.D., All Children's Hospital Psychiatry Eric A Storch, Ph.D., University of South Florida, University of South Florida, College of Arts and Sciences, Dept. of Africana Studies

Keywords: ADHD, Family Adversity, Positive Illusions

Objective: In the current cross-sectional study, we examine the associations of positive biased ratings of symptom severity and life satisfaction with several parent and family factors

Methods: Our sample included 123 children (8-17 years old) and their parents. Parent and child ratings of the child's life satisfaction were evaluated using the 7-item Life Satisfaction Scale. Parent and child ratings of ADHD symptom severity were measured using the Vanderbilt ADHD Diagnostic Rating Scale. The Depression, Anxiety, Stress Scales-Short Form, a 21-item self-report measure, was used to measure maternal levels of depression, anxiety, and stress. Family adversity was assessed by measuring parent psychopathology, marital status, and education level.

Results: Results showed that children's positive biases of symptom severity were associated with high levels of maternal stress and anxiety. Our findings also indicate that children in families with married parents have smaller positive biases of their own life satisfaction than those in families where parents are not married. Interestingly, parents' education level (college educated versus no college degree) was not related to discrepant ratings of symptoms or life satisfaction.

Conclusion: Our results provide further support for the self-protective hypothesis of positive illusory biases. It could be that children with ADHD may show greater positive biases when there is a greater need to protect themselves from adverse family environments. On the other hand, highly stressed mothers may be especially sensitive to their child's symptoms and consequently provide higher symptom ratings and lower child life satisfaction ratings, as observed in the depression-distortion hypothesis (Chi & Hinshaw, 2002).

ipad in the Clinical Setting: Using Interactive Technology as a Bridge to Clinical Education

Jericka Knox University of South Florida College of Arts and Sciences Anthropology

Keywords: iPad; technology; computer-based; patient education

Objective: Technology has a profound effect on how patients can be educated by their doctors by adding an interactive visual to teaching, encouraging patients to feel comfortable to engage their doctor, promoting adherence, and enhancing patient understanding of their health.

Methods: Patient ages 13 to 24 years, attending a pediatric specialty clinic and from diverse educational and socioeconomic backgrounds, were offered computer-based education on several topics during their routine medical visit. Powerpoint presentations were created and online videos were reviewed, scored by educational topic, and viewed by patients on an iPad. After the session, patients were asked to rate their learning experience in comparison to standard provider education by an anonymous survey, rating relevance, accessibility, and degree of difficulty navigating.

Results: Powerpoint presentations on the topics of substance abuse, pregnancy prevention, adherence to medication therapy, and disclosure of STD diagnosis were created. An average of 10 online videos per topic was assessed for accuracy, iPad compatibility, relevance, patient appropriateness, and length. The iPad does not support Adobe Flash, 8 out of 38 videos could not be used. Length ranged from less than 1 minute (min) (24%) to 16 min with an average of 7 min. The majority of the video contents were felt to provide accurate and appropriate information. Collection of patient's impressions were useful to future applications in the clinic.

Conclusion: Use of an iPad has the potential to enhance patient's education and utilize patient's waiting time for health education. The application of this technology was viewed as a helpful, interactive and attractive method facilitating patient-provider interaction.

Research supported by: Department of Pediatrics

Hypothesis: Size Matters: Sequential Mutations in Tumorigenesis may Reflect the Stochastic Effect of Mutagen Target Sizes

Kimberly Long, Toaa Abuelenen, Libia Pava, Maya Bastille, and George Blanck, University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: sequential mutations; tumorigenesis; cancer hallmarks; metastasis; tumor suppressor proteins

Objective: To determine whether the order of tumor suppressor gene inactivations, occurring throughout the development of a tumor, could correlate with mutagen target size.

Methods: We tallied the number of possible mutant amino acids in proteins thought to be inactivated early in tumorigenesis and in proteins thought to be inactivated late in tumorigenesis, respectively.

Results: Proteins thought to be inactivated early in tumorigenesis, on average, have a greater number of alternative, mutant possibilities, which raises the possibility that the sequential order of mutations associated with cancer development reflects the random chance, throughout life, of a mutagen inactivating a larger versus a smaller target. Interestingly, the two sets of proteins representing early and late inactivations did not show any significant difference with their relationships to other proteins involved in tumorigenesis, suggesting that the order of inactivation does not represent specific phenotypic differences in tumorigenesis but rather merely the stochastic effect of mutagen target sizes.

Conclusion: The hypothesis that the temporal order of genetic changes in cancer reflects mutagen target sizes leads to novel considerations of (i) the mechanisms of the acquisition of cancer hallmarks; and (ii) cancer screening strategies

Research supported by: Departmental funds.

The Impact of Arginase-1 and Polyamines on Tau Biology

Kayleigh N. McCarty (College of Arts and Sciences), Guang Yu C. Yang (College of Pharmacy), Jerry Hunt (College of Pharmacy), Daniel C. Lee (College of Pharmacy), University of South Florida College of Arts and Sciences, Dept. of Cell Biology, Microbiology & Molecular Biology

Keywords: polyamines, tau, arginase-1

Objective: This study sought to determine if overexpression of arginase-1 and increased concentrations of polyamines led to the induction of tau species in a cell culture model. The relationship between tau induction and toxicity was also examined.

Methods: BE(2)-M17 cells were cultured and treated with polyamines in 10% FBS media. Treatment lasted for 24 hours, and the cells were harvested for Western blotting. Arginase-1 was transfected for 24 hours in serum free media. Then, the media was removed and replaced with 10% FBS media containing arginase-1 inhibitors and polyamine modulators. These treatments incubated for 72 hours, and the cells were harvested for Western blotting. The lysed cell samples were subjected to SDS-PAGE, and the protein was transferred to a PVDF membrane. The membrane was probed for various phosphotau species and GAPDH. The membrane was incubated in LumiGold enhanced chemiluminescence and exposed to x-ray film. The film was quantified using spot densitometry. LDH toxicity and MTS viability assays were performed on polyamine treated cells.

Results: The arginase-1 transfection and putrescine treatments failed to show any significant change in tau. The polyamine treatments that induced tau were 100 μ M and 300 μ M spermine, 300 μ M and 1000 μ M spermidine, and 100 μ M, 300 μ M and 1000 μ M ornithine. The treatments that showed a significant increase in toxicity were 300 μ M spermidine and 30 μ M, 100 μ M and 300 μ M spermine.

Conclusion: Higher concentrations of polyamines tend to show significant induction of tau. The higher concentrations of polyamines, specifically spermidine and spermine were also associated with a significant increase in toxicity. These results suggest a role for polyamines and tau induction and toxicity.

Quantifying Differential Protein Expression in Drug Resistant Multiple Myeloma

Sayeef Mirza¹, Bin Fang², Yun Xiang², Linda Mathews², Kenneth Shain², John Koomen², ¹University of South Florida, ²Moffitt Cancer Center. University of South Florida, College of Arts and Sciences, Dept. of Africana Studies

Keywords: myeloma, resistance, mass spectrometry, proteomics

Objective: Mass spectrometry analysis of differential protein expression in chemotherapy resistant cell lines of multiple myeloma may explain the development of resistance to different clinical treatments.

Methods: A pipeline method was developed using gel-based protein fractionation followed by peptide sequencing with liquid chromatography coupled to tandem mass spectrometry (GeLC-MS/MS) for cataloging the proteome. However, liquid chromatography coupled to multiple-reaction monitoring mass spectrometry (LC-MRM) assays were then developed for quantification of selected protein biomarkers in cell lysates of doxorubicin resistant multiple myeloma (Dox40).

Results: Increased expression of certain biological pathways associated with doxorubicin-resistance in multiple myeloma. After analysis of candidate biomarkers, peptides are then selected for quantification of each potential protein biomarker and the assays are tested using cell lysates.

Conclusion: Therefore, up-regulation of proteins associated with resistance was conveyed using LC-MRM; with additional development, it may be translated to patient assessment as companion biomarkers to evaluate therapeutic response and the development of drug resistance. These efforts may pave the way for more effective treatments for multiple myeloma that do not develop resistance. While currently at the research stage, this method may be utilized in biomarker discovery studies where up and down regulation of certain proteins are characteristic of specific biological pathways in cancer.

Research supported by: US Army Medical Research and Material Command. Bankhead-Coley Cancer Research program - Florida DoH Office of Undergraduate Research – USF Project LINK-ET (Leaders in New Knowledge-Emerging Technologies) funded by National Cancer Institute

The Current Level of Awareness for Concussions as Reported by Parents of Youth Hockey Players.

Dr. Jeff G. Konin², Alexis Mugno¹ ¹College of the Arts and Sciences ²Department of Orthopaedics and Sports Medicine, University of South Florida Morsani College of Medicine

Keywords: Concussion, Assessment, Youth, Health, Sports

Objective: The purpose of this study is to assess the knowledge of parents of the youth hockey division concerning concussion related awareness. This includes concussion symptoms, side-effects, physical/emotional damage, and treatment.

Methods: A concussion survey was administered in person to parents currently participating in youth hockey. Parents participated on a volunteer basis located at ice hockey facilities throughout the state of Florida.

Results: 52 surveys were completed. Many discrepancies regarding proper procedural care, symptom knowledge, and post-concussion action were found. 44% of parents did not indicate proper procedure regarding return of activity of a youth player after sustaining a hit to the head. 12% of parents correctly indicated proper mouth guard protection. 52% of parents indicated an inaccurate perception of post-concussion symptom relief. 71% of parents were unaware of unusual sense of smell as a symptom. 40% of parents are unaware of trouble sleeping as a symptom. 8% were unaware or considered loss of memory as not a symptom. 15% of parents were unaware of difficulty studying or doing class work being a symptom.

Conclusion: This study concludes there is an inconsistency of knowledge regarding concussion knowledge among the youth hockey parent population. The prevalence of this information is essential to endorse the safety of youth hockey players. Brain trauma caused by concussions can play a critical role in a developing brain. It is crucial for a concussion to be identified as early as possible. Further research should concern the awareness among the coaches, players, and those who have participated in workshops. Further education of parents, coaches and athletes is imperative for a safe environment.

Research supported by:

A Method for Rapid, Efficient Quantification of Evolutionary Conservation for Individual Genes: Relevance to Fusion Gene Detection Algorithms

Libia Pava, Kevin Cronin, George Blanck University of South Florida, Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: evolutionary conservation; cancer fusion genes; genomics; human genome database

Objective: The gene partners forming cancer fusion genes are characterized by (i) large size and (ii) evolutionary conservation, knowledge that could aid in establishing algorithms for predicting which genes have formed a fusion gene. However, an efficient method of quantifying the evolutionary conservation of particular genes, which would allow rapid and convenient assessment of thousands of genes at a time, has been lacking. Using data available at genome.ucsc.edu, we devised a method of quantifying evolutionary conservation of specific genes.

Methods: Averages of the “phasCon” evolutionary conservation scores within the exons of single genes were acquired in two ways. First, the scores that represent the exons were totaled, and a value was calculated based on the number of scores that overlapped exons. Second, an average evolutionary conservation score for each exon in a gene was determined based on the base pair size of the exon.

Results: The above two approaches yielded similar results and can rapidly provide an evolutionary conservation value for all genes with any segment on a chromosome, including segments involved in chromosomal translocations. We have identified two novel translocations, in a lung and pancreatic tumor cell line and are currently applying the above gene size and evolutionary conservation parameters to identify the respective fusion genes. Furthermore, application of this method has revealed that fusion gene partners are unified by high levels of evolutionary conservation.

Conclusion: Rapid, quantitative assessment of evolutionary conservation on a gene by gene basis facilitates chromosomal segment analyses and will likely improve the efficiency of identifying cancer fusion genes.

Research supported by: Departmental funds.

Age Related Changes in Myeloid Lineage Cells in Bone Marrow of Young, Adult and Aged Mice

Daniel C. Lee Ph.D, College of Pharmacy¹; Yashobha Ranaweera²; Dave Morgan Ph.D³; Marcia N. Gordon Ph.D³; Maj-Linda B. Selenica Ph.D² ¹University of South Florida, College of Pharmacy; ²University of South Florida Morsani College of Medicine Molecular Pharmacology & Physiology; ³University of South Florida, Department of Molecular Pharmacology and Physiology

Keywords: Bone Marrow, Age, Myeloid Lineage, Inflammation

Objective: The aim of this study is to identify the age-related factors that mediate infiltration of circulating monocytes into site of inflammation.

Methods: We utilized wild type mice of ages six months, twelve months, and twenty-four months, representing the mouse lifespan. The bone marrow cells were harvested and divided into total bone marrow (TBM) and positively selected CD11b population by using magnetic beads conjugated to CD11b+ antibody. Each population was then stained using conjugated antibodies specific to Ly6C, CD45 and F4/80 macrophage markers and analyzed by flow cytometry and cytospin assays.

Results: We observed a significant enrichment of the CD45 positive cells in the old age mice when compared to the young in the CD11b+ population. The CD45High fraction of both TBM and CD11b+ selected populations was elevated in old age mice when compared with the young mice. Ly6-C positive cells showed a significant decrease with age by 1.5fold in the TBM population and CD11b+ selected cells, respectively. The Ly6C +/High fraction was increased by 1.5fold in old aged mice compared to adult in the TBM population. Meanwhile, we found a twofold increase in age-dependent manner F4/80 high cells in the TBM population.

Conclusion: Overall we found that CD45 High population was significantly increased while Ly6-C expression decreased in aged mice in TBM fraction. From adulthood to old age, CD11b+ selected cells showed an increase of CD45 High cells but decreased the expression of Ly6C +/High .cells. These findings suggest for an age related alternations in expression of cell surface markers of myeloid lineage cells. The impact of these changes in responding to peripheral and central inflammation will be studied in future studies.

Research supported by: NIH grant AG015490

Characterization of Inflammatory Markers in Nasal Epithelial Cells of Tau Transgenic Mice

Devon Placides, Guang Yu C. Yang, Jerry Hunt, Umesh Jinwal, Kevin Nash, Maj-linda Selenica, Daniel C. Lee
University of South Florida, College of Arts and Sciences, Dept. of Cell Biology, Microbiology & Molecular Biology

Keywords: Tau, Inflammation, Aginase 1, Olfactory, Epithelial.

Objective: Alzheimer's disease (AD) is a neurodegenerative disease that currently affects around 5 million people in the United States. Early detection is crucial for the preservation of neurons within the patient. The hallmarks of AD include amyloid beta plaques, tau pathology, neuroinflammation, and synaptic loss. Past studies revealed Lewy body formations in olfactory bulbs and a loss of olfaction associated with AD and PD. Alternative biomarkers from olfactory system may facilitate existing cerebrospinal fluid (CSF) and blood markers for early detection of neurodegenerative diseases. We hypothesize that nasal epithelial cells express neuroinflammatory markers that depict CNS changes associated with tau pathology.

Methods: In these experiments nasal epithelial cells were harvested from 9 month old transgenic mice expressing the tau MAPT P301L mutation (rTg4510) and non-transgenic littermates. Western blot analysis was used to identify different inflammatory activation markers.

Results: Western blot analysis identified several inflammatory activation markers in nasal epithelial cells that significantly changed in tau transgenic mice compared to non-transgenic littermates. These markers included, macrophage galactose-type C-type lectin (MGL-2), chitinase 3-like 3 (Ym1) and Arginase-1 (Arg-1).

Conclusion: This suggests that tau pathology impacts the olfactory epithelium and that certain inflammatory readouts can be detected in nasal epithelial cells. Furthermore, these studies demonstrated proof of principle that CNS disorders may express inflammatory signatures that are specific to certain neurodegenerative diseases and may be used for early detection through olfactory epithelium.

Research supported by: USF new researcher grant.

Characterization of Arginase-1 Expression and Microglia Activation in the CNS of Cre-Lox Arginase-1 Knockout Mice

Yashobha Ranaweera, Maj-Linda Selenica, Guang Yu C. Yang, Jerry Hunt, Gabriela Pena, Marcia Gordon, Dave Morgan, Daniel C. Lee
USF Health Byrd Alzheimer's Institute University of South Florida Honors College

Keywords: Arginase1, Alzheimer's, YM1, CD45, CD11B

Objective: To verify that Arg-1 was successfully removed (deleted) in the microglia and cells of myeloid origin using Cre-Lox Arginase-1 Knockout Mice.

Methods: Bi-genic mice were generated using a transgenic mouse expressing cre-recombinase on the Lysozyme P promoter (LysM; promoter for cells of myeloid lineage) and mice expressing LoxP sites flanked on the Arg-1 gene. Cross-breeding results in recombination and deletion of the Arg1 gene in myeloid cells. Mice of three genotypes we designate as wild-type littermate with no flanked Arg-1 (Arg1 Wt/Wt), Arg-1 flanked with LoxP sites (Arg1 LoxP/LoxP), , and Arg-1 flanked LoxP mice crossed with a cre-recombinase transgenic mouse (Arg1 Cre/LoxP). Mice received an intracranial injection of lipopolysaccharide (LPS) into the hippocampus to activate microglia and induce Arg-1 expression. Brains were harvested three days post LPS injection. Using immunohistochemistry tissue sections were stained with antibodies for Arg1, YM1, CD45, and CD11B.

Results: We show that Arg-1 immunoreactivity was significantly reduced in the CNS of Arg1 Cre/LoxP mice that received LPS compare to Arg LoxP/LoxP, and Arg wt/wt mice suggesting successful deletion of the Arg1 gene. In addition, YM1 and CD45 showed significant reductions in immunoreactivity compared to Arg wt/wt mice suggesting that Arg-1 impacts certain inflammatory profiles during microglia activation. Furthermore, no change in CD11B expression was observed between the mice.

Conclusion: These data indicate the successful deletion of Arg-1 in microglia/macrophages was achieved in Arg-1 cre mice. Furthermore, general activation was achieved by use of CD11B, however the selective markers and functional activation state of microglia was impacted by Arg-1 deletion.

Research supported by:

Effects of Early Initiation of ART on Neopterin Levels in HIV-infected Adolescents

Erik Richardson, Susan Lukas MPH, Bret J Rudy MD, and John W Sleasman MD University of South Florida Morsani College of Medicine Pediatrics

Keywords: HIV, Neopterin, macrophage activation, antiretroviral therapy, ART

Objective: HIV pathogenesis is primarily the result of CD4 T cell attrition but macrophage activation also plays an important role in disease progression and may not be reversed by antiretroviral therapy (ART). Neopterin is a low-molecular protein derived from activated macrophages and can be measured in plasma as a marker of macrophage activation. We sought to determine if initiation of early ART, prior to CD4 T cell decline, has an impact on neopterin levels in HIV-infected youth. Our hypothesis is that early use of ART lowers macrophage activation.

Methods: A cohort of HIV-infected youth (aged 18 – 25) were enrolled in a study to examine the impact of early ART on immune activation. Subjects were randomized (3:1) to Group 1: initiating early ART (CD4>350 cells/ul) or to Group 2: initiating ART according to DHHS guidelines (CD4<350 cells/ul). Healthy controls balanced for age, gender, and ethnicity were recruited. Plasma neopterin levels at three time points: entry, 24 weeks, and 48 weeks were measured using ELISA.

Results: Group 1 achieved viral loads of <200 copies/ml by 48 weeks on ART. Group 2 had stable CD4 T cell counts and remained off ART. Neopterin levels decreased significantly in group 1 from 11.94 ng/ml pre-therapy to 6.560 ng/ml after 48 weeks, ($p<0.0001$), similar to controls 7.543 ng/ml. However, neopterin levels in Group 2 remained elevated at 48 weeks, 10.68 ng/ml at entry, and 10.24 ng/ml after 48 weeks.

Conclusion: Using neopterin as a biomarker, early ART lowers macrophage activation to normal levels by 48 weeks on treatment. By lowering macrophage activation, early ART is likely to minimize the disease complications associated with macrophage activation such as cardiovascular disease and HIV-associated neurocognitive decline.

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Lysosome Accumulation In Endothelial Cells Aggravates Blood-Brain Barrier Impairment In Sanfilippo Syndrome

Sebastian A Sallot¹, Santhia Mirtly¹, Diana G Hernandez-Ontiveros¹, Paul R Sanberg^{1,2}, Svitlana Garbuzova-Davis^{1,2} ¹Center of Excellence for Aging and Brain Repair, ² Department of Neurosurgery and Brain Repair, University of South Florida, Morsani College of Medicine, Tampa FL, USA, University of South Florida, Morsani College of Medicine, Dept. of Neurosurgery & Brain Repair

Keywords: Mucopolysaccharidosis; blood-brain barrier; endothelial cells; lysosomes; microvascular pathology

Objective: Mucopolysaccharidosis type III (MPS III), or Sanfilippo Syndrome, is an autosomal recessive disorder caused by the lack of enzymes needed to breakdown heparan sulfate. Accumulation of heparan sulfate in lysosomes leads to cerebral and systemic organ abnormalities. Determining blood-brain barrier (BBB) condition may aid in understanding neurological mechanisms of disease. Recently, BBB impairment has been shown in a mouse model of MPS III B. One study finding was accumulation of a secondary storage product, GM3 ganglioside, in brain vessel endothelium, leading to BBB breakdown. However, little is known about BBB competence in humans with Sanfilippo Syndrome. In this study, lysosomal accumulation within endothelial cells in the cerebral microvasculature was investigated in tissue from patients with MPS III type A or D and from age-matched controls.

Methods: Patient and control tissues were obtained from the NICHD Brain and Tissue Bank for Development Disorders, Baltimore, MD. Double immunohistochemical staining for lysosomes and collagen IV revealed lysosomal accumulation within endothelial cells forming vessels in the hippocampus, cerebellum, putamen, and primary motor cortex. These structures are known to have neuropathological changes in MPS III.

Results: (1) lysosomal accumulation within endothelial cells in multiple brain structures, (2) more extensive accumulation in the hippocampus, (3) neural cells showing altered morphologies with translocated nuclei, and (4) more severe lysosomal accumulation in MPS III A than MPS III D.

Conclusion: Study results showed endothelial cell damage was caused by lysosomal accumulation. These new findings may indicate BBB dysfunction in MPS III.

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Screening for Inhibitors of the Increased Thioester Hydrolysis Activity of the Mutant Protein Acyl Transferase, DHHC9 R148W

Phillip Sanchez, Robert J. Deschenes and David A. Mitchell University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: Palmitoylation, DHHC9, Ras, X-linked mental retardation (XLMR), palmitoyl acyltransferase (PAT).

Objective: Palmitoylation modifications localize proteins to cellular membranes through the enzyme-mediated addition of palmitate to a protein via a thioester linkage. Defects protein acyl transferases (PAT), the enzyme family that catalyzes palmitoylation, are linked to multiple cancers, diseases and disorders. For example, DHHC9, the PAT involved in human Ras palmitoylation, is linked to colorectal and leukomyloid cancers, and mutations in DHHC9 are linked to X-linked mental retardation (XLMR). We plan to adapt and validate a fluorescence-based NAD coupled assay to measure protein palmitoylation in vitro using High Throughput Screening of compounds within small molecule and natural substance libraries. This is the best way to identify and study palmitoylation.

Methods: We will use a coupled-enzyme assay that measures DHHC9•GCP16-dependent autopalmitylation in a 96- or 384-well format. Compounds identified in this screen are potential DHHC9 palmitoylation inhibitors for in vivo studies. We can purify DHHC9 R148W and DHHC9 P150S, DHHC9 mutations implicated in XLMR. We will compare the rates of autopalmitylation of these mutants with the rates of wt DHHC9.

Results: Compared to wt, the rate of autopalmitylation is 3-fold greater for the DHHC9 R148W mutant. The rate of hydrolysis for DHHC9 P150S is similar to that of wt DHHC9, while its formation of the thioester appears to be slower. The Z'-value for the assay is 0.89.

Conclusion: Our strategy is to screen DHHC9 R148W for inhibitors of its increased thioester hydrolysis activity. Once these candidate inhibitors are in hand, we will test them against wt DHHC9. We aim to identify compounds that inhibit DHHC9 R148W with little to no effect on wt DHHC9.

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Does Variable SP Scoring Input on High Stakes Exam Skew Student Test Results?

Daniella M Schocken, Duke University, and Center for Advanced Clinical Learning, USF Health Morsani College of Medicine, Dawn M Schocken, Center for Advanced Clinical Learning, USF Health Morsani College of Medicine, University of South Florida, Morsani College of Medicine, Dept. of Family Medicine

Keywords: Medical education, exam scores, SPs, inter-rater reliability

Objective: The national USMLE exam uses standardized patient (SP) and student responses to help determine licensure. Current structure of high stakes exams at this institution does not ensure that each individual test date's scores originate from an equal proportion of SP input to student response input. A query was made whether the average test scores on a given date are skewed by the variable weight of the SP input.

Methods: 119 medical students took a Year Three summative exam, the Comprehensive Clinical Performance Examination (CCPX). Each of twelve stations represents a portion of the clerkship experience. The cases are designed to assess student's communication (SP input), History / Physical Exam skills (SP input) and critical reasoning skills (faculty graded). Each of the ten days of student exams is unique with different cases (exam schemata). Both faculty and SPs undergo specialized training to increase inter-rater reliability in scoring these skills.

Results: The ten unique schematas are drawn from a variety of input including SP availability, placement of student cohorts, even case distribution and critical reasoning expectations. Each student receives a combined score including SP and faculty score. Exam scores are validated with independent grading. The data generated from score dates indicate that student's scores are indeed skewed (all dates: mean = 83.5 versus higher SP input: mean = 74.2) when variable SP input is allowed.

Conclusion: Trends indicate that when the SP scores are not standardized (same input value on each case for each date), students in one cohort may do either much better or much worse than the other students, despite a high level of inter-rater reliability. Closer attention to this variability is needed for future exams.

Intravenous Grafts of Amniotic Fluid-Derived Neural Progenitor Cells Induce Endogenous Cell Proliferation and Ameliorate Behavioral Deficits in Ischemic Stroke Rats

Cyrus H. Tamboli¹, Naoki Tajiri¹, Sandra Acosta¹, Paula C. Bickford¹, Marianna A. Solomita^{1 2 4}, Ivana Antonucci², Liborio Stuppia², Loren E. Glover¹, Takao Yasuhara³, Isao Date³, Yuji Kaneko¹, and Cesar V. Borlongan^{1*}, ¹Department of Neurosurgery and Brain Repair, University of South Florida College of Medicine, Tampa, USA, ²Department of Biomedical Sciences, G. d'Annunzio University, Chieti-Pescara, Italy, ³Department of Neurological Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, ⁴Department of Neuroscience and Imaging, School of Advanced Studies G.d'Annunzio Chieti- Pescara, Italy. University of South Florida, Morsani College of Medicine, Dept. of Neurosurgery & Brain Repair

Keywords: stroke, neural stem/progenitor cells, neuroprotection, cell proliferation, neurotrophic factors

Objective: We recently reported isolation of viable neural progenitor cells from rat amniotic fluid. Here, we tested the therapeutic benefits of amniotic fluid-derived stem(AFS) cells in a rodent model of ischemic stroke.

Methods: Adult Male Sprague-Dawley rats were subjected to a one-hour MCAo and received intravenous transplants of rat AFS cells or vehicle. All rats were evaluated behaviorally with Elevated body swing test, Rotarod test, and Morris Water Maze test for 2 months then euthanized for immunohistochemical evaluations.

Results: Statistical analyses revealed significant recovery of cognitive, motor and neurologic function in stroke animals that received the AFS cells compared to vehicle-infused stroke animals ($p < 0.05$). H&E staining revealed significant differences in the infarct area between the two stroke groups. Ki67 demonstrated an increase in Ki67-positive cells along the subventricular zone of the stroke animals that received AFS cells compared to those that received vehicle infusion. Moreover, there is a corresponding increase in cells immunostained with Ki67 and doubled labeled with MAP2. This increased cell proliferation along a neural fate occurred despite very few surviving grafts of AFS cells.

Conclusion: Intravenous transplantation of stem cells derived from rat amniotic fluid rescues of ischemic peri-infarct area via neurogenesis, likely mediating the reduced infarct volume and the recovery of motor, as well as cognitive, function in stroke animals. The present rat donor cell graft-to-rat recipient supports the use of allogeneic transplants in the clinic.

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The Ureter as a Landmark for Robotic Sacrocolpopexy.

Jessica Valceus, Mona McCullough, MD, ME, Katheryne Downes, MPH; Lennox Hoyte, MD, MSEECS. University of South Florida N/A

Keywords: CT, Robotic Surgery, Sacral Promontory, Sacrocolpopexy, Ureter

Objective: Report on the location of the ureters in relation to the sacral promontory at the level of the pelvic brim.

Methods: Female patients undergoing indicated CT urograms were selected for this study. Charts and images from a defined 3-year study period were reviewed. The GE Centricity software was used to evaluate multi-planar CT views and measure the distance from the bilateral ureters to the midpoint of the distal sacral promontory for each subject.

Results: Sixty-three women underwent CT urograms during the study period. Of these, 38 met criteria for inclusion. Among these, the left ureter was 35.9 ± 4.9 mm lateral to the mid-sacral promontory. The right ureter was 29.7 ± 6.2 mm lateral to the sacral promontory.

Conclusion: On average, the sacral promontory is located 29.7mm medial to the right ureter at the level of the pelvic brim. This allows for identification of the promontory for sacrocolpopexy suture placement in obese patients, in whom the right ureter is visualized.

Evidence of Cardiomyocyte Cell Death Following Cerebrovascular Accident

J. R. Vasconcellos¹, H. Ishikawa¹, N. Tajiri¹, K. Shinozuka¹, L. E. Glover¹, A. Mayo-Perez¹, C. Metcalf¹, P. Mavronicolas¹, Y. Kaneko¹, C.V. Borlongan¹ ¹Neurosurgery and Brain Repair, University of South Florida, Tampa, FL, University of South Florida, Morsani College of Medicine, Dept. of Neurosurgery & Brain Repair

Keywords: heart death, stroke, insular cortex, cell death

Objective: A topic of recent interest is the effect of cerebral ischemia on the heart. Although research looking at damage to the cardiac myocytes following cerebrovascular stroke presents mixed findings, a subset of these data has suggested that cardiac compromise may be associated with cerebral stroke in the right insular cortex. In order to test the validity of these findings, we examined brains and hearts from rats that had undergone experimental stroke. Analysis was performed using immunohistochemical staining to determine if cell death markers were present in either or both organs.

Methods: Ten-week old male Sprague Dawley rats were subjected to a one-hour right middle cerebral artery occlusion. After 6 months, the rats were euthanized and prepared for immunohistochemical evaluation using antibodies against mouse/rabbit cell markers of apoptosis, necrosis, and autophagy.

Results: Heart myocytes stained positive for p53 (apoptosis), BCL2 (necrosis), and ATG9A (autophagy). In the corresponding brain sections, the ipsilateral striatum stained positive for p53, BCL2, and ATG9A. The contralateral portion of the brain was negative for BCL2 and p53, but minimally positive for ATG9A.

Conclusion: Our results show the presence of markers for cell death in both the heart and the brain following a right-side cerebrovascular accident. These findings suggest that ischemic cell death in the brain leads to heart cell death, advancing the notion that stroke may cause systemic cellular damage. To this end, management of stroke patients should be approached with treatment regimens targeting the ischemic brain and heart. Further investigation into the existence of a mechanism that links the brain and heart is warranted.

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