The 2009 Lewis A. Barness Lecture & Fellows Forum

ABSTRACT SESSION
ORAL PRESENTATIONS

9:50am-10:10am
Abstract# 4
Zebrafish KiSS1 orthologue is expressed in the hypothalamus in adult zebrafish
Iyer P*, Cannon J

10:10am-10:30am
Abstract# 9
Auditory Brainstem Responses in Preterm Infants
Hernandez M*and Sullivan J

10:30am-10:50am
Abstract# 8
Patient Safety Rounds in Pediatric Inpatient Units Shows Trend Toward Improved Safety
Welch TR; Nimeh JW*; Miner B; Page N

10:50am-11:10am
Abstract# 10
Comparison of Infant Body Composition in Small- and Appropriate-for-Gestational Age Infants Using ‘Air Displacement Plethysmography’ (ADP)
Kumaraswamy L*, Carver J, Rubin LP, Division of Neonatology, Dept of Pediatrics, University of South Florida, College of Medicine, Tampa, FL

POSTER PRESENTATIONS
(Poster authors present by posters)

Abstract# 1
Memory CD27+ B220- B Cell Subpopulation is Decreased in Human Immunodeficiency Virus Disease (HIV), Common Variable Immune Deficiency (CVID), and Systemic Lupus Erythematosus (SLE)

Abstract# 2
Measurements of Plasma Lipopolysaccharide (LPS), Endotoxin Core IgM Antibody (EndoCAb), Soluble CD14 (sCD14), TNFα, and Soluble CD62L (sCD62L) Levels to Assess Microbial Translocation and Immune Activation in HIV-Infected Children and Adolescents

Abstract# 3
IRAK-4 Deficiency: Age Associated Improvement of Symptoms and Responses to Vaccines
Abstract# 6
Diet Liberalization in a 2 Year-Old Child with Classical PKU after Treatment with Sapropterin Dihydrochloride
Diaz-Thomas AM*, Malone JI, Swan K. Pediatric Endocrinology, Diabetes and Metabolism, University of South Florida, St Petersburg, FL, United States

Abstract# 7
"Hail to the Chief" The Roles and Expectations of the Chief Resident
Harris E*, Dabrow S, Maldonado L, M.D, Gereige R.

12:00noon-1:20pm – LUNCH – Fellows Social Networking

ORAL PRESENTATIONS

1:20pm-1:40pm
Abstract# 11
Analysis of FOXP3 Expression in Term and Preterm Infant Cord Blood CD4+CD25+ T cells
Ruiz R, Arbona I*

1:40pm-2:00pm
Abstract# 5
NOVEL MUTATION OF KCNJ11 (PHE35CYS) IS ASSOCIATED WITH TRANSIENT NEONATAL DIABETES AND IS RESPONSIVE TO SULFONYLUREA THERAPY
Lenz AM* and Shulman DI

2:00pm-2:20pm
Abstract# 12
Intravenous ibuprofen treatment for patent ductus arteriosus in preterm infants does not affect cerebral blood flow velocity
Munoz L*, Bruton D, Carver J, and Wadhawan R

* Denotes Presenting Author
Detailed Abstracts

The 2009 Lewis A. Barness Lecture 
&
Fellows Forum

April 23rd, 2009
USF STC

ABSTRACTS

ALLERGY-IMMUNOLOGY

Abstract# 1

Memory CD27+ B220- B Cell Subpopulation is Decreased in Human Immunodeficiency Virus Disease (HIV), Common Variable Immune Deficiency (CVID), and Systemic Lupus Erythematosus (SLE)


Presenter: Panida Sriaroon, MD - Allergy/Immunology Third Year Fellow

Type: Poster Presentation

BACKGROUND: Aberrant B cell activation and differentiation are common features shared by HIV, SLE, and CVID. Increased B cell percentages and polyclonal B cell activation have been observed in HIV while maturation arrest and lower memory B cell proportions have been described in all three conditions. Memory B cells can be further subdivided based on expression of B220, a CD45 isoform.

HYPOTHESIS: Functional B cell defects observed in HIV infection are due to late stage defects in B cell development. We tested the hypothesis that proportion of memory B cells is decreased in HIV, SLE, and CVID.

METHODS: We studied fresh whole blood from 12 healthy controls (HC), 19 subjects with HIV, 8 with SLE, and 9 with CVID. Multiple parameter flow cytometry analysis enumerated CD19/CD27/B220 with additional markers including surface IgM/IgD/IgG, CD21, CD23, CD80, and CD86.

RESULTS: We found no major differences in total CD19+ percentages among the populations. All 3 studied groups had lower CD27+ memory B cells compared to HC (p < 0.05, t-test based ANOVA) specifically in CD27+B220- subpopulation (p = 0.001 CVID vs HC). As expected, class switched CD27+B220- memory B cells were decreased in CVID (p < 0.01 vs HC) while the range varied significantly among HIV+ patients. Proportion of B cell activation markers as defined by the expression of CD80 or CD86 in CD27+ B220- memory B cells was significantly increased in HIV suggesting polyclonal B cell activation. We found no major differences among groups in CD21 expression in naïve or memory B cell subpopulations. However, unlike CD21, HIV+ subjects had significantly lower percentages of naïve CD27-B220+ B cells expressing CD23 (p < 0.01
HIV vs HC). No major differences in B cell subpopulation were observed among HIV+ subjects with or without antiretroviral therapy.

**CONCLUSIONS:** Similar to CVID and SLE, subjects with HIV have reduced memory CD27+B220- B cells. Unlike CVID, class switch recombination is preserved in HIV but this is variable among the cohort. Activation markers are increased in memory B cells in HIV. Unlike T cell, antiretroviral therapy fails to correct B cell activation and differentiation abnormalities.

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**Abstract #2**

**Measurements of Plasma Lipopolysacharide (LPS), Endotoxin Core IgM Antibody (EndoCAb), Soluble CD14 (sCD14), TNFα, and Soluble CD62L (sCD62L) Levels to Assess Microbial Translocation and Immune Activation in HIV-Infected Children and Adolescents**


**Presenter:** Sasawan Chinratanapisit, M.D., Allergy/Immunology Second Year Fellow  
**Type:** Poster Presentation

**INTRODUCTION:** Microbial translocation from the gastrointestinal tract into the systemic circulation may result in HIV-1 induced immune activation. HIV-infected children and healthy donors (HD) were examined to evaluate soluble markers of microbial translocation (LPS and endoCAb), soluble markers of macrophage activation (sCD14 and TNFα), and soluble markers of T cell activation (sCD62L).

**METHODS:** Soluble factors were measured within plasma using ELISA. Samples from ten HIV-infected subjects, before and after antiretroviral therapy, were compared to thirteen HD. Comparisons among groups were analyzed by Student t test and regression analysis by Pearson correlation.

**RESULTS:** Compared to HD, HIV-infected subjects had higher plasma LPS levels (2.81 ± 2.12 EU versus 0.02 ± 0.06 EU, respectively, p < 0.05), but no difference in plasma EndoCAb levels were observed (84.83 ± 120.94 MMu/ml versus 92.32 ± 99.95 MMu/ml, respectively). Successful antiretroviral therapy did not result in significant declines LPS levels (p =0.57). Plasma sCD14 and TNFα were higher in the HIV-infected group compared to HD. sCD14 levels were 1.17 ± 0.79 μg/ml and 0.92 ± 0.20 μg/ml respectively, (p < 0.05) while TNFα levels were 0.0068 ± 0.013 μg/ml and < 0.0001 μg/ml, respectively (p < 0.05). sCD62L was higher in the infected subjects, 0.0012 μg/ml compared to 0.0007 μg/ml in HD (p < 0.05).

**CONCLUSIONS:** As expected, higher LPS levels suggests microbial translocation that persists in spite of effective therapy. There is direct activation of macrophages, as measured by elevated sCD14 and TNFα as well as higher levels of sCD62L, a novel measure of immune activation.

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**Abstract #3**

**IRAK-4 Deficiency: Age Associated Improvement of Symptoms and Responses to Vaccines**  
Presenter: Loren E Isakson, MD, MSc; Allergy/Immunology First Year Fellow  
Type: Poster Presentation

BACKGROUND: In 1998, we reported an IL-12 deficient patient with severe life-threatening strep pneumoniae and other bacterial infections. She was subsequently diagnosed as IRAK-4 deficiency and found to have a profound failure to mount and sustain antibody responses to different antigens.

RESULTS: In the present report, we show that at 14 years of age, the patient had improved clinically, and could be weaned of IVIG two years ago without recurrence of strep pneumoniae infections. The severe sinus infections which required surgical intervention every 3 months with extensive growth of Pseudomonas aeruginosa and Serratia marcescens have improved considerably. This clinical recovery is associated with a brisk response to a tertiary immunization with ØX174 bacteriophage, including amplification and isotype switching, and sustained antibody responses to diphtheria, tetanus and pneumococcal polysaccharide antigens.

CONCLUSION: Sufficiency of innate immunity is vital for defense against infections during childhood as in this case with IRAK-4 deficiency and may also apply to children with other innate immunity deficiencies. With the appearance of adequate adaptive immunity and increasing age, our IRAK-4 deficient patient has overcome increased susceptibility to infections. These observations are consistent with the hypothesis that the “TLR pathway is redundant for adulthood immunity.”

ENDOCRINOLOGY, DIABETES AND METABOLISM

Abstract #4

Zebrafish KiSS1 orthologue is expressed in the hypothalamus in adult zebrafish
Iyer P*, Cannon J

Presenter: Pallavi Iyer, M.D, Endocrinology, Diabetes and Metabolism, Third Year Fellow  
Type: Oral Presentation

BACKGROUND: The process of sexual maturation is initiated in mammals with binding of KiSS1 to its receptor KiSS1r (GPR54). Two forms of zebrafish kisspeptin genes (KiSS1 – the F-F form and KiSS2 – the Y-Y form) have been cloned1,2, suggesting that non-mammalian vertebrates may also utilize a KiSS1/KiSS1r axis. Here we present in situ hybridization localization patterns of zebrafish KiSS1 mRNA expression in the adult zebrafish brains.

METHODS: KiSS1 was cloned from adult zebrafish brain mRNA that had been reverse transcribed to CDNA. PCR was used to amplify a fragment of the zebrafish KiSS1 cDNA, and the complete KiSS1 DNA was cloned using rapid-amplification of cDNA ends (RACE). The cloned sequence was verified by comparison to the published KiSS1 sequences in NCBI GenBank database. Paraffin sections (10 μm) of adult zebrafish brains were used for in situ hybridization with sense and antisense RNA probes.
representing zebrafish KiSS1; hybridization patterns were compared to those of zebrafish salmon GnRH (saGnRH) mRNA patterns.

RESULTS: In the adult zebrafish brain, antisense RNA probes of zebrafish KiSS1 hybridized to mRNA transcripts in cells of the ventral zone of the periventricular hypothalamus and preoptic area. In contrast, zebrafish saGnRH probes hybridized to the preoptic area and anterior hypothalamus. The sense probes of KiSS1 and saGnRH did not demonstrate any detectable hybridization.

CONCLUSION: As in mammalian models, adult zebrafish express KiSS1 orthologues in the hypothalamic nuclei. The expression pattern of KiSS1 along the ventral periventricular hypothalamus appears to abut a zone of hypophysiotropic GnRH (saGnRH) expression along the ventral telencephalon. Future studies will focus on further refinement of the expression patterns of zebrafish KiSS1, KiSS2, their receptors and potential cytosolic signaling molecules.

SOURCES:
2 Kitahashi T, Ogawa S, Parhar IS. Cloning and expression of Kiss2 in the zebrafish and medaka. Endocrinology. 2008 (Epub ahead of print)

Abstract #5

NOVEL MUTATION OF KCNJ11 (PHE35CYS) IS ASSOCIATED WITH TRANSIENT NEONATAL DIABETES AND IS RESPONSIVE TO SULFONYLUREA THERAPY

Lenz AM* and Shulman DI
Presenter: Anne Lenz, M.D, Endocrinology, Diabetes and Metabolism, Second Year Fellow
Type: Oral Presentation

BACKGROUND: Gain of function mutations in the KCNJ11 gene, encoding the Kir6.2 protein subunit of the pancreatic β-cell ATP-sensitive potassium channel, render the KATP channel insensitive to increased ATP levels concomitant with high blood glucose. Therefore, the channel does not close in response to elevated ATP, and insulin release is reduced leading to permanent or transient neonatal diabetes.1

CLINICAL CASE: A 2 month old previously healthy infant presented with oral candidiasis, persistent emesis, and polyuria. Laboratory tests confirmed antibody negative diabetes mellitus: BG 468 mg/dL (n=70-110); Bicarbonate 17 mEq/L (n=17-25); CBG pH 7.33 (n=7.35-7.45); Urinalysis positive for ketones and glucose (n=negative); Islet cell, GAD-65, and insulin antibodies negative (n=negative); HgbA1C=5.4% (n<6). (Hemaglobin A1C likely underestimated hyperglycemia due to fetal hemoglobin). Hyperglycemia improved on 3 units of glargine daily with intermittent sliding scale insulin. Home blood glucose monitoring revealed variable blood sugars from 70-250 mg/dL. Gene analysis for KCNJ11, GCK, and IPF-1 genes (Athena Diagnostics) revealed a mutation in the KCNJ11 gene (nucleotide 104 T>G, amino acid Phe35Cys). The infant transitioned from therapy with glargine to glyburide (0.6 mg/kg/day divided
every 8 hours) at 6 months of age. This therapy was tolerated well with relative euglycemia and adequate growth. At 10 months of age, the child presented with respiratory illness, decreased oral intake and resultant hypoglycemia. Glyburide was discontinued. Euglycemia continued off sulfonylurea therapy based on home glucose monitoring (BG=70-120 mg/dL) and HgbA1C =5.6% at 22 months of age. She continues to grow and develop in an age appropriate fashion without pharmacotherapy.

**CONCLUSION:** This case suggests that the Phe35Cys (104T>G) mutation in the KCNJ11 gene confers a natural history of transient neonatal diabetes, which is responsive to sulfonylurea therapy during the transient period of hyperglycemia.


**Abstract #6**

**Diet Liberalization in a 2 Year-Old Child with Classical PKU after Treatment with Sapropterin Dihydrochloride**

_Diaz-Thomas AM*_, Malone JL, Swan K. Pediatric Endocrinology, Diabetes and Metabolism, University of South Florida, St Petersburg, FL, United States

**Presenter:** Alicia M Diaz-Thomas, MD, MPH, Endocrinology, Diabetes and Metabolism, First Year Fellow

**Type:** Poster Presentation

**ABSTRACT:** Infants and children with untreated classical PKU are at risk for seizures, intellectual impairment and behavioral disorders. Although dietary restriction of phenylalanine remains the foundation of treatment, sapropterin dihydrochloride (Kuvan, Biomarin) is an adjunct treatment of hyperphenylalaninemia independent of dietary intake. Current clinical indications for the use of Kuvan are limited to patients over the age of 4 years. We report on a 30-month-old female with classical PKU who was supplemented with Kuvan (20 mg/kg/day) for 7 months while following her routine dietary management for PKU. Her initial phenylalanine level on Newborn Metabolic testing at 59 hours of life measured 6.4mg/dL. Confirmatory testing performed at DOL 9 yielded a phenylalanine level of 20.1 mg/dL. Urine pterins and serum dihydropteridine reductase levels were normal. The primary management included a low-Phe formula plus other foods estimated to provide 175 mg/day of phenylalanine. This management protocol resulted in biweekly blood Phe levels that ranged between 3 and 8 mg/dl. The parents were very motivated and compliant. The blood Phe levels following the addition of Kuvan averaged between 2 and 4 mg/dl and the phenylalanine/tyrosine ratio improved in spite of increasing the phenylalanine content of the diet to 275 mg/day of phenylalanine. Growth parameters remained stable following diet liberalization and the addition of Kuvan. Additionally, this child had neurocognitive testing (BDI-2) done at 33 months of age which revealed above average performance. No untoward side effects were reported. Target populations for treatment of patients with BH4-responsive PKU should include young children at important early permanent stages of functional cognitive development. Further studies to delineate the effect of early intervention with Kuvan in developing children with PKU are needed at this time.
"Hail to the Chief" The Roles and Expectations of the Chief Resident

Harris E*, Dabrow S, Maldonado L, M.D, Gereige R.

Presenter: Elizabeth Harris M.D., First Year Fellow – General Academic Pediatrics – Primary Care Track

Type: Poster Presentation

OBJECTIVE: To evaluate the role of the pediatric chief resident at programs throughout the country.

METHODS: A 20 item survey was electronically distributed to program directors (PD) and chief residents (CR) at all pediatric programs in the United States. Questions pertained to types of activities performed and the level of importance of administrative, clinical, and educational activities for the chief resident. It also investigated motivating factors to become chief resident, future career plans, and level of job satisfaction.

RESULTS: Surveys were sent to 201 chief residents and 279 Program Directors. 101 CR responses (50%) and 127 PD responses (46%) were received. 98% of CRs felt administrative tasks were very/somewhat important, followed by education (93%), service (77%) and research (21%). Significantly more PDs (81%) than CRs (68%) felt the overall workload for the CR was well-balanced. PDs overestimated the CRs ability to develop clinical skills (79% vs. 63%) and manage stress/burnout (86% vs. 72%). Future career plans for the chief residents included fellowship (35%), outpatient practice (30%), academics (17%), and hospitalist practice (15%). 62% of PDs reported that it was not easy to recruit good CRs. The most significant problems encountered by CRs were lack of administrative support and lack of time spent in educational/clinical activities.

CONCLUSIONS: The primary chief resident role is administrative, but teaching and clinical responsibilities are still important. Although PDs and CRs agreed in most areas, the PDs underestimated the amount of responsibility/demands placed on the CR. It is suggested that the position could be improved by providing more administrative support which would allow more time for teaching and clinical care.

Patient Safety Rounds in Pediatric Inpatient Units Shows Trend Toward Improved Safety

Welch TR; Nimeh JW*; Miner B; Page N

Presenter: Joseph W. Nimeh, MD, MMS - First Year Fellow, General Academic Pediatrics – Academic Hospitalist Track

Type: Oral Presentation

BACKGROUND: Recent patient safety literature has introduced the concept of regular patient safety rounds (PSRs) as an initiative. There are no reports of this in pediatric units, despite the unique safety challenges confronting hospitalized children. Related to its absence of effect on cerebral blood flow.
OBJECTIVES: To discover, discuss, and provide solutions for patient safety issues in our pediatric inpatient units as well as measure the impact of patient safety rounds on the attitudes of those participating in them.

METHODS: We gradually implemented monthly PSRs on four inpatient pediatric units. Participants in these rounds included senior medical and administrative leadership, as well as nurses, child life specialists, pharmacists, and residents. Data collected included responses to a validated Agency for Healthcare Research and Quality (AHRQ) safety survey pre- and post-implementation, as well as summaries of the categories of problems identified.

RESULTS: Over a nearly two year period, PSRs identified 112 discrete problems related to unit safety. These were classified into pre-determined categories as: communication (14%), data acquisition (4%), equipment/environment (10%), family education (4%), medication/orders (32%), and nursing/patient care (36%). The post-implementation survey showed improvement in a wide variety of measures of unit safety culture. Sample changes in agreement responses to the AHRQ survey included: A) Procedures and systems are good at preventing errors (79% to 94%) B) Supervisors consider safety suggestions (87% to 97%) C) Staff members are informed about unit errors (55% to 71%) D) Care information is lost at shift change (55% to 32%) E) Staff members are concerned that errors are held against them (28% to 16%).

CONCLUSIONS: Conclusions: A multi-disciplinary team making regular safety rounds on pediatric inpatient units identified safety issues that might otherwise have been unrecognized, and may have contributed to improvement in the overall safety culture on these units.

NEONATAL-PERINATAL MEDICINE

Abstract #9

Auditory Brainstem Responses in Preterm Infants

Hernandez M*and Sullivan J

Presenter: Margarita Hernandez, MD, Neonatal-Perinatal Medicine, second Year Fellow

Type: Oral Presentation

BACKGROUND: The auditory brainstem response (ABR) consists of a series of electrical potentials in the nanovolt range recorded from the scalp following an abrupt auditory stimulus. They are thought to reflect the sequential activation of the eighth nerve and the auditory nuclei of the brainstem. Latencies are highly dependent on the degree of myelination of the pathway.

ABRs have been used as a clinical and research tool in the neonatal intensive care unit (NICU) to assess a wide variety of neurologic and audiologic risk factors in preterm infants based upon normative values derived from studies performed in the 1980’s and 1990’s. Since that time, improved care of preterm infants has resulted in reduction in the gestational age of viability and in greatly improved. Noise-reduction properties of equipment used to record ABRs has also improved significantly. These improvements in care and technology may alter normative ranges for ABRs in the preterm population. Specifically, inter-and intra-subject variability could be reduced by 1) minimizing the number of infants with clinically silent pathology included in the normative sample and 2)
improving the signal to noise ratio of the recordings. By reducing variability in the normal range, we may be able to improve the predictive value of ABRs in high-risk preterm infants. Finally, there is little normative data available on the 8th nerve action potential in preterm or term infants. This component may provide a better bio-marker for bilirubin toxicity or ototoxicity.

**OBJECTIVES/HYPOTHESIS:** Our primary objective is to define the normal limits of:
- The latency of the 8th nerve action potential (AP) represented by wave I of the ABR
- The amplitude of the 8th nerve action potential
- Brainstem auditory conduction time (BCT), represented by the time delay between wave I and V of the ABR
- Rate of maturation of BCT

Our secondary objective is to determine the effects of demographic and treatment variables in high-risk infants using the normal limits as a reference. We hypothesize that the updated normal limits will enable: 1) more precise statistical separation of infants into postconceptional age groups, and 2) identification of factors that alter the rate of maturation of brainstem conduction time and 8th nerve action potential.

**METHODS:** Using the equipment currently used in the newborn hearing screening program (Vivosonic Integrity for diagnostic ABRs), we are performing one to six evaluations on preterm infants in the NICU. ABR measurements are repeated every week until discharge or until six studies have been performed. Otoacoustic emissions are also performed to detect middle ear dysfunction.

**Subjects:** Preterm infants in TGH NICU

**Groups:** Subjects are divided into age groups (post conceptional age in weeks).

**Inclusion criteria:** Viable preterm infants.

**Exclusion criteria:** Major malformations or problems with skin integrity.

**Measures**
- ABR to click stimuli
  1. Latency and amplitude of the 8th nerve action potential
  2. Brainstem conduction time (BCT)
  3. Rate of maturation of BCT

**DATA ANALYSIS:** Confidence limits will be determined for measures at each postconceptional age. The ultimate goal is to analyze data from thirty subjects in each age group; however, a preliminary analysis of means and standard deviations of the rate of maturation will be performed after we have studied 30 subjects per group. Linear regression analyses will be used to identify clinical and demographic factors that impact the rate of maturation of BCT.

Abstract #10

**Comparison of Infant Body Composition in Small- and Appropriate-for-Gestational Age Infants Using ‘Air Displacement Plethysmography’ (ADP)**

Kumaraswamy L*, Carver J, Rubin LP, Division of Neonatology, Dept of Pediatrics, University of South Florida, College of Medicine, Tampa, FL

**Presenter:** Latha Kumaraswamy, MD, Neonatal-Perinatal Medicine, First Year Fellow
Type: Oral Presentation

BACKGROUND: Recent data suggest that body composition during infancy and the rate of early catch-up growth may have significant implications for the long term development of infants born small-for-gestational age (SGA). Nutritional strategies to promote "healthy catch up growth" have not included assessment of infant body composition, weight-for-length and adiposity. Air displacement plethysmography (ADP) accurately measures body composition in children and adults. More recently, ADP has been adapted for use in infants weighing 1-8 kg (PEA POD, Life Measurement, Inc). We hypothesize that noninvasive measurement of body composition will be useful in evaluating growth quality as well as quantity.

OBJECTIVES: (1) To determine longitudinal changes in body composition in growing SGA and appropriate-for-gestational age (AGA) infants. (2) To determine the relationships among body composition, anthropometric measurements and clinical variables in SGA and AGA infants. (3) To assess the impact of specific maternal factors on newborn infant body composition.

METHODS: Inclusion/exclusion criteria: Term and preterm AGA and SGA babies born at Tampa General Hospital weighing between 1 and 8 kg will be included. Each SGA baby will be matched with two AGA babies of the same gestational age. Infants with chromosomol or significant congenital anomalies will be excluded. Body composition and anthropometric variables will be measured daily (weight) or weekly (length, head circumference, abdominal circumference) during infants' initial hospitalization, and once monthly from discharge to the time when infants reach body weights of 8 kg. Maternal medical charts will be reviewed to obtain information regarding maternal conditions and obstetric history.

Descriptive statistics will be used to describe normative body composition and anthropometric data, repeated measures analysis of variance will be used to measure differences within subjects over time, and multiple regression will be used to examine the relationship of infant body composition to nutritional, neonatal and maternal factors.

Abstract #11

Analysis of FOXP3 Expression in Term and Preterm Infant Cord Blood CD4+CD25+ T cells
Ruiz R, Arbona I*

Presenter: Ileana Arbona, M.D., Neonatal-Perinatal Medicine, First Year Fellow
Type: Oral Presentation

BACKGROUND: CD4+CD25+FOXP3+ regulatory T cells (TREGS) play an important role in immune regulation. TREGS regulate/suppress immune responses and play a role in autoimmunity, transplant rejection, and allergic diseases. Depletion of TREGS induces effective tumor immunity, enhances immune responses to invading microbes, triggers allergic responses, and breaks feto-maternal tolerance during pregnancy in murine models. While it has been demonstrated that TREGS levels are higher in human cord blood compared to adult peripheral blood, little is known about TREGS levels during human gestation.
OBJECTIVE: To measure TREGS percentages in cord blood and to relate those values to demographic data and gestational age.

DESIGN/METHODS: In this on-going study, umbilical cord blood is obtained from infants born at 24 to 42 weeks gestational age and mononuclear cells are isolated. Extracellular (CD4 and CD25) and intranuclear (FOXP3) staining are performed, and CD4+CD25+FOXP3+ T cells are identified and enumerated by flow cytometry. Additional markers will be used to further characterize TREGS including CD45RO (memory cells), CD45RA (naïve cells), and CD31 (thymic origin).

RESULTS: Data from 17 infants between 35 and 41 weeks gestation revealed a mean percentage of TREGS of 5.8 ± 0.2%. There is a significant negative correlation between TREGS percentages and gestational age (r²=0.35, p=0.013)

CONCLUSIONS: These data indicate that the percentages of TREGS in fetal blood decrease with advancing gestational age, and support findings from animal studies that TREGS may play an important role in maintaining feto-maternal tolerance. On-going studies will determine if TREGS levels relate to clinical outcomes in preterm infants.

Abstract #12

Intravenous ibuprofen treatment for patent ductus arteriosus in preterm infants does not affect cerebral blood flow velocity

Munoz L*, Bruton D, Carver J, and Wadhawan R

Presenter: Luis Munoz, M.D., Neonatal-Perinatal Medicine, Second Year Fellow
Type: Oral Presentation

BACKGROUND: Patent ductus arteriosus (PDA) is a common clinical problem in very low birth weight infants (VLBW). The use of intravenous cyclo-oxygenase (COX) inhibitors like indomethacin or ibuprofen as medical therapy for PDA is currently the standard of care. While the effects of indomethacin on systemic circulatory beds, including the cerebral circulation have been widely studied, ibuprofen, being a newer agent for this indication has not been as well studied. Clinical trials have shown indomethacin, administered within 24 hours of birth, to be effective in prophylaxis of intra-ventricular hemorrhage (IVH) in preterm infants. Ibuprofen has not been shown to have this beneficial effect.

HYPOTHESIS: IV ibuprofen for the treatment of PDA will not result in reduction of middle cerebral artery blood flow velocity (MCABFV)

METHODS: Ongoing prospective study of VLBW infants (<1500 gm birth weight) at a level III NICU at All Children’s Hospital. Infants are enrolled in this study when they are diagnosed by an echocardiogram as having a hemodynamically significant PDA needing pharmacological therapy. Doppler ultrasound is used to measure MCABFV, ductal size and Rp/Rs ratio. These measurements are performed before and 30 minutes after the administration of the first dose of the drug. Doppler measurements are then repeated with the third dose at the same time interval.

RESULTS: Preliminary data is available for 10 patients. Mean gestational age of enrolled infants is 24.5 weeks of gestation, with a mean birth weight of 820.5 g. Interim data analysis shows that ibuprofen has no effect on MCABFV. The mean pre and post MCA peak systolic velocity (MCAPSV) in the enrolled infants was 0.39 m/s and 0.42 m/s for dose 1. For dose 3, the mean pre and post MCAPSV was 0.38 m/s and 0.4 m/s.
None of these differences were statistically significant. Similarly, the MCA mean velocity was unchanged before and 30 minutes after the drug administration for both the first and the third dose.

**CONCLUSION:** Our results confirm that there is no reduction of MCABFV after ibuprofen administration. This lack of effect on cerebral blood flow may help explain the inefficacy of ibuprofen in IVH prophylaxis.