Finding Potential Alzheimer’s Treatments in Unlikely Places

Neuroimaging Center: Cornerstone of a “CRISP”

Q&A With Paul R. Sanberg, PhD, DSc
Senior Associate Vice President for Research & Innovation at USF

Alzheimer’s Research at USF: Unstoppable

Early Diagnosis Yields Savings for Dementia Patients

Jun Tan, MD, PhD
Robert A. Silver Chair in Developmental Neurobiology
Professor, Director of Developmental Neurobiology Laboratory
Silver Child Development Center
Welcome

Here at the USF Health Byrd Alzheimer’s Institute, our mission is to provide outstanding diagnostic evaluation and treatment, offer comprehensive educational opportunities, and perform cutting edge research, with the ultimate goal of curing Alzheimer’s disease and related dementia.

Building on the more than 25 years of service that the Suncoast Center has offered to the Bay area, we are renovating one floor of the Institute over the next year to launch our newest program: a “Dementia Diagnosis CRISP” (Clinical and Research Integrated Strategic Program).

The CRISP program will provide a comprehensive multidisciplinary diagnostic clinic that will transform memory-related health services for patients and families throughout Florida. In addition, family-centered care will offer patients information about the impact of Alzheimer’s across the whole of family life, from adult daycare options, legal issues, stress management, competency for driving and daily activities, to treatment choices. Every visitor will be offered opportunities to participate in clinical trials or other research activities at the Dementia CRISP.

The cornerstone of the clinic will be the Neuroimaging Center housing a sophisticated PET scan machine. New research has enabled the use of PET imaging to visualize the nerve-killing Alzheimer’s amyloid proteins in the brain years before symptoms such as memory loss begin to appear. Early treatment will be vital in preventing the onset of the disease.

Our goal is to expand the frontiers of dementia care through research leading to innovations in prevention, early diagnosis, and intervention for our patients. PET screening offers the possibility of early diagnosis to people at high risk based on genetics, family history or life experiences that increase risk (such as brain trauma associated with athletics or military service). PET screening can also be offered to those who simply want an early evaluation and risk analysis performed. Critically, this new PET technology is rapidly becoming the standard for evaluating the effectiveness of experimental drugs being developed to prevent and remove the amyloid deposits. Success in establishing the CRISP will make the Alzheimer’s Institute the only center in the world offering all of these services in a single visit.
Can this man outsmart Alzheimer’s?

Dr. Jun Tan and his team think outside the box to find potential treatments.

In unlikely places, Dr. Jun Tan is finding potential treatments for Alzheimer’s disease. The USF Health researcher and his team have found that an extract of green tea can inhibit a process that kills brain cells. They also developed a clever method, akin to a skin patch, to prevent the serious side effects of a once-promising vaccine injection. And now they are isolating which aspects of human umbilical cord blood cells appear to block the creation of the proteins believed to cause Alzheimer’s.

“Alzheimer’s disease is a trickster, able to harm and kill neurons using the brain’s own immune defenders,” Tan explains. It seems that when a switch, CD40, on the surface of microglia (the brain’s immune cells) is turned “on,” they cease their usual defensive work: they stop cleaning up the amyloid beta protein tangles that kill the neurons. Instead, Tan said, the microglia begin to produce small proteins called cytokines, which damage neurons.

Tan looks at two ways of solving the problem. The first is to reduce the production of the harmful substances. One method involves plant compounds called flavonoids, and in particular EGCG, which is found in green tea. Tan’s team found that in mice, EGCG turns off the CD40 switch and stops the cascade of neuron damage.

Tan and his team found that human umbilical cord blood cells also appear to turn off the CD40 switch. They now are working under a five-year, $1.5 million grant from the National Institute on Aging to figure out how that happens.
The Science Behind PET Imaging

PET scans are images of the body, but they differ from X-rays and CT scans as much as a movie differs from a photograph.

They display images of the body at work, allowing doctors to see not just the structure but also the function of organs or tissues, giving physicians a powerful diagnostic tool for problems from cancer to heart disease or Alzheimer’s disease.

PET is an acronym for Positron Emission Tomography, a system of nuclear medicine imaging. To the patient, the test is deceivingly simple: An injection of a substance commonly called a tracer, and then 30 to 60 minutes of lying still in a massive, doughnut-shaped machine. That “doughnut” houses devices that record energy given off by the tracer, a radioactive compound that links to or is absorbed by the target tissue.

Modern PET scanners usually perform a simultaneous CT (computed tomography) scan. The computer combines the record of the tracer’s energy over time with the CT scan of the body’s structure. The product is a three-dimensional image that shows the body at work. In cancer, tumors stand out because they process sugars, the fuel of cells, more rapidly.

Traditional neurological PET scans show which parts of the brain are active and which are dying. The location of those active and inactive areas can help doctors distinguish between Alzheimer’s disease and other forms of dementia.

Doctors can diagnose heart disease with everything from simple tests of cholesterol and blood pressure to sophisticated tools like stress tests and catheterization. Imagine, though, if the only way to spot the problem was to wait for a devastating, possibly fatal heart attack.

Until recently, that has been the predicament of the doctors who treat Alzheimer’s disease: They could diagnose the condition only when the symptoms manifested, meaning that the disease was already in an advanced state. Now, technology is giving Alzheimer’s physicians the same diagnostic power as their cardiologist colleagues. Positron Emission Tomography, better known as PET scans, can diagnose Alzheimer’s disease as much as a decade before symptoms appear.

While the process is still developing, Dr. Dave Morgan, CEO at USF Health Byrd Alzheimer’s Institute, is confident that PET scanning will revolutionize the detection and treatment of the disease. “This permits us to make a positive diagnosis of Alzheimer’s disease before the symptoms appear,” he said. “It’s going to allow us to predict who’s at risk five years before symptoms appear, possibly 10 years.”

That makes PET scanning one of the top priorities as the Institute seeks to finance and build out its nationally recognized facility.

A new look at the living brain

A century ago, Dr. Alois Alzheimer developed his theories about the disease after the autopsy of a patient revealed the telltale protein plaques, now known as amyloid in the brain. But with PET scans, doctors can now see the amyloid plaques that Dr. Alzheimer saw long before the patient’s death and even before the disease manifests itself. “We can actually see the amyloid in the living brain,” said Dr. Amanda Smith, who directs clinical programs at the Institute.

Ligands – molecules or compounds commonly called tracers – are injected into a patient, and travel to the brain. In the brain, the ligand (or tracer) attaches itself to the amyloid plaques, Morgan explains. The tracer gives off radiation, which the PET scanner can detect and use to develop a clearer image of the brain. “It gives you a picture of where the amyloid is in the brain,” he said. He and other researchers see this as a key to determining
who is at risk for developing Alzheimer’s disease.

“Being able to predict Alzheimer’s disease is only half the battle,” Morgan said. “The other half is being able to reduce the levels of amyloid in the brain, and the Institute is participating in some 15 separate trials of substances that may do exactly that,” he said. “In some, PET scans have shown that the study drugs reduced amyloid levels when compared with a placebo.”

Smith noted that one medication, already approved by the Food and Drug Administration for other neurological diseases, has been shown to reduce amyloid levels. “Tests are underway to see if it also reduces the symptoms of Alzheimer’s,” she said.

Smith indicated that PET scanning and early diagnosis may be crucial to any success, because it allows treatment to begin before amyloid deposits reach a level of no return. “It may be that once people have symptoms, it’s too late,” she said.

Mission-Critical, Patient-Friendly

Morgan sees PET scanning as crucial to the central clinical program at the Institute, which has the acronym CRISP: Clinical and Research Integrated Strategic Program. On the clinical side, PET scans would be a key piece of a comprehensive, patient-friendly treatment at USF Byrd. Patients could come to the center and be escorted through a series of examinations and evaluations by psychologists, neurologists and other specialists.

“We want to provide, in a single setting, the ability to walk in in the morning and walk out at lunchtime, and have had a thorough workup by physicians, including a PET scan,” he said. “As far as we know, nobody in the world is doing this the way we want to do it.”

Having the PET scan system in place at the Institute would make Alzheimer’s assessment and treatment much easier on patients. “It would really provide, for the families, a minimal amount of parking and driving, and ease their way through the medical maze,” he said.

It would be equally important to the Institute’s research side. Morgan sees PET scan technology as a key for attracting top-notch researchers to the Institute and improving its ability to develop better treatments and tests.

Smith points to the continuing development of improved ligands, the tracers used in neurological testing.
Q: What does it mean to the Tampa Bay region to have a major research university like USF here?

A: As a leading public research university, and one of the fastest growing in federal funding, the University of South Florida has an energized partnership with business and industry in this area, which has a significant effect on economic development in the region. And that partnership extends to cultural, arts, health, sports, marine, and eco-sustainability issues.

Within USF, we have a number of Centers and Institutes that focus on specific issues, with each providing a venue for faculty, researchers and students to come together to solve a common problem. To give you a few examples, we have expertise in diabetes, biological defense, drug discovery, infectious disease, small business development, and neuroscience, especially as related to neurodegenerative disorders.

Q: What role does the USF Research Park play in this process?

A: The USF Research Park, also directed by Dr. Casto, is truly a unique complex. It houses the flagship facility of the Tampa Bay Technology Incubator. The Park and the Incubator exist to support technology research and function as a catalyst for economic development. It addresses the needs of local high technology employers in life sciences, engineering and other technologies.

Q: How is USF providing graduate researchers with opportunities to address real-life problems?

A: Graduate research at USF provides students with opportunities to work alongside internationally renowned faculty and researchers in a variety of settings. The Dean of the Graduate School, Karen Liller, PhD, is committed to students contributing to efforts that address real-life problems on local, national and global levels. They get to participate in work that will literally “change the world.”

Q: Can you provide an example of how USF CONNECT serves private industry?

A: USF CONNECT focuses on the needs of Tampa Bay’s entrepreneurs at all stages of the business life cycle. We are a single point of contact for businesses seeking resources such as technology transfer, financing, relocation assistance, or marketing and management. USF CONNECT’s network of local serial entrepreneurs, bankers, attorneys and mentors help local entrepreneurs by sharing what it takes to build a successful business. Since 2005, USF CONNECT has provided incubation for more than 35 companies that have generated more than 230 high-wage jobs.
Don Porter personifies old Florida: Raised on a ranch that he still manages, overseeing cattle herds and orange groves, steeped in the state’s history. 

But he also sees Florida’s future, as a leader in medical research and innovation. And in the wake of his mother’s death, that vision led his family to support Alzheimer’s research at USF.

Their donation of $2.85 million in 2004 established the James H. and Martha Porter Lead Annuity Trust. Martha Porter was just 54, Don remembers, when she started to show Alzheimer’s symptoms. After first writing it off as simple forgetfulness, the family realized it was more than that.

They tried to care for her themselves, at home, but as her condition worsened, they added one caregiver, then a second, then a third. Realizing that even around-the-clock, in-home care was insufficient, they finally relented and found a nursing home to provide for her until her death at age 76.

That long struggle taxed the family financially, and even more so emotionally, Porter said, and it impressed upon them the need to find a treatment or cure for Alzheimer’s disease.

With their homestead, the Wiregrass Ranch, just some 20 miles away, the Porters saw the promise of the fledgling Institute as the place that could find that cure. Don Porter is even more positive about its potential today.

“I think the outlook, the purpose, the sense of direction is very upbeat,” he said. “We’re very pleased with what we’re seeing at the Institute, even in these difficult times.”

Porter sees two significant strengths: The skills of the scientists in the Institute, led by CEO Dr. Dave Morgan, and the energy of USF Health leadership, under USF Health Senior Vice President Dr. Stephen K. Klasko.

“It has struck us that the quality of the research going on is quite good and they have talented people in the labs,” he said. The family’s funding was intended to back that research, not bureaucracy, and has been spent as they intended. “The team at the Institute have been good stewards,” he said.

Meanwhile, Klasko and other USF officials have aggressively pursued state and national grants, and they have begun establishing partnerships with other institutions.

“The most compelling thing I’m seeing is Klasko and Morgan seem to be committed to enlarging the umbrella, and I think over time that will pay handsome dividends,” Porter said.

“There is not a comparable facility anywhere in the country devoted to finding a cure for Alzheimer’s disease. It will become even more respected if they can keep the funding lifeline strong.”
Nearly a half-million Floridians already face perhaps the cruellest fate imaginable: The gradual but inevitable erasure of their memories and their personalities.

Alzheimer’s disease has stricken 5.3 million people nationwide, about 450,000 of them here in Florida. And as the ranks of retirees and baby boomers age, that statewide figure is expected to climb to 600,000 Alzheimer’s patients by 2025. While the disease will devastate patients and their families, it also has the potential to cripple the state. Researchers estimate the disease costs Florida more than $2 billion a year in Medicaid payments. And the tide of patients threatens to overwhelm the network of in-home care providers and nursing homes.

The USF Health Byrd Alzheimer’s Institute plans to meet the disease’s daunting challenge by expanding its accomplished research and innovative patient care. It is seeking $29.5 million in funding via the USF: Unstoppable campaign, an opportunity to invest in the facility’s future and provide the tools it needs to better diagnose and treat – and someday, even cure – Alzheimer’s disease.

Noting the disease’s demographics, Steven D. Blair, Chief Development Officer for USF Health, explains, “The USF: UNSTOPPABLE campaign provides an opportunity to be part of groundbreaking translational research and treatment for a disease that will likely affect you in a profound way.”

There are many ways to support Alzheimer’s research at USF, and every dollar matters. Institute officials stress that much of the funding achieved to date has not been from single, multi-

“With the continued support of the community, the end of this disease should be inevitable.”

Steven D. Blair, Chief Development Officer for USF Health
million dollar contributions, but the result of combining many smaller donations. The Institute has earned a potent reputation and plaudits for its research and clinical care. This recognition is rooted in the Tampa Bay region but extends far beyond into the realm of national and international esteem. The role of private contributions in supporting these achievements will continue to be essential. Some of the largest priorities of the Institute, with projected costs, are listed below.

**Neuroimaging Center**
*Projected cost: $2 million*

Central to the future of both the clinical and research sides of the institute is the emerging technology of Positron Emission Tomography, or PET, scanning.

Scientists have learned that the telltale pathology of Alzheimer’s – protein tangles in the brain – can appear years before symptoms manifest. In the past three years, breakthroughs in PET scanning have given doctors the ability to see those tangles and develop treatments for use earlier, when they may be most effective.

For USF Health Byrd Alzheimer’s Institute researchers, having PET scanning in-house will speed and enhance their work, and allow them to participate in more trials of potential treatments and diagnostic methods. Having cutting-edge technology also makes USF a more attractive destination as it tries to draw more of the world’s leading researchers.

**Establish named, endowed chairs**
*Projected cost: $3 million each*

The best way to recruit and retain leading scientists is to establish endowed chairs, positions with permanent funding to support advanced research. The Institute hopes to establish three such positions, named for the donors, to provide for physicians and scholars.

**Build and outfit new laboratories**
*Projected cost: $16.5 million*

The dazzling USF Health Byrd Alzheimer’s Institute facility is still largely unfinished. To accommodate a rapidly growing corps of scientists and staff, the Institute needs to build out laboratories on its fifth and sixth floors and outfit them with specialized equipment, including a confocal microscope, a small animal magnetic resonance imaging (MRI) system and other state-of-the-art equipment.

**Patient dignity program**
*Projected cost: $2 million*

At the heart of the Institute are the people and families it cares for. Preserving their dignity during such an emotionally challenging time is integral to the Institute’s mission. USF envisions a Patient Dignity Program that will assist and educate patients as they visit the Institute. USF Health students would guide patients through the Institute’s Eric Pfeiffer Suncoast Alzheimer’s Center and USF Memory Disorders Clinic, and inform them about what to expect during their testing and clinical care.

**USF: UNSTOPPABLE**

Throughout its history, generous donors have helped the USF Health Byrd Alzheimer’s Institute make opportunities available to students and faculty, which they in turn have transformed into benefits for the world.

Together, these forward-thinking individuals, families and institutions are helping the world’s largest facility dedicated to caring for Alzheimer’s patients and their families to ultimately defeat this crippling disease.

“This campaign gives us a great opportunity,” Blair said. “While we are proud of USF’s talented faculty and students who drive the University’s innovative research and award-winning academic programs, we also know that private donations provide substantial power to the engine. Nowhere else on our campus, or on any campus in the United States, do we have a facility where Alzheimer’s research is being done, where patients are being seen, and where feedback from those patients goes back toward new discoveries. With the continued support of the community, the end of this disease should be inevitable.”

For ways to get involved in the Alzheimer’s Institute or the USF: UNSTOPPABLE campaign, see “How to Give” on page 10.
Institute Tours

An interesting way to learn more about the Institute is by taking a facility tour. Visit the Discovery Labs to see our researchers at work in the pursuit of a cure for Alzheimer’s. Tour our Medical Clinic and learn about the clinical trials, services, and care we provide to patients and their families – all under one roof. Along the way, you will learn about Prevent Alzheimer’s Now, our revolutionary plan to create a multidisciplinary diagnostic program for patients and their families at the Institute.

Tour dates

The following tour dates are scheduled for the remainder of calendar year 2010. All tours are from 11:30 a.m. - 1:30 p.m. and include lunch.

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If you would like to schedule a tour of the Institute, please contact Holly Lisle, Associate Director of Development, at (813) 974-0890 or email her at hlisle@health.usf.edu. There is no cost for the tour, but reservations are required as space is limited.

How To Give

The USF Foundation welcomes gifts of all sizes on behalf of the Institute. Outright gifts and planned gifts can benefit both the university and the donor, via potential tax benefits.

Outright gifts

Outright gifts are the simplest way to help, and immediately go to work on behalf of the university. Donors can make checks payable to the USF Foundation. The donor can designate the gift for Alzheimer’s by a note in the memo line of the check or in a letter, and may designate the gift for a specific department or program.

Donations can be mailed to:
University of South Florida
ATTN: Development Department
12901 Bruce B. Downs Blvd.,
MDC 70
Tampa, FL 33612-4742

Donors may also use the pre-addressed envelope bound into copies of Brain Research Discoveries magazine. Donations also can be made online, using a credit or debit card. Visit the Web site at giving.usf.edu and click the Make A Donation link. Many corporations will match gifts made by employees, retirees or even spouses, allowing the donor to double or triple the value of their gift. It only requires the donor to request a matching gift form and send it along with the gift.

Planned giving

Planned giving involves donating assets and is usually part of a donor’s estate plan. Options include simple bequests, memorial and honorary gifts, endowed gifts, charitable gift annuities and charitable remainder trusts. Such gifts usually involve legal documents and require the advice and assistance of a professional financial consultant. The USF Foundation offers more information at its Web site.

Corporate & foundation giving

Donating to USF can also benefit corporations and foundations. Through corporate giving, businesses can build partnerships, participate on USF advisory boards, and develop relationships with outstanding students who are preparing to enter the workforce.

Foundations can fulfill their missions by working with USF to find projects and goals that meet or align with their funding initiatives.

The USF Foundation has staff trained in coordinating these gifts and developing opportunities that help both the university and the donor organization.
Tan’s theory is that antibodies in the cord blood cells interfere with the bonding between the CD40 switch and a triggering molecule. And, as a result, the protein accumulation and neuron death that are the hallmarks of Alzheimer’s are stopped. Under the grant, in addition to isolating which aspects of the blood cells produce the desired effect, they also plan to develop a “cocktail” to administer to mice engineered to have the symptoms of Alzheimer’s disease. That would allow scientists to create a synthetic drug, producing the same results without using actual umbilical cord blood.

Tan’s other approach to solving the Alzheimer’s problem is to enhance the body’s ability to defend against the disease in the first place.

An injectable vaccine developed in the late 1990s reduced deposits of amyloid beta and tau, another protein tied to Alzheimer’s disease, in the brains of mice. Their memory and learning ability improved. Tests also showed improved cognitive abilities in human patients. But development of the vaccine stopped after safety trials in humans found that it caused inflammation, bleeding or death in a small percentage of subjects.

Subsequent study showed that the problems likely stemmed from T cells, a class of the blood’s immune cells, that the vaccine allowed to infiltrate the brain. Tan theorized that delivering the vaccine through the skin might reduce that problem, because the skin contains cells that reduce T cell production.

The result was reduced amyloid, with no T cell infiltration or microhemorrhage in the brain. “These data suggest that transcutaneous (through the skin) immunization constitutes an effective and potentially safe treatment strategy for Alzheimer’s disease,” the authors wrote.

The study, published in the Proceedings of the National Academy of Sciences in 2007, drew positive response worldwide. Tan praised his co-authors, including Dr. Dave Morgan of the USF Health Byrd Alzheimer’s Institute, and said he believes in a collaborative approach with researchers from different backgrounds. “We have a good team at USF,” he said. “This is a good environment for Alzheimer’s research, it’s the top.”

Jun Tan, MD, PhD, is the Robert A. Silver Chair in Developmental Neurobiology and Professor / Director of the Developmental Neurobiology Laboratory, Silver Child Development Center, USF Health Department of Psychiatry and Neurosciences.

Collaborators: Dr Doug Shytle, Associate Professor, and Dr. Paul Sandberg, Sr. Vice President for Research & Innovation.

Some of the most effective ligands, like Pittsburgh Compound B, are chemically fragile and difficult to use in patients. But several companies are developing new tracers, including two in trials running at the Institute. “What we are hoping is that these new ligands will get FDA approval, and they will transform how we treat and diagnose Alzheimer’s disease,” Smith said. “This is a revolution. We want to be at the forefront.”
Is it serious? Is it Alzheimer’s?

Significant memory problems are not a part of the normal aging process, and may reflect an underlying illness. Is it serious? Is it Alzheimer’s?

For Alzheimer’s patients, and for family and friends feeling overwhelmed by the disease’s unrelenting grip, two world-class facilities – the USF Suncoast Alzheimer’s Center and the USF Memory Disorders Clinic – provide a variety of clinical, educational and support services, at a single location.

- Expert clinical care
- Diagnosis of memory problems
- Family education and support
- Caregiver support groups
- Medication review
- Clinical trials of new medications

Call for more information, to schedule a memory screening, or to volunteer for a clinical trial.

USF Suncoast Alzheimer’s Center: (813) 974-4355
USF Memory Disorders Clinic: (813) 974-3100

Alzheimer’s Foundation of America
National Memory Screening Day®
November 16, 2010 • 8:30am – 3:30 pm

Call To Reserve Your Appointment for a Free Screening:
(813) 974-4355

Until Alzheimer’s is a memory.