Clinical Trials Offer Hope to Alzheimer’s Patients

USF Health / Byrd Merger: “Limitless” Opportunity for Research & Treatment

Investigating The Role of “Chaperones” In Cell Function

Q & A With USF President Judy Genshaft

Featured from left to right:
Dave Morgan, PhD
Chief Scientific Officer,
USF Health Byrd Alzheimer’s Institute

Judy Genshaft, PhD
President, University of South Florida

Stephen K. Klasko, MD, MBA
Sr. Vice President for USF Health
Dean, USF College of Medicine
Welcome

I’m pleased to share with you the inaugural edition of Brain Research Discoveries, the news magazine of the USF Health Byrd Alzheimer’s Institute. Founded as a public corporation, this remarkable translational research center joined forces with the University of South Florida in July 2009. This union permitted the rapid relocation of multiple NIH-funded Alzheimer’s researchers to the Institute staff. The number of principle investigators has tripled. Grant funding has quadrupled. The affiliation also permitted the fusion of several clinical operations at USF that provided service to Alzheimer’s patients into a single location. The new Comprehensive Clinical Center located within the Institute includes the Suncoast Alzheimer’s Center, the Memory Disorders Clinic and the Alzheimer’s Disease Research Center. This coalescence increased patient visits to the Institute by a factor of 10, and offers patients participation in 15 clinical trials testing new treatments.

The Institute is one of the few in the world in which laboratory scientists are co-located with clinical researchers and service providers in a truly translational research model. The mission of the Institute is to discover new therapies and provide the highest quality patient care, leading to a cure. Even though we have expanded rapidly in the last year, there are many opportunities for additional growth. One major initiative is to develop a Neuroimaging Center as part of a state-of-the-art Dementia Diagnosis facility. This multidisciplinary clinic will provide patients with age-associated memory concerns and their families access to multiple medical specialists in a single visit. Moreover, the clinic will provide information to family members regarding the benefits of occupational therapy, legal counseling, nutritional advice and caregiver education. The Neuroimaging Center with PET scanner will permit screening of patients for Alzheimer’s risk before they show symptoms, a time when medications will be most effective.

As you read about our achievements, I hope you’ll share my excitement about the discoveries we’re making in our work to make Alzheimer’s just a memory.

Dave Morgan, PhD
Chief Scientific Officer

Spring 2010

Clinical trials – medical research involving people – test possible interventions that may diagnose, prevent, treat or cure a disease. In this case, the man is participating in one of many trials under way at the Institute, receiving injections of a drug called Filgrastim, which already is used to stimulate the body’s production of white blood cells. But a team of scientists, led by Dr. Juan Sanchez-Ramos, found that the drug also reduces the protein known as beta amyloid, which is believed to trigger Alzheimer’s disease. In lab mice, the drug reversed memory impairment and stimulated learning.

Researchers say the trial is an example of what they expect to become common: Scientists develop a drug in the Institute’s labs, and then test it and eventually treat patients in the Institute’s clinic.

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New treatments, promising clinical trials offer hope to Alzheimer’s patients in the Tampa Bay region.

In a treatment room on the first floor of the USF Health Byrd Alzheimer’s Institute, an Alzheimer’s disease patient is advancing the fight against the illness simply by having a medicine injected under his skin.

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“It’s vital for people to understand that we’re all working together,” said Dr. Amanda Grant Smith, who is medical director of the Institute, and completed her internship, residency in psychiatry, and fellowship in geriatric psychiatry at the USF College of Medicine. “The people who work with the mice and the people who work in the labs on the third and fourth floors and the people in the clinics have a sense of what each other is doing. Projects from the labs can evolve into projects that are being tested in the clinic. That’s happening right now. That’s why this institute is so fantastic. That’s why it’s a national model for how things should be.”

Dr. Amanda G. Smith
Medical Director, USF Health Byrd Alzheimer’s Institute

Translating science upstairs to treatment downstairs.

For the complete story visit:
www.byrdinstitute.org/Discoveries
Sherrill Tomasino envisions a future without Alzheimer’s.

Six years ago, Sherrill Tomasino lost her father, William, to Alzheimer’s disease. Her mother, Ruth, also developed the disease. Tomasino, a University of South Florida trustee, also has a great-granddaughter, Ada, now almost a year old. She hopes the little girl never has to watch her parents decline the way she has. And that’s why Tomasino supports the Institute and is pushing for others to do the same: “I don’t want Ada to ever hear the word ‘Alzheimer’ except as a historical reference.”

Ruth, now 90, is living in a local assisted living community, in a section for people with memory disorders. She still plays the piano at times, to the delight of other residents and their families.

Through her frequent visits to her mother in her assisted living community, and her time in the hospital with her father, Tomasino has come to know many others who have struggled when their loved ones were diagnosed with the disease.

“I learned about the life of a family member of someone with Alzheimer’s disease. I learned how devastating the disease can be, not only to my family but to others,” she said.

The experience led Tomasino to learn more about the Alzheimer’s Institute, contribute to its funding, and volunteer for a spot on the Byrd-USF affiliation board. As both a trustee and as someone touched by Alzheimer’s, she observed Byrd’s previous struggles and is convinced that the Institute is now positioned to make a difference, both in treating people suffering from the disease and in performing research that can lead to a cure.

Some 18 months after the Byrd Institute merged into the USF Health system, three memory clinics are under one roof, as are labs conducting groundbreaking research into the nature of Alzheimer’s.

Now the Institute’s clinicians and researchers are forming seamless teams to treat and someday cure the cruel, crippling and ultimately fatal disease that affects nearly a half-million Floridians.

“Overall, it’s been a resounding success,” said Dr. Stephen K. Klasko, Sr. Vice President for USF Health and Dean of the USF College of Medicine.

Klasko cited a number of achievements since the merger:

- Institute researchers will receive $6 million in federal research grants, triple the amount they received in 2007.
- The Institute recently convened the first meeting of the Florida Alzheimer’s Network, a consortium of researchers from across the state, and identified dozens of potential partnerships.
- Clinical operations – which combined the USF Memory Disorders Clinic, the Eric Pfeiffer Suncoast Alzheimer’s & Gerontology Center and Byrd’s clinic – treated some 1,800 patients in the past year.
- Together, the clinical and research teams provide the Institute with an almost unequaled advantage: “This is one of the few examples anywhere where clinic faculty and research faculty are sharing lunch,” said Dr. Dave Morgan, chief scientific officer. “They’re both working together and meeting informally to move the ideas in the labs more rapidly into treatments in patients.”

When the Institute officially joined USF, ending its independent status and six years of political struggles and funding battles, Klasko put a transition team in place and trimmed staff. By early 2009, clinical and research teams scattered around USF began to move into the Fletcher Avenue center, which Morgan says is probably the largest building in the world devoted to Alzheimer’s research.

Klasko – who also has an M.B.A. degree from the Wharton School at University of Pennsylvania – now hopes to strengthen the revenue side of the Institute.

Institute’s merger into USF Health represents “limitless” opportunity for research and treatment.

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The center has received no state funds for two years. Its costs have been covered by the remnants of past appropriations, reimbursement from the clinics’ patients, and through researchers’ salaries as USF faculty. Without renewed state support, the center’s fate is “stagnation,” Morgan said.

“We would continue to operate, but we would not grow and fulfill the real mission of this institute, to serve the residents of Florida.” The Institute was created in part to support treatment and research statewide, and in January assumed that leadership role by convening the first meeting of the Florida Alzheimer’s Network. Some 45 researchers from all over Florida compared notes and laid the ground-work to share ideas and facilities.

One example, Klasko said, came from talks with Florida State University scientists, who offered time and training on the school’s powerful magnetic resonance imaging device. That corresponds with research and clinical trials now underway, examining ways to use positron emission tomography, or PET scanning, to identify people at risk of Alzheimer’s disease long before symptoms appear.

To continue that research and its statewide service, the Institute plans to seek $5 million in state funding. Klasko said. About $1 million would go toward developing that diagnostic imaging facility; another $1 million would help USF Health recruit new faculty; expand existing programs and build out the rest of the Fletcher Avenue center.

Another $1 million would be set aside as matching funds for the federal Alzheimer’s Disease Research Center grant, which brought it $7.5 million in National Institute of Aging funds over the past five years. Without state support, that federal re-certification is highly unlikely, Klasko said.

“The state did a brilliant thing in setting this up,” Klasko said. “It would be sad to waste this opportunity, because the opportunity is limitless.”
To Alzheimer’s disease researchers, they are known as the trigger and the bullet. Most research, at the Institute and elsewhere, centers on a protein known as beta amyloid, the trigger in the disease analogy. But scientists Chad Dickey has targeted the bullet itself. His research appears to have identified ways to eliminate its deadly presence.

The bullet is a protein called tau, which normally gives nerve cells their structure. In the brains of Alzheimer’s patients, though, it malfunctions, forming tangles that eventually kill the cells and create the symptoms that lead to memory loss and death. “You have to have amyloid for the tau dysfunction to start, but it’s the tau dysfunction that ultimately kills the neuron,” said Dickey, an assistant professor of molecular medicine at USF Health.

“Amyloid triggers it, but then tau takes on a life of its own. And so stopping the amyloid late in the disease may have no impact on people who have moderate Alzheimer’s disease. You really have to target the tau at that point.” To disarm it, he and his team have focused on tau’s unwitting accomplices, a class of proteins known as chaperones that were largely ignored until about 20 years ago.

Among other roles, chaperones monitor the activity of other proteins in a cell, helping newly made proteins fold into the proper shape, and helping dispose of old proteins. That latter function is where problems arise. “They make sure everything is in order,” Dickey said. “They grab onto these proteins and hold onto them and try to fix them, but they’re not fixable.

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Q & A With USF President Judy Genshaft

Q The Institute’s merger with the University of South Florida is almost complete. In what ways does this enhance USF’s general role of educating and serving the community? And how does it fit with your goal of making USF a hub of bioscience and entrepreneurship?

A USF has always been about real-world science. That’s why we’ve enthusiastically embraced the Alzheimer’s Institute. Alzheimer’s disease is growing into such an epidemic, that it threatens to create suffering for half our population as we age. USF Health takes its mandate to help block the disease, prevent it, and treat it. Our communities, especially in Florida, need those successes, and they need them soon. If we can just prevent Alzheimer’s, we’ll give millions of families the ability to work hard and long. We’ll give businesses a creative workforce of us all as we age. And we’ll create evidence-based opportunities for therapies to keep that disease out of our lives.

Q You have worked closely with Stephen Klasko, Sr. Vice President for USF Health and Dean of the College of Medicine in the merger. What does USF bring to Alzheimer’s research and what does that tell you about the Institute’s potential, in both its research and clinical functions?

A Immediately after the Institute transferred to USF, we filled the built-out space with the top Alzheimer’s researchers in the world. USF has that strength. Now we need to build out the rest of the building and make it the state’s home for preventing and treating this epidemic disease. That’s our potential: To stop the suffering for millions of people who find the promise of active, productive aging turned to darkness by Alzheimer’s.

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Q & A With USF President Judy Genshaft

Q “It’s like trying to put a puzzle together, a puzzle where you don’t have the box top to see what the final product looks like. You don’t even know if you have all the pieces.”

Chad Dickey, PhD

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Researchers investigate the role of “chaperones” in cell function.
Donor Profile: Tomasino
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“It’s as if Byrd was there, ready to do something, and then USF poured water on this slightly wilted plant and it just came to life,” she said.

USF offers the state-of-the-art facility the stability and credibility of faculty affiliation, she explained. Unifying the teams of scientists and patient care staff once scattered across USF has stimulated new thinking and lines of research.

And Stephen K. Klasko, Sr. Vice President for USF Health and Dean of the USF College of Medicine, has energized the staff and sparked efforts that have led to some $6 million in federal grants. Now, Tomasino said, the Alzheimer’s Institute needs an injection of support for it to bloom. “We are at a critical point. We have an incredible building, we have it well staffed, but there is room for much more. This is a time when people can make a difference.”

Chaperones...
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anymore. For some reason, the chaperone proteins just can’t get rid of the bad protein that is accumulating.”

So he and his team looked at ways to make chaperones work better. They theorized that increasing the activity of one such protein, HSP 70, would increase its bonding to tau and clear tau from the nerve cells. So they tested the abilities of several compounds to stimulate or restrict HSP 70’s activity.

But as often happens, their results were a surprise. Instead of reducing tau levels, activating HSP 70 actually preserved tau in the cells. Conversely, inhibiting HSP 70 activity reduced tau.

In a paper published in Sept. 2009 in The Journal of Neuroscience, Dickey and his co-authors outlined what they believe happens: Inhibiting HSP 70’s folding function forces tau to be recycled from the cell.

One of Dickey’s goals now is to use their findings to develop more effective compounds that more specifically target HSP 70. And that may also lead to treatments for other diseases: HSP 70 appears to have a role in proteins linked to Huntington’s disease, ALS (Lou Gehrig’s disease), and breast cancer.

As a USF graduate raised in nearby Temple Terrace, Dickey hopes to see his own research being tested in the clinic and developed into treatments. He predicts there will be classes of chaperone-based therapies for a variety of diseases in the next few decades. As a scientist, though, he most enjoys the challenge of unfolding the complex relationships inside the cell. “The mechanistic questions are what I love,” he said. “It’s like trying to put a puzzle together, a puzzle where you don’t have the box top to see what the final product looks like. You don’t even know if you have all the pieces. There are always going to be questions, because it’s so intricate.”

Q & A with Judy Genshaft
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Q: You have set a course of winning more federal research funds for USF, and that already is paying dividends. How can the state of Florida and private benefactors help build on that support, and why is it important?

A: USF already beat the pack in gaining new federal funding for research. Our faculty brought in federal dollars faster than any other university from 2000 to 2007. In the last few years we’ve added partners to ensure this research gets out to the public — that people are helped by it. Great examples are our new partnerships with SRI (a spin-off from Stanford), and Draper Laboratories (a spin-off from MIT). Now we’re spinning off our own firms as well, including one that has developed a major medication to assist people with depression.

There’s no question that the opportunity is here to shape our future, and to shape Florida’s future. Anyone who wants to be engaged in the effort to make life better will find a great partner in USF.

Help us make more discoveries.
Please support the vital work of the USF Health Byrd Alzheimer’s Institute with your gift today.

Contact our development office at 813-974-0890 or visit www.byrdinstitute.org for more information or to make your gift securely online. Thank You!