

Dean's Report

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Stellar team at Keck School leads race for Alzheimer's treatments

Fueled by both a growing awareness about Alzheimer's and new medical technology, research has yielded discoveries about Alzheimer's at a rapid clip in recent years. Scientists have uncovered the cause, identified genes and lifestyle factors that put people at risk, revealed the way in which the disease progresses and have discovered that the pathology of the disease begins long before symptoms appear.

What has eluded scientists so far is an effective treatment for Alzheimer's. The researchers at the Keck School of Medicine of USC believe a breakthrough is near and are pushing forward to develop the most cost-effective therapy that will finally change the course of care for the 5.3 million Americans who suffer from this most common form of dementia.

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Dean Carmen A. Puliafito, MD, MBA, and Alzheimer's disease research pioneer, Berislav Zlokovic, MD, PhD

Advancing Alzheimer's treatment options through collaboration



Paul Aisen, MD

Paul Aisen, MD, the founding director of the USC Alzheimer's Therapeutic Research Institute (ATRI), is the newest member of the Keck School of Medicine of USC whose focus is Alzheimer's disease research. He recently spoke with the *Dean's Report*, and answered a few questions about

joining USC and the progress of Alzheimer's disease research over the last 25 years.

Q: What excites you about joining the faculty at the Keck School of Medicine of USC?

A: I think Keck is the perfect home for my research group. We have enjoyed terrific support at all levels, allowing us to get our studies running in record time. And the academic environment is likewise terrific, as we build collaborations with outstanding leaders in Alzheimer's disease research, including Arthur Toga, Paul Thompson and Helena Chui.

Q: There is already a significant amount of research going on at Keck Medicine through the Alzheimer's Disease Research Center, USC Stevens Institute of Neuroimaging and Neuroinformatics and the Zilkha Neurogenetic Institute. How do you think the ATRI fits into that landscape?

A: ATRI's mission is to accelerate the development of effective treatments for Alzheimer's disease. We work on

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Stellar team at Keck School leads race for Alzheimer's treatments

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That figure speaks to the urgency of Alzheimer's disease research, says Lon Schneider, MD, professor of psychiatry, neurology and gerontology at the Keck School, and why it has so many initiatives devoted to better understanding of the disease.

Schneider is clinical director of the Alzheimer's Disease Research Center, funded by the National Institute on Aging, part of the National Institutes of Health. Keck School of Medicine scientists and physicians participate in two federally funded programs — the Alzheimer's Disease Cooperative Study and the Alzheimer's Disease Neuroimaging Initiative, while Keck Medicine of USC participates in the Alzheimer's Disease Genetics Consortium, a research project funded by the National Institute on Aging.

Researchers at the Keck School also pursue individual research projects aimed at finding treatments that will benefit the millions of Americans and their families who are struggling with Alzheimer's.

For example, Terrence Town, PhD, professor of physiology and biophysics at the Keck School, and his team recently showed that blocking an immune suppressor called interleukin-10 activates a beneficial immune response that appears to clear the brain of the toxic plaque buildup that is the hallmark of Alzheimer's disease.

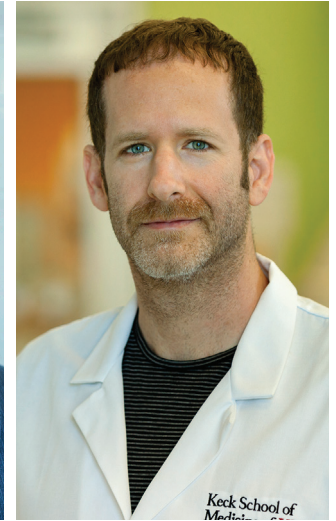
Town's lab is part of the Zilkha Neurogenetic Institute (ZNI), which is led by Berislav Zlokovic,

MD, PhD, another pioneer in Alzheimer's disease research whose work has illuminated the role that blood vessels in the brain play in the development of dementia.

In 2015 alone, Zlokovic's team of researchers has published new findings in three major journals. They were able to show that the blood-brain barrier becomes leaky with age using high-resolution imaging of the living human brain. They also showed that deficiencies of a protein called GLUT1, which helps move glucose across the blood-brain barrier, leads to vascular injuries that exacerbate the effects of Alzheimer's disease. Zlokovic, holder of the Mary Hayley and Selim Zilkha Chair for Alzheimer's Disease Research, discovered that a deficiency of a protein known as PICALM in cerebral blood vessels is associated with a diminished capacity to clear plaque formed by amyloid-beta protein from the brain.

With Zlokovic's body of research in the field, there is now significant evidence that vascular dysfunction is an early event in Alzheimer's disease.

Powerful new technology in the field of brain imaging is also helping to advance understanding of Alzheimer's disease by offering



Terrence Town, PhD, and Lon Schneider, MD

researchers the ability to track changes in the living brain.

Paul Thompson, PhD, professor of neurology, psychiatry, radiology, engineering and ophthalmology at the Keck School, leads ENIGMA (which stands for Enhancing Neuro Imaging Genetics through Meta-Analysis), the world's largest brain-mapping project. Recently, utilizing information from the

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“I think there is a lot to be hopeful about and I believe there is going to be a breakthrough on the treatment front.”

– Lon Schneider, MD

Paul Aisen expresses optimism for patients with Alzheimer's disease

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new methods (trial designs, outcome measures, analytical approaches), and design and implement multicenter trials. We look forward to collaboration with all of the research groups at the Keck School — all will contribute to our therapeutic studies.

Q: Take us back to the early days of your career when you decided to pursue research on Alzheimer's disease. What was it like to be involved in Alzheimer's research then?

A: I think I was very fortunate to enter academic medicine just as the field of Alzheimer's therapeutic research was beginning. I had the opportunity to participate in the earliest studies, contributing to the development of the first drugs to be approved for the disease. Over the past 25 years, I have worked with remarkable investigators around the world on setting the stage for a new generation of therapies that we hope will bring this terrible disease under control. I don't think there is any more important or more exciting work in medicine.

Q: What changes have been most beneficial to advancing research?

A: The important advances are too many to name. But let me focus on one area: PET imaging. There are two primary abnormalities in the Alzheimer's disease brain: plaques, made of aggregated protein called amyloid, and tangles, deposits within brain cells made up of a protein called tau. For the past 10 years, we have been able to

study the accumulation of amyloid plaques in the brain using PET scans. This changed our entire perspective on the disease, and revolutionized drug development. We now know that amyloid, the root cause of the disease, accumulates 15 years before the onset of symptoms of Alzheimer's disease. So we are now conducting our anti-amyloid trials during this asymptomatic phase when removal of amyloid is likely to be very effective. For the past two years, we have been able to visualize tangles as well, with a different type of PET scanning. With these two neuroimaging tools, we can analyze the course of the disease as never before, allowing accurate diagnosis very, very early, and enabling the accurate tracking of disease progression.

Q: You have been quoted recently saying that you think there is reason for optimism for patients with Alzheimer's disease. What do you see on the horizon that gives you hope?

A: With our new neuroimaging tools, and very promising therapeutic agents, I am confident that we will have effective treatments within the coming years. Ultimately, I believe we will be able to screen people in mid-life for evidence of amyloid dysregulation, so that we can administer treatments to prevent the accumulation of amyloid in brain, just as we treat elevated cholesterol to prevent the accumulation of plaques in arteries. We will be able to change the course of the most feared disease of aging.

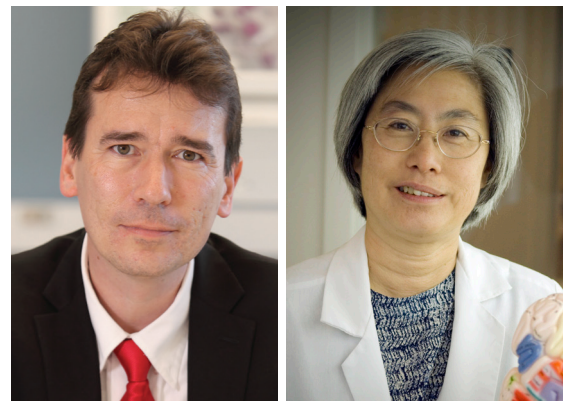
Keck School researchers pursue new treatment options for Alzheimer's

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ENIGMA group, Thompson was able to show that a common variant in one gene, TREM2, speeds brain cell loss in elderly people and in those with Alzheimer's disease.

There are also several clinical trials underway at Keck Medicine to test potential future treatments.

"We are committed to giving our patients the highest quality of care," says Helena Chui, MD, McCarron Professor of Neurology and chair of the Department of Neurology at the Keck School. "Our practice benefits by having access to top researchers in the field who are finding ways to better diagnose and treat Alzheimer's disease."



Paul Thompson, PhD, and Helena Chui, MD

USC Norris Gala raises more than \$2 million

USC Norris Comprehensive Cancer Center raised more than \$2 million at its 2015 star-studded black tie gala fundraiser held Oct. 10 at the Beverly Wilshire Hotel and sponsored by donors Ray and Shauna Mirra. The event honored philanthropists Dana and David Dornsife with the Visionary Award and physician-scientist Parkash Gill, MD, with the Research Innovation Award for his groundbreaking cancer research. Funds raised support the innovative cancer research at the 43-year-old USC Norris Comprehensive Cancer Center, where 250 clinical cancer trials are conducted each year.

Photos by Steve Cohn.



1. Dean Carmen A. Puliafito and actress Fran Drescher
2. Dean Puliafito with actor Pierce Brosnan
3. Dean Puliafito joins David and Dana Dornsife on the red carpet with USC President C. L. Max Nikias and USC Norris Director Stephen B. Gruber
4. Dean Puliafito and actor Joe Piscopo
5. Dean Puliafito and comedians David Spade and Dana Carvey
6. A sellout crowd enjoys the special evening

