



An Exciting New Target for Alzheimer's Therapy

Study funded by Alzheimer's Disease Research suggests new ways of shutting down toxic protein



Researchers at the University of California, San Diego School of Medicine have identified a novel protein that can trigger a dramatic increase in toxic amyloid plaques in the Alzheimer's brain. The study, supported by Alzheimer's Disease Research, suggests an important potential target for treating the disease.

The amyloid-beta protein is produced when the amyloid precursor protein is "cut" by two enzymes. Because these enzymes also perform beneficial work in the brain, inhibiting them can create negative side effects.

So the research team led by David E. Kang, Ph.D., focused instead on RANBP9, an enzyme that helps amyloid beta shuttle from the brain to the body, where it is broken down into harmless waste products. The researchers found that, by removing RANBP9 from a cell, they were able to reduce amyloid beta production by 60 percent.

"This study is the first to identify RANBP9 as a target to potentially

inhibit ... amyloid beta peptide generation," wrote Madepalli K. Lakshmana, Ph.D., the study's lead author. "As such, a small molecule drug that can reduce the RANBP9 could offer an effective treatment for Alzheimer's disease," preventing contact between amyloid precursor protein and the enzymes that transform it into brain plaque.

The researchers say they will now work to verify their findings in animal models.

Kathleen Honaker, Executive Director of Alzheimer's Disease Research, praised the work of Dr. Kang and his team for "reminding all of us of the tireless and dedicated work of scientists around the globe working to cure this devastating disease."

Alzheimer's Disease Research has contributed \$687,819 toward the work of Dr. Kang and his colleagues.

Inside This Issue

- **In Memoriam** 2
Anne Cataldo
- **President's Corner** 2
Body and mind
- **"Crystal Balls" for Alzheimer's Disease** 3
Findings underscore downside of Western diets
- **Heart Disorder Tied to Alzheimer's Disease** 3
Study shows atrial fibrillation increases dementia risk
- **Research Roundup** 4
- **Become a Year-Round Force in Alzheimer's Disease Research** 4
Monthly giving helps ADR reduce overhead



In Memoriam

Anne Cataldo

We were deeply saddened to learn of the passing of Anne Cataldo, Director of the Laboratories for Molecular Neuropathology at McLean Hospital, Belmont, Massachusetts.

Dr. Cataldo's research into the cell biology of Alzheimer's disease – furthered in part by grants from Alzheimer's Disease Research – has left a lasting scientific legacy. As one of her colleagues recently wrote, "Dr. Cataldo will not only be remembered for her originality, technical skill, and accomplishments as an investigator, but also for her enthusiasm, warmth, and creativity." She will be missed.



**Please visit
our website at
www.ahaf.org/alzheimers**

Visit the site to learn more about what's new in the world of research, as well as important information about risk factors for Alzheimer's disease.



Please share this newsletter with someone you know who might be interested in learning about some of the latest advancements in research to prevent, treat and cure Alzheimer's disease. The *Alzheimer's Disease Research Review* is published by Alzheimer's Disease Research, a program of the American Health Assistance Foundation, a nonprofit organization located at 22512 Gateway Center Drive, Clarksburg, Maryland 20871, 301-948-3244, 800-437-2423, www.ahaf.org.

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President's Corner

Body and mind

If Alzheimer's disease has taught us nothing else, it has taught us how impossible it is to separate our brains from the rest of our bodies.

In this issue of *Alzheimer's Disease Research Review*, for example, you'll learn about a simple test – balancing on one foot – that can tell us as much about a patient's cognitive decline as the most sophisticated scientific assay. You'll also find fresh evidence of the critical role that diet plays in slowing the disease's onset.

Month after month, the same message comes back: to take care of our brains, we must take care of our bodies.

And to take care of our bodies, we have to cram our brains with as much information as they can hold. For that reason, I urge you to become as knowledgeable about this disease as you can.

Read this newsletter. Visit our website at www.ahaf.org/alzheimers. And if you have any remaining questions about Alzheimer's disease, please don't hesitate to ask us. Working together, I believe we can overcome this terrible scourge.

Brian K. Regan, Ph.D.

“Crystal Balls” for Alzheimer’s Disease

Scientists pioneer new diagnostic and predictive tests



A team of scientists at the University of Pennsylvania School of Medicine has developed a test that can both diagnose Alzheimer’s disease and predict the course of an individual’s cognitive decline, according to a study published in the *Annals of Neurology*.

By measuring concentrations of amyloid beta peptoid and tau protein in samples of cerebrospinal fluid, researchers were able to detect the disease at its earliest stages and to predict whether mild cognitive impairment would convert to Alzheimer’s disease over time.

“Validated biomarker tests will improve the focus of Alzheimer’s clinical trials, enrolling patients at earlier stages of the disease to find treatments that can at least delay – and perhaps stop – neurodegeneration.” said study leader Leslie M. Shaw, Ph.D. “In addition, prevention trials can test methods to delay or block cognitive impairment from converting to full-blown Alzheimer’s.”

In related news, scientists with the University of Georgia and partner institutions have uncovered new linkages between two antibodies and the severity of Alzheimer’s disease symptoms.

In a study published in the *Journal of Gerontology*, the researchers said that antibodies created in response to amyloid beta and RAGE (Receptor sites for Advanced Glycosylation End products)—two molecules involved in the immune system—were found at much higher levels in the brains of people with Alzheimer’s. The findings raise the possibility of someday developing a diagnostic blood test for the disease.

Heart Disorder Tied to Alzheimer’s Disease

Study shows atrial fibrillation increases dementia risk

People with atrial fibrillation are at significantly higher risk of developing Alzheimer’s disease, according to a study by Intermountain Medical Center in Salt Lake City.

The study, which looked at more than 37,000 patients, found that patients with the common heart rhythm disorder were 44 percent more likely to develop dementia than people without the disorder. Atrial fibrillation patients under age 70 were 130 percent more likely to develop Alzheimer’s disease. Moreover, patients with

both atrial fibrillation and dementia were 61 percent more likely to die during the study period than dementia patients without the heart disorder.

Atrial fibrillation occurs when the upper chambers of the heart beat out of rhythm and very rapidly, which may cause blood to pool and possibly clot. If the clot leaves the heart, a stroke can result.

“Now that we’ve established this link, our focus will be to see if early treatment of atrial fibrillation can prevent dementia or the development of Alzheimer’s disease,” said study co-author John Day, M.D.

Research Roundup

Diabetes, high cholesterol can speed brain's decline

Alzheimer's patients with a history of diabetes and high levels of cholesterol, particularly LDL (low-density lipoprotein) cholesterol, appear to experience faster cognitive decline than other people with the disease, says a new study from Columbia University Medical Center.

"These findings indicate that controlling vascular conditions may be one way to delay the course of Alzheimer's," said senior author Yaakov Stern, Ph.D. "Preventing heart disease, stroke and diabetes – or making sure these conditions are well managed in patients diagnosed with them – can potentially slow the disease progression of Alzheimer's."

Published in the Archives of Neurology, the findings were part of a 10-year, multi-ethnic study of cognitive aging and dementia in northern Manhattan.

Scientists find explanation for Alzheimer's-epilepsy link

An estimated one-third of Alzheimer's patients suffer from some form of epilepsy. Now, for the first time, scientists with Scotland's University of Aberdeen may have figured out why.

Beta-amyloid protein – the main component in the plaque that forms on the Alzheimer's brain – causes

the brain's nerve cells to short-circuit and fire off too many electrical signals, researchers say. When these neurons are unable to communicate with each other, the brain becomes more susceptible to seizures.

"Some drugs used in the treatment of memory impairment can unfortunately lower a patient's seizure threshold while anti-epileptic drugs can impair the already compromised cognitive functions of Alzheimer's patients," said neurobiologist Tibor Harkany. "It may be that we need to look for new drugs that treat both diseases at the same time."

Simple test could predict cognitive decline

A patient's ability to balance on one leg may determine how quickly his or her cognitive health declines under the influence of Alzheimer's disease, according to a study published in the *Journal of Alzheimer's Disease*.

The study found that patients unable to stand on one leg for five seconds showed much greater cognitive decline than patients able to stand for longer.

"Our results reinforce ... the growing evidence suggesting a link between physical performances and cognitive decline," said senior investigator Yves Rolland of France's University of Toulouse. "If these results are confirmed by other data, the one-leg balance test could be adopted in clinical practice to identify Alzheimer's disease patients at high risk of rapid cognitive decline."

Become a Year-Round Force in Alzheimer's Research

Monthly giving helps ADR reduce overhead

Many of our donors find that the easiest and most efficient way to give to Alzheimer's Disease Research is to make monthly contributions of \$10, \$20, \$50 or more.

Automatic payments are particularly effective because they save you and us the cost of stamps and envelopes – reducing our overhead and allowing us to allocate more of every dollar to the fight against Alzheimer's disease.

Becoming a monthly donor is easy to do. For more information on this unique way of giving, please contact Cristel Siaobungco at 1-800-437-2423.

Thank you for thinking of Alzheimer's Disease Research!