ALZHEIMER'S RESEARCH REVIEW

A publication for friends and donors of Alzheimer's Disease Research *Summer 2006*

Supporters Play a Vital Role in Alzheimer's Disease Breakthrough

Research funded by ADR reveals Alzheimer's beginnings

The discovery that Alzheimer's disease may have its beginnings in the trafficking structures that exist within brain cells **"opens a new window on the causes of Alzheimer's disease,"** says researcher Dr. Gunnar Gouras.

Dr. Gouras's research – funded in part by Alzheimer's Disease Research, a program of the American Health Assistance Foundation, and **donors like you** – was reported in the April 26 issue of the *Journal of Neuroscience*.

What makes these findings so startling is the fact that many in the research community were not aware of just how early in the process neurological decline, due to Alzheimer's disease, can begin.

"Our work is showing that, long before this extra cellular phenomenon occurs, beta-amyloid is building up inside neurons – specifically, on intracellular trafficking structures called multivesicular bodies," explains Dr. Gouras, lead researcher on the project, as well as an associate professor of neurology and neuroscience at Weill Medical College of Cornell University, where the study was conducted.

Dr. Gouras' team used cell biological approaches to examine nerve cells extracted from the brains of "transgenic" mice – mice genetically engineered to develop a disease very similar to Alzheimer's disease.

Next, brain cells were extracted from the mice before they developed symptoms indicating advanced Alzheimer's disease.

Using an electron microscope, researchers detected a buildup of beta-amyloid protein at the outer membrane of an intracellular trafficking structure called the "multivesicular body."

In basic terminology, this finding shows that **Alzheimer's disease may have its beginnings in the trafficking structures that exist within brain cells.**

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Inside This Issue

For more information on projects being funded by Alzheimer's Disease Research, visit us on the web at: www.ahaf.org

President's Corner

Investing in a cure makes sense

Alzheimer's disease is not just a personal tragedy for the families affected by it – it is a financial tragedy as well.

In terms of health care expenses and lost wages of both patients and their caregivers, the cost of caring for people with Alzheimer's disease nationwide is now thought to be around $100 billion per year.

On an individual level, the average cost for the illness from diagnosis to death – which can be as long as 20 years – is $174,000, the third most expensive disease in the United States.

As you well know, the aging of America also contributes to the number of people with Alzheimer's disease. Thanks to incredible medical advances over the last several decades, Americans are living far longer. In fact, the U.S. Census Bureau estimates that nearly 19 million Americans will be age 85 or older by the year 2050; some experts suggest that the number could even be higher.

All of these statistics make research into new treatments and a cure for Alzheimer's disease an excellent investment for individuals, foundations, and the government. Not only will a cure save billions in lost income and health care expenses, but it will also spare millions from the suffering caused by Alzheimer's disease.

For all you do to make that cure a reality, I thank you.

Brian K. Regan, Ph.D.
President

Alzheimer's beginnings

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Experts have known for some time that a buildup of beta-amyloid protein "plaques" around and between neurons is a common indicator of Alzheimer's disease. Now it seems that neurological problems may begin much earlier than previously thought.

Says Dr. Gouras, "The brain cell isn't killed, but it is impaired in its function. And all of this occurs long before we see any evidence of plaque buildup outside the cell."

Explains lead researcher Dr. Claudia Almeida, a graduate student when the study was conducted, "the multivesicular body is an endosome – a kind of cargo-carrying body that's used late in endocytosis, the process by which the cell internalizes

nutrients and other substances coming in from outside."

Once the researchers were aware of the abnormal buildup of beta-amyloid within the brain cell, they were eager to learn how it impaired nerve cell functioning.

They found that multivesicular impairment seems to "gum up the works" when it comes to an important trafficking mechanism called the ubiquitin-proteasome system.

This disruption within the ubiquitin-proteasome system impacts the cell's ability to internalize nutrients.

"This system used to be thought of as the cell's 'garbage disposal'– cutting up and ridding the cell of its biochemical waste," explained co-researcher Dr. Reisuke Takahashi, a pathologist researcher at the lab where the research was conducted.

This buildup within the brain cell – along with the impairment of the ubiquitin-proteasome system – could provide researchers with new avenues to explore in the causes and potential treatments of Alzheimer's disease.

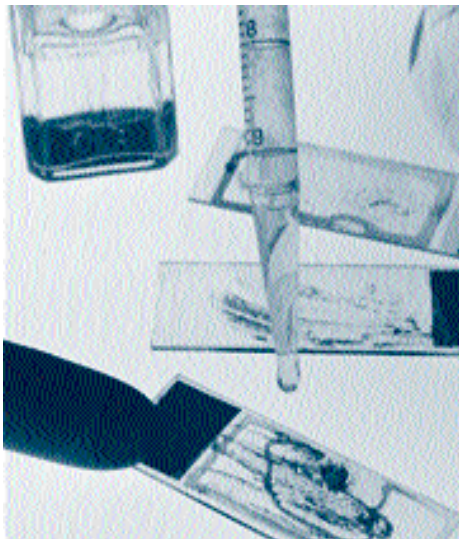
Dr. Gouras's research may also have implications in diseases well beyond Alzheimer's disease. A breakdown in the ubiquitin-proteasome system has long been implicated in a number of degenerative brain diseases, including Parkinson's disease.

What does all this mean to the millions of families who live with Alzheimer's disease?

Not only do we now know far more about the causes of Alzheimer's disease, but, according to Dr. Gouras, the research also provides us with "new targets that researchers might focus on to help prevent it in its earliest stages."

This study was supported by grants from the American Health Assistance Foundation, the Alzheimer's Association and the National Institutes of Health.

Adapted from the following source: Weill Medical College of Cornell University



Real Life...Real Questions

Our experts respond to your questions about Alzheimer's disease

Q: What happens if one lets Alzheimer's disease run its course?

A. At first, not much happens. In fact, a person can have Alzheimer's disease for quite some time before it is detected.

The earliest signs can be as mild as slight forgetfulness, trouble remembering names or recent events, or an inability to use former math skills to solve simple problems.

However, over time, these symptoms get worse.

In the second stage of the disease, a person with Alzheimer's disease may become slow of speech. Forgetfulness becomes more pronounced and troublesome. Daily tasks – such as brushing one's teeth or combing one's hair – can become difficult and frustrating. Of course, these are only generalities – the disease takes its own individual course with each person it affects.

In the final stages of Alzheimer's disease, a person may become aggressive or anxious, crying frequently. Alzheimer's disease patients may wander far from home, with no idea where they are or how they got there. And there is a chance they will not recognize even the familiar faces of a spouse, son, or daughter.

Not only can an early diagnosis and treatment help to slow the progression of the disease, it also allows families to plan for the future. While the loved one with Alzheimer's disease still has all their faculties, you will be able to discuss their wants and needs, as well as what might be best for the family as the disease worsens.

Q: How close are we to understanding the cause of Alzheimer's disease?

A. We've made great progress – but we still have a ways to go.

For example, we still don't know the "normal" function of the amyloid precursor protein (APP), which is involved in the production of beta-amyloid proteins in the diseased brain. The beta-amyloid proteins produced in the brain of an Alzheimer's disease patient becomes part of plaques, which are likely toxic to nearby brain cells.

We also don't yet know why Alzheimer's disease largely strikes the elderly and why the disease progresses more rapidly in some patients than in others. The more quickly scientists can determine the exact function of the key players and/or what controls the rate of Alzheimer's disease progression, the sooner we will know the actual cause(s) of the disease.

Evidence seems to indicate that Alzheimer's disease has many causes; somehow these numerous factors combine to result in the progression of the disease in a way that differs from person-to-person depending upon age, gender, lifestyle choices, and genetic disposition.

Q. Is the risk of developing Alzheimer's disease greater for women than for men?

A. What we know for certain is that age is the biggest risk factor for Alzheimer's disease; the older you are, the higher the risk of Alzheimer's disease onset.

But are women more at risk than men? Studies are at odds as to whether that is the case or not.

One study published in the *American Journal of Epidemiology* in 2001* suggests that women and men have the same risk of Alzheimer's disease onset. On the other hand, smaller studies have indicated that women may actually be at slightly higher risk for Alzheimer's disease.

Regardless of which sex is at higher risk, women seem to

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Real Questions

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bear most of the burden of Alzheimer's disease. Scientists are still studying why women have a higher prevalence of Alzheimer's disease when there does not seem to be anything about gender differences that puts women at higher risk.

Perhaps women really are at a slightly higher risk, as some studies have indicated. Or perhaps, since women generally live longer than men, the toll that Alzheimer's disease can take on them and their families is simply that much greater.

*Hebert, et al., American Journal of Epidemiology, Vol. 153, No. 2

Q: What is the difference between dementia and Alzheimer's disease?

A. Many people use the broad category of "senility" or "dementia" to describe all lapses of memory or intellectual problems associated with aging.

But that was before we had as much insight as we do now into the world of the aging.

Today, we recognize that dementia is a symptom of many different diseases, Alzheimer's included. Some types of dementia can be brought on suddenly by stroke, dehydration, or a medication interaction; not only that, in a few cases, dementia is not only treatable but reversible.

Alzheimer's disease, on the other hand, is not reversible, though there are a number of treatments that can slow the progress of the disease. Early diagnosis is critical to determining whether the cause of dementia is Alzheimer's disease or not. The ability of the medical community to diagnose Alzheimer's disease in its earliest stages is advancing at a rapid pace.

Alzheimer's Disease Research frequently posts questions from our friends and readers on our website at www.ahaf.org. There is also a search function on the website that allows you to search through our archives for answers to specific questions.

To submit a question, please go to www.ahaf.org and select the Alzheimer's Disease Research Link, What's New and Real Life Questions where you'll find a Real Life Questions form to fill out.

Consider a Charitable Gift Annuity

It benefits you and ADR!

If you're 55 years of age or older – and you want to play a major role in helping to cure Alzheimer's disease – you may want to consider a charitable gift annuity.

A charitable gift annuity is an agreement between you and Alzheimer's Disease Research in which you transfer cash or appreciated assets. In return, you (or a person of your choice) will receive guaranteed fixed income for as long as you live – as well as significant tax savings.

You can set up a charitable gift annuity with as little as $5,000 and receive payments when you choose – annually, quarterly, or monthly. One of the greatest advantages is that in the year that you fund the annuity, you are entitled to an income tax deduction for a portion of the entire amount! Better yet, part of each payment you receive is tax free.

You can choose to have payments made to yourself or another party of your choice – or both! It's completely up to you.

Would you like to learn more about the benefits of a charitable gift annuity? There's no obligation at all. Simply contact Gayle Handiboe, Manager of Development, at ghandiboe@ahaf.org or 1-800-437-2423.

Thank you for thinking of Alzheimer's Disease Research!

Research Update

Study suggests restricting carbohydrates may prevent Alzheimer's disease

A study which appears in the July 2006 issue of the *Journal of Biological Chemistry* suggests that restricting calories – in particular, carbohydrates – may help in the prevention of Alzheimer's disease.

In an experimental mouse model, researchers at the Mount Sinai School of Medicine showed that beta-amyloid peptides in the brain can be reduced by restricting caloric intake – primarily based on low carbohydrate food.

As one might expect, a high caloric intake based on saturated fat was shown to increase levels of beta-amyloid peptides.

As most people familiar with Alzheimer's disease are aware, men and women with Alzheimer's disease exhibit elevated levels of beta-amyloid peptides. These beta-amyloid peptides cause plaque buildup in the brain, which is the primary characteristic of Alzheimer's disease.

"Both clinical and epidemiological evidence suggests that modification of lifestyle factors such as nutrition may prove crucial to Alzheimer's Disease management," says Giulio Maria Pasinetti, M.D., Ph.D., Professor of Psychiatry and Neuroscience, Director of the Neuroinflammation Research Center at Mount Sinai School of Medicine and lead author of the study.

"We hope these findings further unlock the mystery of Alzheimer's," says Dr. Pasinetti, "and bring hope to the millions of Americans suffering from this disease."

NOTE: THIS RESEARCH UPDATE HAS BEEN PROVIDED TO OUR READERS FOR INFORMATIONAL PURPOSES ONLY. THIS STUDY WAS CONDUCTED IN MICE AND, TO DATE, THERE HAVE BEEN NO HUMAN TRIALS. PLEASE BE SURE TO CHECK WITH YOUR OWN DOCTOR BEFORE MAKING ANY CHANGES TO YOUR DIET.

Adapted from the following source: Mount Sinai School of Medicine

www.ahaf.org

Simply click on the Alzheimer's Disease Research link 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. If you'd like to receive additional copies, please contact us 1-800-437-2423.

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