

# Alzheimer's Disease Research Review

Better Health Through Research

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## Protein Discovery Opens Door to New Drug Therapies

Support from Alzheimer's Disease Research helps yield another clinical breakthrough

In a remarkable new development, scientists with the Fisher Center for Alzheimer's Research have discovered a new protein that stimulates the production of beta-amyloid plaque. Called gamma secretase activating protein (gSAP), it may offer a key therapeutic window for stopping the toxic buildup that kills brain cells in Alzheimer's disease patients.

"Existing drugs may mask symptoms for a time but do nothing to stop the relentless downward progression of Alzheimer's," says Dr. Paul Greengard, director of the Fisher Center and an honorary board member of Alzheimer's Disease Research (ADR), as well as an alumni of a very productive 1986 project. "What is needed are safe and effective medications that will halt the cause of the underlying disease. It is our hope that this gamma secretase activating protein will greatly add to the creation of safe and effective Alzheimer's treatments."

One such potential treatment is an anti-cancer drug similar to Gleevec, which is already on the market and approved for use in cancer treatment. The hope is that the new drug suppresses beta-amyloid production by binding to gSAP and which, unlike other beta-amyloid inhibitors, is not toxic to nerve cells.

"The findings of Dr. Greengard and his team are an exciting new step toward creating safe and effective Alzheimer's disease treatments," says Brian Regan, Chairman of Alzheimer's Disease Research.

Alzheimer's Disease Research has contributed \$48,000 toward Dr. Greengard's laboratory research over the years. "Support from Alzheimer's Disease Research was invaluable to my research and the work of my colleagues," says Dr. Greengard.

## Arthritis Sufferers Get an Alzheimer's Disease Benefit

### Protein isolated by scientists could lead to new drug therapy

A protein triggered by rheumatoid arthritis dramatically reduces the development of Alzheimer's disease and associated memory loss in laboratory mice, says a new study by the University of South Florida.

The study, published in the *Journal of Alzheimer's Disease*, originally sought to explain why people with rheumatoid arthritis, a chronic disease that inflames joints and surrounding tissue, are less likely to develop Alzheimer's disease.

In the past, some scientists have theorized that the anti-inflammatory drugs taken by arthritis patients may halt Alzheimer's disease in its tracks. However, the South Florida researchers conclude that the arthritis releases a particular signaling protein, called GM-CSF, which stimulates the body's immune system to attack and remove beta-amyloid deposits in the brain.

"Our findings provide a compelling explanation for

why rheumatoid arthritis is a negative risk factor for Alzheimer's disease," said principal investigator Huntington Potter, Ph.D., a professor at the university's Byrd Alzheimer's Institute.



Dr. Potter adds that Leukine, a recombinant human form of GM-CSF approved by the FDA, has been used for years to help cancer patients generate more immune cells, although it has not yet been tested for Alzheimer's disease. "Our study, along with the drug's track record for safety, suggests Leukine should be tested in humans as a potential treatment for Alzheimer's disease," says Dr. Potter.

Alzheimer's Disease Research has contributed a total of \$200,000 to Dr. Potter's previous research studying the formation of beta-amyloid aggregations.

## Beta Amyloid Inhibitors Get a Green Light



Contrary to some scientists' fears, interrupting a promising new drug treatment does not exacerbate Alzheimer's disease, according to a clinical trial partially funded by Alzheimer's Disease Research.

A class of drugs known as gamma secretase inhibitors has been shown to block the proteins that create beta-amyloid, a main ingredient in Alzheimer's disease plaque. Unfortunately, the harmful side effects associated with some of these drugs mean that patients cannot take them continuously. When physicians temporarily stop administering the drugs to human patients, previous studies have shown that levels of beta-amyloid in the blood surge. This raised concerns that the drugs might actually speed the progress of Alzheimer's disease.

But in a recent trial with animal subjects, scientists with Washington University School of Medicine in St. Louis and Merck & Co. Inc., found that when they stopped administering the drugs, beta-amyloid levels rose in the blood but not in the central nervous system.

"This is important because it eases some concerns that have been raised about this potentially useful class of medications," says senior author Randall Bateman, M.D., a Washington University neurologist.

Alzheimer's Disease Research has contributed \$150,000 toward Dr. Bateman's work.

# Research Roundup

## Life-extending protein could also suppress Alzheimer's disease

A protein that appears to boost longevity in laboratory animals could also be of potential value in treating Alzheimer's disease, according to a new study by the Massachusetts Institute of Technology (MIT).

MIT scientists found that activating a protein called sirtuin in Alzheimer's disease-prone mice significantly suppresses the memory loss associated with the disease. Conversely, mice with no sirtuin begin to lose their memory at a much earlier age.

Sirtuin has been extensively studied in recent years because it seems to maintain the health of the body's organs while protecting them from disease. Drugs that activate sirtuin are already on the market, but these drugs are of no use in fighting Alzheimer's disease because they can't cross the blood-brain barrier. However, the chief executive of Sirtris Pharmaceuticals, a biotechnology company based in Cambridge, Mass., has told *The New York Times* that his company is developing sirtuin-activating compounds that can target the brain.

## FDA approves higher doses of Aricept

The U.S. Food and Drug Administration (FDA) has approved a new higher-dose Aricept tablet for treating moderate to severe Alzheimer's disease.

The FDA's decision comes on the heels of a large head-to-head trial conducted by Indiana University School of Medicine, which found that a 23-milligram Aricept pill produces more cognitive improvement in patients than the 10-milligram Aricept.

Currently the recommended starting dose for Aricept is 5 milligrams, once a day. After four to six weeks, that dosage can be increased to 10 milligrams. As a result of the FDA decision, moderate-to-severe Alzheimer's disease patients will, after a certain interval, be eligible to have their dosages raised to 23 milligrams.

Aricept is manufactured and distributed by Pfizer and Eisai. The drug's most common adverse side effects are nausea, vomiting, diarrhea and anorexia.

## HIV and Alzheimer's disease may share dementia factors

A common type of dementia found in roughly 20 percent of advanced HIV patients may share molecular features with Alzheimer's disease, concludes a study by Australian researchers.

The study, published in Alzheimer Disease Research's official journal, *Molecular Neurodegeneration*, found that a significant number of proteins that were abnormal in HIV-infected brains also appeared abnormal in Alzheimer's disease brains.

"Every day we see more reports that bridge two diseases that we otherwise thought were unrelated," says Dr. Guy Eakin, Vice President of Scientific Affairs for Alzheimer's Disease Research, "and point to the successes that scientists have had in digging ever deeper into the causes of Alzheimer's and other diseases."

The Australian study and other Alzheimer's disease related reports can be found at <http://www.ahaf.org/research/journal/molecular-neurodegeneration.html>.

## Chairman's Corner

There's an old saying that, if your memory loss concerns just you, it's probably nothing to worry about. If it concerns the people around you, that's another matter.

Over the course of Alzheimer's disease, friends and family members are often the first to notice changes in the memory and cognition of their loved ones. If someone you love is declining, you owe it to that person – and to yourself as a potential caregiver – to take him or her to a doctor.

## Staying Vigilant

Even if the diagnosis is Alzheimer's disease, there are steps that can be taken now to protect your loved one's health – and even improve brain function.

So don't wait. Remember: The longer people stay healthy, the better their chances of being around for that next medical breakthrough. The breakthrough that Alzheimer's Disease Research is even now working toward.

 Brian K. Regan, Ph.D.

# Feel Good and Give Back

A planned gift can help fight Alzheimer's disease ... and secure your own future



Through thoughtful planned giving, you can help the world's leading scientists search for a cure for Alzheimer's disease while also passing along the values that have guided your life.

Whether you send a check, donate stock or include Alzheimer's Disease Research in your will, your gifts will put you front and center in the fight to discover treatments that will benefit millions. You may also be able to reduce your estate taxes and leave a larger inheritance for your loved ones.

For additional information, or if you want to discuss the many giving options available, please contact Barbara Spitzer, Gift Planning Officer, at 800-437-2423 or e-mail her at [bspitzer@ahaf.org](mailto:bspitzer@ahaf.org).

## Thank you for thinking of Alzheimer's Disease Research!



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