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Test of Alzheimer's Drug Gets Large Federal Grant

By PAM BELLUCK

In the most significant sign yet of a broad shift in the focus of Alzheimer's research from treating to preventing the disease, the federal government announced on Wednesday its largest grant so far to test an Alzheimer's drug on healthy people at greatest risk for the most common form of the disease.

The \$33.2 million grant, and several other prevention studies awarded federal money in the last year, follow years of unsuccessful trials of treatments on people who already have dementia. Those failures have led to the realization that these drugs appear to be ineffective by the time memory and thinking problems have taken hold. At the same time, scientific advances have allowed researchers to identify people at risk for Alzheimer's long before symptoms emerge.

With five million Americans suffering from Alzheimer's and their ranks projected to surge as baby boomers age, federal health officials consider the disease such a priority that Dr. Francis S. Collins, director of the National Institutes of Health, scraped money together when forced budget cuts slashed the Obama administration's promise of \$100 million in additional funding for Alzheimer's for 2013. Dr. Collins said he dipped into the budgets of the 27 N.I.H. agencies to supply \$40 million awarded Wednesday for several Alzheimer's research projects. Another \$5 million was provided by the [National Institute on Aging](#).

"The worst thing we could do would be to just hunker down and hold off tackling very important problems," Dr. Collins said, adding, "Obviously, this is high-risk research, but goodness, the stakes are so high that we felt we had to go forward even in the face of the most difficult budget environment that anyone can remember in the N.I.H."

The idea is to approach Alzheimer's with a strategy similar to that used for heart disease and other conditions, said Laurie Ryan, program director for Alzheimer's disease clinical trials at the National Institute on Aging, part of the N.I.H. "We're going to look at people at risk, just like we do with people who have high cholesterol and are at risk for cardiovascular disease," she said. "If we intervene now, can we prevent or at least delay the disease?"

The \$33.2 million grant, part of the government's [national Alzheimer's plan](#), will help finance a clinical trial to test a treatment on people 60 to 75 who have no symptoms of the disease, but do have two copies of a gene known to greatly increase the risk of getting it as people age.

The project, led by Dr. Eric M. Reiman and Dr. Pierre N. Tariot of the [Banner Alzheimer's Institute](#) in Phoenix, will test a drug or placebo on 650 adults in several locations, mostly in the United States. All of the participants will have two copies of the gene, ApoE4, having inherited it from both parents.

Studies have found that more than half the people with two ApoE4 genes will develop Alzheimer's, compared with about one-fourth of people with one copy and 10 percent of people with no copies. People with two copies also develop symptoms earlier, around age 68, years before most people with one copy and more than a decade before most people without the gene.

People with two ApoE4 genes make up only about 3 percent of the population, but because they develop the conventional late-onset form of Alzheimer's, they are important to study. About 25 percent of people possess one copy of the gene.

The [Banner project](#) has not yet chosen the drug to be tested, but it will be a treatment that attacks amyloid, a protein that accumulates in plaques in the brains of people with Alzheimer's.

Expected to begin in 2015, the project will ultimately cost more than \$100 million, most of which is expected to be financed by the pharmaceutical industry, with some money from nonprofit sources, Dr. Reiman said. Researchers will use sophisticated tests to measure whether the drug helps delay memory or cognitive decline over five years, although Dr. Reiman said the tests may be able to record some results in as little as two years. The study will also measure brain and neurological changes over time.

Jamie Tyrone, 53, a retired nurse in Ramona, Calif., said she felt traumatized when she learned while participating in a different research effort that she has two copies of ApoE4.

"For the first time I feel hopeful," she said. While too young to participate in the trial, she recently formed a nonprofit organization called Beating Alzheimer's by Embracing Science ([Babes](#)), which will soon have its inaugural fund-raiser, featuring the celebrities Helen Reddy and Marilu Henner.

She said the new trial "means so much to me because if this study has a positive outcome, guess what — I can be treated and I don't have to live in fear anymore."

The new grant is the latest of several grants for Alzheimer's prevention studies. In 2012, the N.I.H. awarded \$16 million to a project led by the same researchers and Dr. Francisco Lopera, a Colombian neurologist. The researchers will test an anti-amyloid drug on members of a Colombian family, the largest extended family in the world with a gene mutation that causes them to develop Alzheimer's early, showing cognitive impairment by around age 45. In that trial, expected to start this year, family members as young as 30 will receive the drug, [Crenezumab](#), manufactured by Genentech, which is financing the largest portion of that \$100 million trial.

Earlier this year, the N.I.H. gave a significant grant to a study that, like the Banner trial, will focus on people at risk for common late-onset Alzheimer's. Led by Dr. Reisa Sperling, who runs the Alzheimer's program at Brigham and Women's Hospital in Boston, the trial will test the anti-amyloid drug solanezumab on 1,000 people in various locations who do not have symptoms of Alzheimer's but do have amyloid plaques in their brains. The three-year trial will receive about \$7 million in federal money its first year, and a possible total of \$36 million.

On Wednesday, the N.I.H. also awarded \$1.5 million to a trial of three anti-amyloid drugs on people with rare gene mutations that lead to early-onset Alzheimer's. The trial, run by the [Dominantly Inherited Alzheimer Network](#) led by Dr. Randall Bateman of Washington University in St. Louis, may receive a total of \$6 million over four years.

Dr. Ronald Petersen, director of the Mayo Clinic's Alzheimer's center, who is not involved in these prevention trials, said the studies complemented each other and had the potential to answer questions about the role of amyloid as a potential cause of Alzheimer's and whether attacking it can prevent dementia.

"That doesn't mean we abandon people who need treatment," Dr. Petersen said. "But from a public health perspective, if you want to prevent millions of people from getting the disease, this is the way we have to go."

This article has been revised to reflect the following correction:

Correction: September 18, 2013

A headline with an earlier version of this article misstated the form of Alzheimer's disease that the Alzheimer's Prevention Initiative will focus on. It is late-onset Alzheimer's, not early-onset.



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