



Cure Alzheimer's Fund Closes 2008 with a Huge Win

Dear Friends,

We set out three years ago to jump start progress toward a cure for Alzheimer's disease and we are succeeding.

- The Alzheimer's Genome Project™ (AGP), targeting the full set of Alzheimer's genetic risk factors, identified 70 new genes, a tremendous result and truly breakthrough research. New genes open extensive novel scientific avenues for better understanding the disease and development of effective therapies.
- Publications announcing these results have begun and findings will continue to be announced in coming months.
- Other funded work, such as the AlzGene tool that allows researchers around the world to share and analyze information, is driving progress forward in unprecedented ways.



(L to R) Jeff Morby, Phyllis Rappaport, Jacqui Morby, and Henry McCance

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Current treatments address only symptoms of the disease. Cure Alzheimer's Fund provides fast and flexible funding to outstanding researchers who pursue new high-potential ideas for effective intervention. To use a football analogy, we give researchers the opportunity to throw a 40-yard pass instead of struggling for slow gains of a few yards at a time. Our investment in the AGP allowed that kind of 40-yard pass.

Because of our AGP accomplishments, we must significantly increase funding to take advantage of important new knowledge platforms. Already, we are identifying the next ambitious goals that will push research closer to a cure.

Cure Alzheimer's Fund needs your continued support to maintain the momentum. Our urgency is heightened because Alzheimer's is the only major disease with increasing rates of mortality and 78 million baby boomers are approaching the age of high risk. We welcome your partnership. Please join us as we support research to cure this disease in our lifetime.

Best wishes for a happy and healthy holiday season,

Henry McCance, Jeff and Jacqui Morby and Phyllis Rappaport

Major Findings Linking New Genes to Alzheimer's Disease Announced in Publication of Four Papers from the Alzheimer's Genome Project

Four papers published this fall in leading science journals refer to the identification of new genes that confer risk for, or protection against, Alzheimer's disease:

Bertram L and Tanzi RE. Thirty Years of Alzheimer's Disease Genetics: Systematic Meta-analyses Herald a New Era. *Nature Reviews Neurosci* 2008; 9:768-78.

Bertram L, Lange C, Mullin K, Parkinson M, Hsiao M, Hogan MF, Schjeide BM, Hooli B, DiVito J, Ionita L, Jiang H, Laird N, Moscarillo T, Ohlsen KL, Elliott K, Wang X, Hu-Lince D, Ryder M, Murphy A, Wagner SL, Blacker D, Becker KD, Tanzi RE. Genome-wide association analysis reveals putative Alzheimer's disease susceptibility loci in addition to APOE. *Am. J. Hum. Genet.* 2008; In Press.

Schjeide BM, McQueen MB, Mullin K, DiVito J, Hogan MF, Parkinson M, Lange C, Blacker D, Tanzi RE, Bertram L. Assessment of Alzheimer's disease case-control associations using family-based methods. *Neurogenetics* 2008; In Press.

Schjeide, B.-M.M., Hooli, B., Parkinson, M., Hogan, M.F., Divito, J., Mullin, K., Blacker, D., Tanzi, R., and Bertram, L. Follow-up of genome-wide association results suggests GAB2 as an Alzheimer's disease susceptibility gene. *Arch. Neurol.* 2008; In Press.

The genes described in these four papers are subsets of 70 AD candidate genes identified thus far by Dr. Rudy Tanzi and his colleagues at Massachusetts General Hospital as part of the Alzheimer's Genome Project™. These newly identified genes appear to function individually, or in some cases interactively, to increase or protect against risk for Alzheimer's disease. This first milestone achievement of the Alzheimer's Genome Project represents one of the most important breakthroughs in Alzheimer's research in recent history, and will greatly facilitate the development of effective therapies for the disease.

In particular, the four papers describe how newly available technology is improving understanding of the genetic mechanisms underlying the disease. The study described in the *American Journal of Human Genetics* is the largest genetic analysis of Alzheimer's disease carried out to date. The paper reports five DNA markers exhibiting genetic association with Alzheimer's, one of which corresponds to the gene for APOE, the only gene previously established to increase risk for late-onset Alzheimer's. Of the other four novel sites, the strongest marker was located on chromosome 14 and was further supported by an independent analysis comparing 1,400 Alzheimer's patients with healthy controls.

"The genetic association of Alzheimer's with this novel chromosome 14 gene, which like APOE appears to influence age of onset, is sufficiently strong to warrant intensive follow-up investigations into its role in the process of nerve cell death in this disease," says Tanzi. "This gene also is in the general vicinity of the presenilin-1 gene, which we know is an early-onset Alzheimer's disease gene. We don't know if that proximity is a coincidence, and we currently don't know what the new gene does, although there is some indication it may control the activity of other genes."

Another of the identified markers is in a gene known to cause spinocerebellar ataxia, a movement disorder that involves the death of nerve cells in other parts of the central nervous system, and a third is in a gene involved with the innate immune system, part of the body's defense against bacteria and viruses. The fourth marker is in a gene that produces a synaptic protein—not surprising, since it is known that loss of synapses correlates well with dementia in Alzheimer's.

"Virtually all current research into therapies is based on the Alzheimer's genes that we already know about, so each new gene we find not only enhances our ability to predict and diagnose the disease, but also provides valuable new clues about biochemical events and pathways involved in the disease process," adds Tanzi, who was

Publication Genome Project™

a co-discoverer of all three of the known early-onset Alzheimer's genes. The team is continuing to investigate the implications of these novel genes as well as the possible impact of less strongly associated genes also identified in this study.

This is exciting, groundbreaking research that should advance our knowledge of the causes of Alzheimer's disease and guide the development of novel therapeutics to treat and prevent the disease. "This project is the most comprehensive search for the genes that cause Alzheimer's disease published to date," Tanzi said. "Our hope is to use this new information to not only better diagnose and someday predict risk for Alzheimer's, but to also learn from these genes the biological causes of Alzheimer's. The knowledge gained from understanding the Alzheimer's-associated defects in these genes will almost certainly accelerate the development of novel therapeutics and hopefully lead to a potential cure for this devastating disease." ■

Congress Extends Charitable Gifting Program

In September Congress extended the popular charitable gifting program that allows seniors ages 70½ and older to make a tax-free contribution of up to \$100,000 from an IRA to a qualified charity. The charitable individual retirement account rollover provision was instituted in 2006 as part of the Pension Protection Act and now extends into 2009.

If you'd like to explore this as a possible way to give to Cure Alzheimer's Fund, please contact **Tim Armour**, tarmour@curealzfund.org, or **781-237-3800**.

Our Website Got a Facelift—Check It Out

The new look includes video clips of our scientists describing their work and founders discussing the origins of Cure Alzheimer's Fund.



Financial Report

Inception in 2004 to Date (rounded to nearest \$1,000)

Total Funds Raised	\$10,445,000	100%
Allocated for Research	\$8,212,000	79%
<i>Distributed to research</i>	\$6,933,000	
<i>Budgeted for continued research projects</i>	\$1,279,000	
Reserve	\$500,000	5%
Administrative Expenses Paid for By Founders*	\$1,732,000	17%

Current Year to Date

Total Funds Raised	\$1,836,000
Distributed to Research	\$2,136,000

* All Administrative Expenses are paid for by the organization's founders: all non-founder donations go directly to fund research.

Research UPDATE

To date, we have funded **20 projects** in
10 major research labs.

In 2008, we funded **11 grants**,
including continuing projects.

3 additional projects are pending review
with planned distribution by December 31, 2008.

Visit www.curealzfund.org/research
for detail on research projects.

Help us fund research with the highest probability
of slowing, stopping or reversing Alzheimer's disease.

Donations can be made through our website www.curealzfund.org
or sent directly to our office.

For gifts of securities or direct wire transfers, please contact
Tim Armour at **877-CURE-ALZ (287-3259)** for further information.

Cure Alzheimer's FUND

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Mission Statement

To fund research with the highest probability of
slowing, stopping or reversing Alzheimer's disease.

Research Consortium

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CHARITY DESIGNATION

Cure Alzheimer's Fund® is a "doing business
as" name for the Alzheimer's Disease
Research Foundation, a 501(c)(3) public charity
with federal tax ID # 52-2396428.

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Edna Frances 'Tookie' Watts



Jesus Perez



Dorothy Mae Smith



Anne LaPorta



Cure Alzheimer's Fund received gifts in honor or in memory of the following in 2008.

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Research Consortium Dinner

Cure Alzheimer's Fund's Research Consortium gathered Nov. 16 in Washington, D.C., for presentations on funded research and a discussion of progress in Alzheimer's disease research.

(L to R) Dr. Rudolph Tanzi, Dr. Sangram Sisodia, Dr. Virginia Lee, Dr. David Holtzman, Dr. Sam Gandy (Consortium members not pictured: Dr. Charles Glabe and Dr. Ilyas Kamboh)

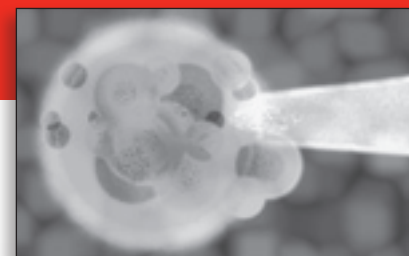


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It is critical to capitalize on recent research success.

Results of the Alzheimer's Genome Project™ are leading to better understanding Alzheimer's disease. Only by understanding the mechanisms of the disease can we get to a cure.

DONATE TODAY and give researchers the funding they need to end Alzheimer's disease.