



A Giant Step Forward: Cure Alzheimer's Fund Backs Whole Genome Sequencing

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the way in an exciting

new area of study that

is just in its infancy."

—Jeffrey Morby

Following the enormous success of its Alzheimer's Genome Project™ (AGP), Cure Alzheimer's Fund recently announced a new \$5.4 million grant to Massachusetts General Hospital to initiate a state-of-the-art whole genome sequencing (WGS) that will further reveal the genetic mechanisms of Alzheimer's disease.

It is the largest single private scientific grant ever invested in whole genome sequencing of families suffering from Alzheimer's.

Whole Genome Sequencing

WGS uses new technology to go beyond encoding genes to map out the entire genome—including the 98.5 percent that until very recently was widely regarded as "junk DNA." This is where many genetic switches controlling the genes are found, themselves triggered by other genes and by environmental inputs. It is a much wider approach than the previous genomewide association (GWAS) approach. While GWAS only can identify candidate genes that appear in at least 1 percent of the general population, WGS can find rarer genes—and instances where switches (as opposed to actual genes) are the culprit.

The new study, led by Rudy Tanzi, Ph.D., chairman of the Cure Alzheimer's Fund Research Consortium, will take 12 to 18 months. In that time, researchers hope to obtain the complete sequences of more than 1,500 subjects from about 400 families affected by Alzheimer's. The genomes of family members with Alzheimer's will be compared with the genomes of those who don't have Alzheimer's to identify the genetic sites that influence Alzheimer's risk.



L-R: Peter Slavin, president of MGH; Jeff Morby, chairman and co-founder of Cure Alzheimer's Fund; Henry McCance, director and co-founder of Cure Alzheimer's Fund; Rudy Tanzi, professor of neurology, Harvard Medical School, director, Genetics and Aging Research at MGH, and chair, Cure Alzheimer's Fund Research Consortium; and Merit Cudkowicz, professor of neurology, Harvard Medical School, chief of neurology, MGH, and head of MassGeneral Institute for Neurodegenerative Disease (MIND).

Importance of the Project

While the first phase of the Alzheimer's Genome Project™ determined *which* genes influence Alzheimer's, this new phase will determine *how* these genes confer increased risk of—or in some cases, protection against—the disease. "The data from the WGS initiative will drive much faster development of therapies, both to prevent the disease and arrest its progress," said Cure Alzheimer's Fund Chairman Jeff Morby. "This approach is highly efficient. While the dollar commitment is significant, the cost per discovery will be quite low."

Morby added: "We will be leading the way in an exciting new area of study that is just in its infancy. No one else in the private sector in this area of study will be on our timetable or have our sample size. It will make a huge contribution to the field and will definitely bring us closer to solving the mystery of Alzheimer's."

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The findings will not be proprietary, but will be made freely available to the scientific community worldwide. "We are taking advantage of cutting-edge technology to discover how our genes determine susceptibility to Alzheimer's disease," said Tanzi, "and will use this knowledge to guide drug discovery efforts."

This new effort also is perfectly in sync with larger national efforts, and is in keeping with the grand reach of Cure Alzheimer's Fund. "We are not focused on incremental progress, but instead are going for the 'long pass downfield' for a significant impact," said Morby. "Our projects have established new paradigms for understanding the very basic causes of Alzheimer's."

Find Out More About the WGS Project

Tune In to Our Next Free Webinar, Feb. 27

Please join us on Wednesday, Feb. 27, at 2:30 p.m. EST for a discussion about the Cure Alzheimer's Fund Whole Genome Sequencing Project and its expected impact on the disease. The interactive discussion will be moderated by David Shenk and will feature Rudy Tanzi, Ph.D.; questions will be encouraged from listeners. To register or for more information, visit www.curealz.org/webinar. ■

Calendars for a Cause

When Maggie Campbell's mother-in-law, Nancy Drapeau, was diagnosed with early-onset Alzheimer's disease last summer at age 59, Campbell decided she wanted to do something to help. Originally from Omaha, Neb., Campbell is a bookbinder and letterpress printer in Brooklyn, N.Y.

Inspired by her mother-in-law's garden in Dubuque, Iowa, Campbell designed and created a set of limited edition, handmade 2013 calendars and perpetual calendar books to raise money to fight Alzheimer's disease. The calendars are hand-printed and bound into an accordion-fold book designed for wall hanging. "Nancy is an incredible gardener and I wanted to use the Queen Anne's Lace I had gathered at her home for the cyanotype backgrounds," explains Campbell.

Campbell used Charity Navigator to find the right place to donate. "I was so happy to come across Cure Alzheimer's Fund. I

wanted to support an organization that was doing groundbreaking work and where the focus was so clear," says Campbell. "This whole project is an attempt to do something to mark a new path in all of our lives, and to give back in a way that is meaningful and lasting. It has been a labor of love."

If you're interested in purchasing a 2013 calendar, please visit <http://shop.brooklynbookbinder.com/collections/2011-calendars>.

\$15 from each calendar and \$5 from each book of days will be donated to Cure Alzheimer's Fund to support continued efforts to research, prevent and cure Alzheimer's disease. ■



Campbell's special-edition calendars.



Nancy and Charlotte (Maggie's daughter) in Dubuque, summer 2012.



Maggie (third from right) in Iowa with her in-laws and daughter.

We are very appreciative of Gerry's, Maggie's and the Cassidy family's efforts on behalf of our organization. Community support like this is critical to the success of our mission.

—Tim Armour, chairman and CEO of Cure Alzheimer's Fund

A Birthday Letter

When Gerry Nogelo of Vero Beach, Fla., turned 70 on Nov. 8, 2012, she only had one wish—to find a cure for Alzheimer's disease. So she mailed more than 40 letters to her friends and family asking them to make a donation to Cure Alzheimer's Fund in honor of her birthday. She wrote:

"I am asking you to consider sending a donation to Cure Alzheimer's Fund in honor of my 70th birthday. It would be the most important and blessed gift you could give to me. Every little bit will help find a cure."

Nogelo lost her mother, her aunt and her uncle to the disease. "They all started showing signs of the illness around age 75," explains Nogelo. "I took care of my mother for eight years and my aunt for 11 before they both passed away."



Gerry at her friend's home in Florida.

Nogelo found out about Cure Alzheimer's Fund through her friend, Phyllis Rappaport, co-founder of the organization. "Cure Alzheimer's Fund is very efficient and effective. Its scientists are able to use their time doing research instead of writing grant proposals, and the organization chooses its research recipients carefully. But a cure is still years away," explains Nogelo. "I know firsthand the amount of care that is needed and it requires a huge amount of resources. It's such a devastating disease and we have to find a cure." ■



Family Makes Donation for Christmas

Instead of exchanging Christmas gifts at their annual "Cassidy Swap" last Christmas, the Cassidy family decided to pool the money they would have spent on presents and donate it to Cure Alzheimer's Fund.

Peter Cassidy of Marblehead, Mass., age 77 and patriarch of the Cassidy clan, was diagnosed with Alzheimer's disease in 2008. He is the father of eight, grandfather of 21 and the great grandfather of two, ranging in age from 3 months to 30 years.

Cassidy's wife, Pam, recognized the Alzheimer's signs earlier than most would have, given that she had watched her mother, two aunts and an uncle all suffer from the disease years earlier. "I suspected early on that Peter had it when he began having trouble with bills, money and numbers, in addition to demonstrating other classic Alzheimer's behaviors. Peter realized he was making mistakes, but didn't know why."

After a bad experience with a neurologist who "insulted and frightened them," the Cassidys found Dr. John Growdon

at Massachusetts General Hospital. "Dr. Growdon was so kind and understanding, and he put us at ease." That's when the Cassidys first learned about Rudy Tanzi and Cure Alzheimer's Fund. "While I have always given to Alzheimer's disease funds, Cure Alzheimer's Fund is different," explains Pam Cassidy. "I know in my heart that every dime goes to research. Rudy and his team have an interest that goes far beyond lab work. They are on a heartfelt mission to find a cure."

Today, Cassidy is her husband's full-time caregiver. She can't leave him alone, but since most of his children and grandchildren live nearby, they support her as much as they can.



The Cassidy clan.

"If I need to go out, I send out an e-mail, and someone always offers to help." Fighting Alzheimer's disease has become a Cassidy family mission and for them, acting on behalf of a loved one was more gratifying than any present they might have received. ■

Financial Update

	This Quarter	YTD*	Inception to date
Fundraising	\$4,868,284	\$6,720,970	\$30,122,867
Expenses paid for by the founders	\$526,678	\$1,445,573	\$5,995,026
Funded research	\$1,000,000	\$3,375,343**	\$18,096,484

*Numbers shown are preliminary for the period.

**Because much of our 2012 support arrived in Q4, we expect to see a significant increase in our research funding in the first quarter of 2013.

Research Update

Research funded during the fourth quarter of 2012

Project	Researcher	Distribution Amount
Whole Genome Sequencing	Rudy Tanzi, Ph.D. Mass General/Harvard	\$750,000
Novel Soluble Gamma-secretase Modulators for the Treatment of AD	Steven Wagner, Ph.D. University of California, San Diego	\$150,000
Antibody Signature of Alzheimer's Disease: Promise of an Early Diagnostic Test	Lucas Restrepo, M.D. University of California, Los Angeles	\$100,000
Total Distributed to Research for 4Q 2012		\$1,000,000

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

Donations can be made through our website, www.curealz.org/donate, 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.

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Fund research with the highest probability of preventing, slowing or reversing Alzheimer's disease.

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FEATURED RESEARCHER

Giuseppina Tesco, M.D., Ph.D.



Each quarter we feature a researcher who has received funding from Cure Alzheimer's Fund. These profiles tell their story—their background, the research projects they're working on and why their research is important to finding a cure. Last quarter we heard from Research Consortium member Steven L. Wagner, Ph.D., project scientist, principal investigator, University of California, San Diego School of Medicine. This quarter we are featuring funded researcher Giuseppina Tesco, M.D., Ph.D., assistant professor of neuroscience, Alzheimer's Disease Research Laboratory, Department of Neuroscience, Tufts University School of Medicine.

Early Days

Born in Prato, Italy, in the heart of Tuscany, Giuseppina Tesco grew up with an older brother and two very open-minded parents. “My mother and father gave me a lot of freedom to make my own decisions about what interests I wanted to pursue,” says Tesco. “They were open to anything I wanted to do.”

Her interest in research began in high school when she would go to the library to study molecular biology, independently of what she was learning at school. “Molecular biology opened up a whole new universe for me and it made me want to know more.”

Education

After high school, Tesco went to the University of Florence, where she earned her M.D. and then Ph.D. in neuroscience. “In Italy we don’t have college, so I went directly to medical school and did my residency in neurology there as well. My medical training was critical, but it also made me realize that I preferred being in a lab more than working with patients,” says Tesco. While in medical school in Florence, she sought out a lab opportunity in the field of psychiatry, but there wasn’t one. However, the neurology department, one floor below, had a research opening in a lab studying Alzheimer’s disease (AD). Tesco jumped at the chance.

While she was finishing her residency, Tesco met leading National Institutes of Health (NIH) Alzheimer’s scientist Daniel Alkon, M.D., at a conference in Florence. He offered her an opportunity to do her post-doctoral training on a Fogarty Fellowship at NIH in Bethesda, Md. “The

work was similar to what I had been doing in Florence,” she says, “but I knew I would never have the same research opportunities in Italy as in the U.S.

“The move was really exciting for me,” she says. Tesco spoke only some English, but she learned quickly. At NIH she studied alterations of calcium levels in skin cells obtained from AD patients. Then she got a post-doctoral position at Massachusetts General Hospital working with Rudy Tanzi, Ph.D., to study the molecular aspects of Alzheimer’s disease in relation to its genetic components. “He has been a great mentor,” she says. “Rudy has always been dedicated to raising the next generation of scientists. I joined his lab as a post-doc and became an independent investigator in the unit that he is now directing.”

Cure Alzheimer’s Fund

In 2007, Tanzi asked Tesco to join Cure Alzheimer’s Fund’s research efforts to focus on a traumatic brain injury project. Since then, Cure Alzheimer’s Fund has supported two of her critical research projects: Traumatic Brain Injury and Stroke Relationship to Alzheimer’s Disease and Understanding the Role of the Gene ADAM10 in the Pathogenesis of Alzheimer’s Disease After Head Trauma.

Through her research, Tesco discovered a common pathway that is activated in

the brain when patients suffer from either Alzheimer’s disease or acute brain injuries. “It wasn’t enough for me to know that there was a correlation—I needed to know why,” she says. Now, she wants to understand why traumatic brain injuries sometimes lead to other neurodegenerative diseases such as Parkinson’s disease or chronic traumatic encephalopathy. “I believe that your genes determine both *if* you will develop a disease and *which* disease you might develop, but I still need to know more. Cure Alzheimer’s Fund’s unique approach supports innovative research that can be high risk, but it can also lead to some very important findings.” Her next goal is to understand the mechanisms that link acute brain injury to chronic neurodegeneration to help get closer to the prevention and cure for Alzheimer’s disease.

In 2009, Tesco took a position at Tufts University in the neuroscience department, which allowed her to combine her knowledge of cell biology with the kind of research that is based on neuronal activity. At Tufts she has studied the disease in mouse models and has done a deep study on neurons, which she calls a great opportunity to advance the science.

Personal Life

While Tesco doesn’t have any history of Alzheimer’s disease in her family, her father suffered a severe brain injury last year after he had a heart attack and fell. “He’s turning 80 and I’m very aware of what happens to elderly people who suffer traumatic brain injuries. But it’s also very important for people to know that the brain can heal itself—I’ve seen that with my own father. The brain has so many resources. We should never give up on the brain.”

When asked what she does outside of work, Tesco laughs and says, “I’m not a total nerd.” She enjoys dragging her friends to the observatory to look at the stars. She reads mystery novels, watches TV, travels and sails, but photography is her favorite hobby. She also likes to cook, but to be a good cook, she says, “you have to have the best ingredients—just like being a scientist.” ■

“I also go back to Italy as often as I can, and even though there is an ocean in between, my family still supports me. Being a scientist is like being a musician—I’m always thinking about my work, because it’s my passion.”



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Fall Symposium Recap

Last October, 150 people gathered at the Mandarin Oriental Hotel in Boston—and about 120 people tuned in to watch on the Web—to hear about the latest progress on the Alzheimer's research front with members of the Research Consortium. Researchers Rudy Tanzi, Ph.D., chair of the Cure Alzheimer's Fund Research Consortium, Sangram Sisodia, Ph.D., and Steve Wagner, Ph.D., presented their findings and discussed and debated the roadmap to Alzheimer's disease therapies. The symposium was moderated by David Shenk, author of the national bestseller *The Forgetting, Alzheimer's: Portrait of an Epidemic*, and the audience was encouraged to ask questions. "It's clear by the nature of the questions we received that people are becoming more and more educated on the challenges of getting to a cure. That's why continued support is more important than ever," says Tim Armour, chairman and CEO, Cure Alzheimer's Fund.

If you missed the symposium, visit <http://curealz.org/symposium> to watch it online and read questions and answers from the audience.

