Cure Alzheimer's FUND
targeting breakthrough research

Alzheimer's Disease Genes: How Many Do We Know and What Can We Do With Them?

Rudolph E. Tanzi, Ph.D., Joseph P. and Rose F. Kennedy Professor of Neurology, Harvard Medical School; Director, Genetics and Aging Research Unit, Massachusetts General Hospital

It is important to remember that all genes are "good"; it is only the variants in the DNA of these genes that can influence one's lifetime risk for a disorder such as Alzheimer's disease.

The four known Alzheimer's genes.

Over the past several decades, it has become increasingly clear that inheritance plays a major role in Alzheimer's disease.

The roughly 25,000 genes in the human genome are composed of deoxyribonucleic acid (DNA) packaged into 24 different chromosomes, 1–22, X and Y. A gene's job is either to make proteins or control the activity of other genes. Over many generations, the DNA of a gene can mutate to create a "variant." A very rare DNA variant is called a "mutation," while a variant that is common in the population is called a "polymorphism."

DNA variants allow for all of us to be a little different from each other. There are about 3 million variants that differ between any two individuals. Variants in certain genes can directly cause a disease like Alzheimer's, can increase susceptibility to disease or even can confer protection against disease. One's risk for most age-related diseases such as cancer, diabetes, heart disease, stroke and Alzheimer's is strongly influenced by our genes. For all of these age-related diseases, we know of mutations that guarantee onset of these diseases with no need for input from any other genes or environmental factors. And we know of polymorphisms that can increase (or decrease) one's susceptibility to the disease, but without guaranteeing onset of the disease. In this latter case, other genes and environmental factors usually work together to determine when and whether one will get disease. Any gene that can contain a variant(s) that significantly influences one's susceptibility to Alzheimer's, whether it be to guarantee the disease or serve to increase (or decrease) risk, is called an "Alzheimer's gene." It is important to remember that all genes are "good"; it is only the variants in the DNA of these genes that can influence one's lifetime risk for a disorder such as Alzheimer's disease.

In the 1980s and '90s, my laboratory co-discovered the three known genes that can carry mutations causing early-onset (younger than 60 years of age) familial Alzheimer's disease. These three genes, known as APP, PSEN1 and PSEN2, can harbor any of more than 200 different gene mutations that guarantee onset of Alzheimer's at a relatively early age with no need for additional input from other genes or environmental factors. These mutations are rare, accounting for only 1 percent to 2 percent of Alzheimer's cases. Inheritance of one of these mutations from just one parent virtually guarantees onset of Alzheimer's, usually by age 60. If a parent carries such a mutation, each child has a 50 percent chance of inheriting the same mutation and getting early-onset Alzheimer's disease with virtual certainty before age 60. Genetic testing is available for the early-onset Alzheimer's gene mutations, but is usually reserved for those who have a family history of early-onset Alzheimer's.

The fourth known Alzheimer's gene is APOE.

In the early 1990s, investigators at Duke University found that a common gene variant (polymorphism) of APOE, called epsilon 4, can increase risk for late-onset (older than 60 years of age) Alzheimer's disease. This variant is present in about 20 percent of the general population, but in greater than 50 percent of Alzheimer's patients. Unlike the early-onset AD gene mutations, this variant does not guarantee Alzheimer's, but only serves to increase risk. Inheriting one copy of the variant (from one parent) increases risk fourfold (vs. the general population), and two copies (from both parents) increases risk tenfold. Importantly, a person can inherit the APOE epsilon 4 gene variant from one or both parents and never get Alzheimer's in the span of a normal lifetime.

With regard to genetic testing for the common late-onset form of Alzheimer's, we are not yet able to do so reliably. This is because the APOE epsilon 4 gene variant is not sufficient on its own to predict one's risk for Alzheimer's reliably. Other genes and environmental factors need to combine with the APOE epsilon 4 gene variant to cause Alzheimer's. Some gene variants can exacerbate, while others mitigate, the risk for Alzheimer's conferred by the APOE epsilon 4 gene variant. We do not yet know the full set of gene variants that can increase or decrease risk for Alzheimer's when inherited together with the APOE epsilon 4 gene variant. Thus, APOE gene testing is not recommended as a sole means for predicting Alzheimer's risk. The other late-onset Alzheimer's genes must first be identified in order to reliably test for risk for late-onset Alzheimer's disease.

So how many other Alzheimer's genes are there?

We know that the four known Alzheimer's genes, APP, PSEN1, PSEN2 and APOE, account for roughly 30 percent of the inheritance of Alzheimer's. Thus, 70 percent of the genetics of Alzheimer's remains undefined. Cure Alzheimer's Fund (CAF) researchers and others have been engaged in comprehensive projects to find the other Alzheimer's genes. Once we have all of the Alzheimer's genes in hand, we will be able to more reliably predict one's lifetime risk for the common late-onset form of Alzheimer's disease. However, one might ask, "Why bother to

test if there is nothing we can currently do to prevent, stop, or reverse it?" This is certainly a fair question, since we still do not have drugs that stop the disease process in Alzheimer's. We only have drugs like Aricept and Namenda that modestly and temporarily alleviate the symptoms of cognitive decline, but without affecting the progress of the disease.

We need to find better, more effective therapies for Alzheimer's, but how do we get there?

First we need to identify all of the genes and variants involved in influencing risk for Alzheimer's disease. Studies of the known Alzheimer's disease genes have provided the vast majority of information being used to guide novel drug discovery aimed at preventing, stopping and maybe even reversing Alzheimer's disease. Every new Alzheimer's gene defect we find provides new clues regarding the cause of the disease and what we need to do to stop the disease. Thus far, all four genes have pointed to a small protein called "Abeta" as the cause. Abeta is normally made in the brain, but is found in excessive amounts in the brains of Alzheimer's patients, e.g., in senile plaques that litter the Alzheimer's brain around nerve cells. Small clumps of Abeta can gum up the connections between nerve cells known as synapses. Billions of nerve cells in the brain form trillions of synapses, making up our neural network. The neural network, in all its complexity, is needed for all brain function, including memory and learning. Excessive Abeta disrupts synaptic communication between nerve cells, leading to loss of memory and learning and eventually dementia. Dementia is defined as global and catastrophic cognitive failure; Alzheimer's disease is the most common form of dementia in the elderly.

Beyond the original four Alzheimer's genes.

Most drug discovery for Alzheimer's today is based on studies of the four original Alzheimer's genes. But we know there are many more Alzheimer's genes yet to be identified. Since 2005, CAF has supported a project called the Alzheimer's Genome Project™, carried out in my laboratory at Massachusetts General Hospital. The goal of this project is to study 5,000 families with multiple members who are affected with the common late-onset form of Alzheimer's disease in an effort to identify

all of the other Alzheimer's genes. In addition to the Alzheimer's Genome Project™, the International Genomics of Alzheimer's Project (IGAP), in which we are members, uses tens of thousands of individual Alzheimer's cases from the general population in the United States and Europe to find common DNA variants that influence risk for Alzheimer's. The family-based method of our Alzheimer's Genome Project™ and the population-based method of IGAP have identified some of the same Alzheimer's genes, but also find different ones with different effects on risk.

In the family-based studies of the Alzheimer's Genome Project™, we are able to find not only common DNA variants that influence one's risk for Alzheimer's, but also rare mutations that profoundly affect risk for the disease or directly cause it. The Alzheimer's Genome Project™ places a high priority on finding these rare but very potent gene mutations because, historically, among the four known Alzheimer's genes, it has been the rare early-onset familial Alzheimer's gene mutations that have been most effectively guiding drug discovery efforts. This is mainly because hard-hitting mutations have clear-cut adverse effects on biological systems, which can be elegantly recapitulated in animal models. This then allows for more effective drug discovery and development.

One of the first new genes to be identified in the Alzheimer's Genome Project™ was ADAM10.

This gene was specifically chosen for testing as a potential Alzheimer's gene because, like the four original Alzheimer's genes, it affects the production of Abeta in the brain. We identified two rare mutations in this gene that strongly predispose adults to Alzheimer's disease at around age 70. These two mutations were found in only seven of 1,000 AD families tested. Thus, they are very rare. We recently have demonstrated these two mutations dramatically impair the activity of ADAM10. ADAM10 normally blocks the production of Abeta. Accordingly, we have found these two rare mutations greatly enhance Alzheimer's amyloid pathology in animal-based models of the disease. With the validation of these mutations to be "pathogenic," or disease causing, the Alzheimer's Genome Project™ considers ADAM10 to be the fifth Alzheimer's gene.

Also beginning in 2005, with CAF support and as part of the Alzheimer's Genome Project™, we carried out the first family-based "genome-wide association study" for new Alzheimer's genes. This entailed a screen of the entire human genome in patients and their relatives in thousands of Alzheimer's families. The first phase of this study was completed in 2008 and led to the identification of more than 100 new Alzheimer's candidate genes. We reported the top four Alzheimer's candidate genes from this study in 2008; it was named by *TIME*/CNN to be one of the Top 10 Medical Research Breakthroughs of 2008.

The CAF Alzheimer's Genome Project™.

This was the first large-scale study of the human genome performed on the world's largest collection of families affected by Alzheimer's disease. It was also the first genome-wide study for Alzheimer's in the world to discover novel Alzheimer's gene candidates with statistically significant results and confirmation in thousands of subjects from families with a high incidence of Alzheimer's disease. The four new Alzheimer's genes reported by the Alzheimer's Genome Project™ in 2008 were ATXN1, CD33, GWA14Q34 and DLGAP1. ATXN1 is known to carry mutations that cause another neurodegenerative disease called spinal cerebellar ataxia, a movement disorder. We found that when this gene is inactive, Abeta levels increase dramatically, leading to cognitive decline in mouse models. Another gene, CD33, is perhaps the most interesting, since it controls the brain's innate immune system and inflammation in the brain. In a related study funded by Cure Alzheimer's Fund, Abeta was found to play a role in the brain's innate immunity system. CD33 regulates the brain's immune system and, concurrently, levels of Abeta. We now are developing CD33 as a drug target for Alzheimer's based on the genetic findings of the Alzheimer's Genome Project™. It should be emphasized that without the Cure Alzheimer's Fund Alzheimer's Genome Project™, we likely never would have guessed that genes like ATXN1 and CD33 might be involved with Alzheimer's.

As part of the current activities of the Alzheimer's Genome Project™, we now are testing these genes, as well as more than 100 other new Alzheimer's candidate genes coming out of our genome screen, to identify all of the DNA variants and mutations that influence risk for Alzheimer's in the 5,000 Alzheimer's families under study in the Alzheimer's Genome Project™. We specifically are searching for DNA mutations and variants in these genes that very strongly affect risk for onset of Alzheimer's. As new defects are found in these genes, we not only will increase our ability to reliably predict risk for Alzheimer's but, more importantly, we will garner new clues regarding the causes of Alzheimer's and, in doing so, gather new ideas and biological targets for novel drug discovery aimed at preventing, stopping and reversing the disease.

In the parallel screen for new Alzheimer's genes conducted by the IGAP, the DNA from tens of thousands of individual Alzheimer's patients was compared with the DNA of elderly subjects without Alzheimer's to find common variants that influence risk for Alzheimer's. In 2009, this led to the identification of four new Alzheimer's gene candidates called PICALM, CLU, CR1 and BIN1. More recently, in April 2011, IGAP found four more Alzheimer's genes called CD2AP, MS4A, EPHA1 and ABCA7. In addition, researchers found Alzheimer's risk to be influenced by the gene CD33, which first was reported by our Alzheimer's Genome Project™ in 2008.

It should be noted for the sake of clarity that the IGAP had stated in reports and press releases that it had increased the number of known late-onset genes from "five to ten." However, these numbers only pertained to studies of individual Alzheimer's patients in the general population, and not the family-based Alzheimer's genes reported by the Alzheimer's Genome Project™. The IGAP considered the original five late-onset Alzheimer's genes to be APOE, PICALM, CLU, CR1 and BIN1. It then considered the next five to be CD2AP, MS4A, EPHA1, ABCA7 and CD33. However, as mentioned above, CD33 already had been identified in our Alzheimer's Genome Project™ in 2008.

All the new Alzheimer's gene candidates reported by the IGAP carry common DNA variants that confer only tiny effects on risk.

Specifically, the new genes contain common DNA variants that are present in a large proportion (30 percent to 70 percent) of the general population, but only increase or decrease risk by a mere 10 percent to 20 percent. In contrast, the epsilon 4 variant in APOE, which is present in 20 percent of the population, increases risk by 400 percent to 1200 percent!

With regard to the CD33 gene, which was identified as an Alzheimer's gene in both our Alzheimer's Genome Project™ in 2008 and the IGAP in 2011, each project actually discovered different Alzheimer's-associated DNA variants in this gene. In our family-based Alzheimer's gene study, we originally reported a relatively uncommon variant in CD33 that increases risk for Alzheimer's in a subset (fewer than 100) of the 5,000 Alzheimer's families we studied. In contrast, the IGAP discovered a very common variant in CD33, present in about 50 percent of the population, that conferred only marginal protection against Alzheimer's (decreasing risk by only 11 percent). The fact that we now know of two different Alzheimer's-associated DNA variants in the CD33 gene from multiple Alzheimer's samples increases the odds that CD33 is a bona fide Alzheimer's gene.

As with all of the new genes found in the genome-wide association screens of the Alzheimer's Genome Project™ and IGAP, the next critical step is to identify all of the DNA variants and mutations in these genes that increase or decrease risk for late-onset Alzheimer's disease. CAF continues to support these efforts. We currently are screening more than 100 new Alzheimer's candidate genes found in the Alzheimer's Genome Project™, along with those found in the IGAP, to identify all of the DNA variants and mutations in these genes that influence risk for Alzheimer's disease. Elucidating the full deck of Alzheimer's-associated gene variants and mutations is necessary to fully understand all of the biological processes that are affected in Alzheimer's disease. This will give us the best odds of reliably predicting the disease early in life (with appropriate counseling and legal protection). But, most importantly, the full set of Alzheimer's genes and the knowledge of how they biologically influence risk for disease will continue to provide the most critical information needed to guide the development of new and effective therapies aimed at preventing, stopping or reversing Alzheimer's disease.

Finally, it should be noted that even if a DNA mutation in an Alzheimer's gene is rare or restricted to a small subset of families, most researchers think new drugs

A Journey to Remember

Glenn Caffery Runs Coast to Coast to Honor His Father's Memory and to Raise Money for Alzheimer's Research

On May 19, 2011, Glenn Caffery, age 49, set out from Seaside, Ore., to run 3,312 miles across the country to Westerly, R.I. He is running to honor his father—Dick Caffery—whom he lost to Alzheimer's disease in 2002, and to raise money to help find a cure for this devastating illness. "Watching my father suffer made me feel so helpless," says Caffery. "Since he's passed away, I've felt like I needed to do something to help, and running across the country felt like something."

The diagnosis.

Caffery's father was diagnosed with early-onset Alzheimer's at age 55 in 1989. At the time, neither Glenn, his mother or his two sisters had any knowledge of the disease. According to Caffery, "my father was always high performing and good at masking his symptoms, so none of us ever suspected anything." For a couple of years he says his dad seemed to be his same old loving dad, except for his memory issues, but then his progression was pretty rapid. He stopped sleeping and became increasingly agitated and paranoid. "My mom bore much more than she ever should have," says Caffery. "But she was always a passionate advocate for my dad, as were many of his friends."

A cause close to his heart.

A seasoned long-distance runner, Caffery recently underwent surgery for his arthritic hip. With the school year ending at UMass Amherst, where he teaches in the Department of Resource Economics, he decided the time was now or never. "When my dad was alive," he says, "I was really busy with my family and my job. When he died I wasn't able to process the whole experience. A big element of my cross-country run is to finally have a chance to do that." Caffery is hoping to meet people from all walks of life who have been touched by Alzheimer's and hear their stories.

The run.

Caffery has run his share of marathons and his body has naturally good endurance, but this run is different— both physically and mentally. His plan is to run about 50 miles a day for 10 weeks at what he calls a comfortable pace, and finish at the end of July. "You can't train to run 50 miles a day," he says, "but a lot of conditioning will happen in the early stages of my run. Unlike a marathon, which takes a toll on the body, this kind of running— 'ultra running'—respects your body more." He has mapped out his route across the United States and will stop in Minneapolis and Ann Arbor, Mich., where his two daughters live, and in Wallingford, Conn., where his mother still resides. He will be running with no support, using only a jog stroller for supplies and camping equipment and staying with friends or people he meets along the way.

Why Cure Alzheimer's Fund?

"I'm stunned by how little money goes to Alzheimer's research given the magnitude of the pain, the burden and the numbers of people who suffer from it," says Caffery. "I chose to donate all the money I raise to Cure Alzheimer's Fund (CAF) because every single dollar will go to fund research." Because of his father's experience with Alzheimer's, Caffery is incredibly motivated to stop Alzheimer's so it doesn't affect his daughters. "It's been frustrating how many dead ends there have been, but in the last few years it seems like we've turned a corner," he says. His wife, mother, sisters and daughters are all supporting him in their own ways and, says Caffery, "my dad will always be with me as well." ■

As of June 20, Caffery was in Wyoming, heading for South Dakota. You can follow his progress at **alzrun.org** and join his fundraising efforts by making a donation to Cure Alzheimer's Fund at **www.curealzfund.org/donate**.

Running4Answers Makes Huge Strides for Cure Alzheimer's Fund

The second annual Running4Answers road race, held in Roseland and Essex Fells, N.J., in early April, was another incredible success—thanks to Carolyn Mastrangelo and Barbara Geiger, co-founders and organizers of the event. This four-mile race brought families together to honor loved ones whom they had lost to Alzheimer's and helped to raise money toward finding a cure. This year donations increased 30 percent to an amazing $30,000!

Carolyn and Barbara already are talking about how to take Running4Answers to the next level, and we thank them for their dedication to CAF. For more information, check out www.racingnj.com/Results.html. ■

Alzheimer's Disease Genes: How Many Do We Know and What Can We Do With Them?

continued from page 3 »

or therapies for Alzheimer's based on what is learned from that mutation will be useful in preventing and treating all cases of Alzheimer's. As noted above, in the Alzheimer's Genome Project™, we place a high priority on family-based gene studies of Alzheimer's, since there we have the highest odds of finding DNA mutations with very strong effects on risk for Alzheimer's, akin to those of the early-onset familial Alzheimer's disease gene mutations discussed above. These mutations are most useful for driving successful drug discovery, since their biological effects on the disease process are of much greater impact and more clear-cut in terms of mechanism by which they cause disease. They also lend themselves to more useful animal models for drug testing. Ultimately, the full list of Alzheimer's genes emerging from the family-based genetic studies of the Alzheimer's Genome Project™ and the population-based studies of IGAP are getting us closer and closer to someday being able to eradicate Alzheimer's disease using a strategy of early prediction and early intervention. ■

Alzheimer's Genes Identified to Date (Total of 17): Early-onset familial Alzheimer's disease genes (onset before age 60):

APP (1987)*

PSEN1 (1995)*

PSEN2 (1995)*

Late-onset genes (onset after age 60):

APOE (1993)

ADAM10 (2008)**

ATXN1 (2008)**

CD33 (2008)**

GWA14Q34 (2008)**

DLGAP1 (2008)**

PICALM (2009)***

CLU (2009)***

CR1 (2009)***

BIN1 (2010)***

CD2AP (2011)***

MS4A (2011)***

EPHA1 (2011)***

ABCA7 (2011)***

* Co-discovered in Tanzi laboratory

** Discovered by the Cure Alzheimer's Fund Alzheimer's Genome Project™ in Alzheimer's families—these genes are expected to contain DNA variants that significantly increase risk for Alzheimer's.

*** Discovered by the IGAP—these genes are expected to contain DNA variants that are common in the general population but that have only tiny effects on risk for Alzheimer's.

N.B. The Alzheimer's Genome Project™ also has discovered more than 100 additional Alzheimer's candidate genes that are in the process of being confirmed and validated. In addition, Cure Alzheimer's Fund supports a website called AlzGene (alzgene.org), in which we are tracking all of the Alzheimer's candidate genes reported in the scientific literature, including their ongoing testing for confirmation as bona fide Alzheimer's disease genes.

With regard to functional effects, the above list of 17 Alzheimer's genes can be divided into four major categories based on their known or predicted biological effects on Alzheimer's risk:
1. Production and clearance of Abeta: APP, PSEN1, PSEN2, APOE, ATXN1, CD33, CLU, ADAM10, PICALM, CD2AP
2. Cell signaling and protein trafficking: PICALM, BIN1, EPHA1, CD2AP, DLGAP1
3. Cholesterol metabolism: APOE, CLU, ABCA7
4. The innate immune system and inflammation: APOE, CD33, CLU, CR1, MS4A4, EPHA1, BIN1

Cure Alzheimer's Fund Expands Its Team

After five years as a start-up organization, Cure Alzheimer's Fund (CAF) is entering a new phase of growth and development. Our research agenda is more ambitious than ever, with projects leading to new research that brings us closer to a cure.

Our more ambitious research agenda requires the need for greater capacity to identify and manage new funding sources. In addition to Julie Winton, our marketing and development associate who joined us a few months back, the founders of CAF have enthusiastically agreed to fund two additional senior, experienced nonprofit managers and fundraisers to help drive our success through the next five years. As has been the case in the past, the founders will cover all expenses incurred in this expansion, with all third-party contributions going directly to research.

The New Team

We are delighted to welcome the following contributors to the CAF team. We are very lucky to have them with us.

Julie Winton, Marketing and Development Associate, CAF

With demonstrated success in marketing content and design, event planning and promotional strategies, Julie will take the lead for CAF in our social media outreach, communications program and administrative operations. With 10 years of experience at such firms as Lotus Development Corp., Acacia Marketing Group and PI Worldwide Inc., Julie is a welcome addition.

Sally Rosenfield, Senior Vice President, CAF

For the past decade, Sally has held senior and managing director positions in the nonprofit sector—most recently with Hadassah, the largest women's volunteer organization in America, and prior to that with Camp Ramah, the informal education arm of the Conservative movement of Judaism. At both organizations, Sally successfully managed the entire enterprise and built membership, participation and fundraising. We welcome her expertise and passion for service.

Mike Curren, Senior Vice President, CAF

Mike joins us from the Massachusetts Hospital Association, where he was senior vice president for operations and member relations. Prior to that, Mike was vice president for the Northern Division of the American Diabetes Association and executive director and area director for the March of Dimes Birth Defects Foundation in New England. Mike is a certified association executive with experience and achievement in all areas of nonprofit management and fundraising. He has taught nonprofit management and development at the graduate school level and has been involved with a variety of constituencies generating resources for his organizations from a variety of sources.

All of these professionals have strong entrepreneurial instincts and track records, accolades from past colleagues and constituents and unquestionably deep commitments to causes they care about. Julie, Sally and Mike join Laurel Lyle, CAF's director of fundraising programs; Karen Robertson, our bookkeeper; and Tim Armour, president and CEO. We look forward to an exciting and productive next few years! ■

THE NEXT FRONTIER
ONE MIND FOR BRAIN RESEARCH

On May 23–25, 2011, the inaugural Next Frontier conference was held at the Sheraton Hotel in Boston and featured presentations from America's pre-eminent researchers, clinicians, scientists and policy makers outlining a new road map to unlock the mysteries of the mind and serve as a national call to action for dramatic increases in funding and coordination of brain research.

Rudi Tanzi, chairman of CAF's Research Consortium, was on the planning committee and both Jeff Morby, chairman and co-founder of CAF, and Tim Armour, president and CEO of CAF, attended, along with several members of CAF's

Research Consortium, including David Holtzman, M.D., Washington University School of Medicine; and Roberto Malinow, University of California, San Diego. Senior members of the federal government also were represented, including Dr. Francis Collins, director of the National Institutes of Health, and Vice President Biden.

The goal of the conference is to raise $500 million each year from private philanthropy and $1 billion per year from the government over the next 10 years. You can read about the detailed ten-year plan at www.1mind4research.org. ■

Financial Update

	2nd Quarter*	YTD 2011	Inception to date
Fundraising	$191,336	$910,710	$19,960,252
Expenses paid for by the founders	$148,448	$275,945	$3,836,048
Funded research	$0	$500,000	$13,171,141

These numbers are as of June 6, 2011

Marathon for Cure Alzheimer's Fund

On Sunday, May 29, Brian Gray ran the Vermont City Marathon alongside his father to honor the memory of his maternal grandmother, who passed away in 2003 from Alzheimer's disease. Despite the hot, sticky weather, Brian and his dad managed to finish the race in less than four hours—their personal goal—as 30,000 race attendees cheered them on. Brian and his father also met their fundraising goal and raised more than $2,000 for Cure Alzheimer's Fund. We congratulate them on their achievement and thank them for their commitment to our cause. ■

Jim and Brian Gray on race day

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/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.

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

Research Consortium
Rudolph E. Tanzi, Ph.D., Chairman, Research Consortium, Harvard Medical School/ Massachusetts General Hospital
Sam Gandy, M.D., Ph.D., Mount Sinai School of Medicine
Charles Glabe, Ph.D., University of California, Irvine
David Michael Holtzman, M.D., Washington University, St. Louis
M. Ilyas Kamboh, Ph.D., University of Pittsburgh
Virginia M.-Y. Lee, Ph.D., MBA, University of Pennsylvania
Robert C. Malenka, M.D., Ph.D., Stanford University
Roberto Malinow, Ph.D., University of California, San Diego
Sangram S. Sisodia, Ph.D., University of Chicago
Thomas C. Südhof, M.D., Stanford University

Scientific Advisory Board
Caleb Finch, Ph.D., University of Southern California
Paul Greengard, Ph.D., The Rockefeller University
John S. Lazo, Ph.D., University of Pittsburgh
John C. Mazziotta, M.D., Ph.D., UCLA
Marsel Mesulam, M.D., Northwestern University

Board of Directors
Jeffrey L. Morby*, Pittsburgh, PA, Chairman
John S. Lazo, Ph.D., Pittsburgh, PA
Henry F. McCance*, Boston, MA
Jacqueline C. Morby*, Pittsburgh, PA
Phyllis Rappaport*, Boston, MA
Tim Armour, Wellesley Hills, MA, President
*Founder

Administration
Tim Armour, President
Mike Curren, Senior Vice President
Sally Rosenfield, Senior Vice President
Julie Ann Winton, Development and Communications Associate
John Epeneter, Controller
Laurel Lyle, Manager, Fundraising Programs
Karen Robertson, Accountant

Cure Alzheimer's FUND

34 Washington Street, Suite 200
Wellesley Hills, Massachusetts 02481

877-CURE-ALZ (287-3259) • www.curealzfund.org

Alan Summits Everest!

After two previous attempts to summit Mount Everest, the highest peak on Earth, Alan Arnette finally succeeded on May 26, 2011. Everest was the third stop on his 7 Summits Climb for Alzheimer's: Memories are Everything campaign—in which he plans to climb the highest peak on each continent to raise money to fight Alzheimer's. Although his journey is certainly not all downhill from here, summiting Everest is a significant milestone that Arnette now can look back on with a smile.

"It has been a wonderful experience that can be summarized in one word—humbling," says Arnette. "The summit was nice, but my climbs are all about the cause. I want to thank my followers for their support, and more importantly for their generous donations." He heads for Mount McKinley or Denali (Koyukon Athabaskan or "The High One") in Alaska next and planned to depart on June 25, 2011. ∎

To support him in his efforts, make a donation at www.curealzfund.org/7summits, www.alanarnette.com/ or www.climb4ad.com/campaign-overview.

Alan Arnette on the summit of Mount Everest, May 26, 2011

Arnette pointing out his signature on the Rum Doodle Everest summitter board.