



Two Sides to Abeta

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For the last 27 years, Abeta, a fatty protein that is created in the brain, has been identified as the leading cause of Alzheimer's disease. As a result, the majority of efforts aimed at developing a cure have targeted Abeta as the enemy. But recent studies have indicated that simply wiping out Abeta in the brain is not the solution.

Everything in moderation.

While too much rain can cause flooding, not enough can cause a drought. Yet nature depends on rain for its very existence. Similarly, studies have shown that Abeta, previously thought to be an unequivocal "bad guy" in Alzheimer's pathology, may play a pivotal role in the brain.

"Too much Abeta in the brain acts like a plugged-up kitchen sink," explains Rudy Tanzi, Ph.D., Harvard Medical School/Massachusetts General Hospital and chairman of Cure Alzheimer's Fund Research Consortium. Treating an overabundance of Abeta means either slowing production (fixing the leak) or hastening clearance (unclogging the drain).

"Too much Abeta creates plaques and tangles, which kill brain cells, choke synapses, impair cognition and lead to Alzheimer's," says Tanzi.

On the other hand, explains Robert Moir, Ph.D., Harvard Medical School/Massachusetts General Hospital, "not enough Abeta can impair the body's natural immune system." In its non-toxic form, Abeta appears to be a vital antimicrobial peptide (a portion of a protein) that protects the body from deadly infections. In fact, one experimental drug that eradicated Abeta in the brain led to meningitis, a deadly side effect.

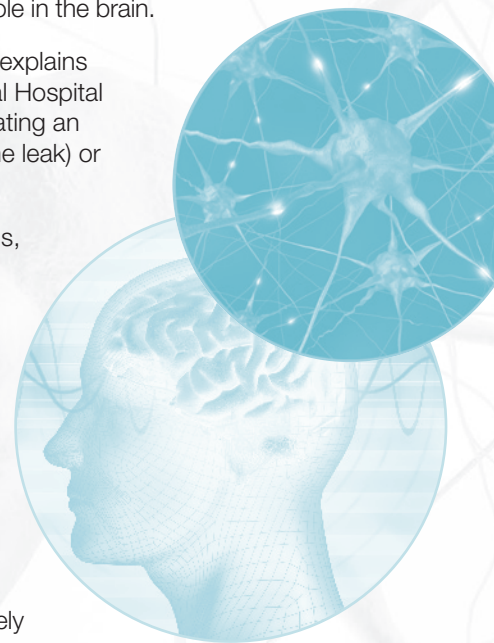
In finding a cure for Alzheimer's, researchers are working to determine how to keep Abeta production at safe levels without completely wiping it out, which makes drug discovery that much more complex.

Statins.

When scientists first discovered that too much cholesterol in the blood caused heart disease, high cholesterol became the target. But scientists also learned that while an overproduction of LDL (low-density lipoproteins) is life-threatening, HDL (high-density lipoproteins) are important for keeping people healthy. Like Abeta, eliminating cholesterol completely was not the answer.

As a result, scientists developed statins, such as the drug Lipitor, to reduce the risk of heart disease. By controlling cholesterol production, cases of heart disease have dropped substantially. "We need the equivalent of a 'statin' for Alzheimer's disease," says Tanzi.

Today, Cure Alzheimer's Fund is funding research on a class of drugs called gamma secretase modulators involved in the production of Abeta—to modulate production within tolerable limits without eliminating it altogether—the same type of function that statins perform for cholesterol. The goal is to develop a drug that can lower the incidence of Alzheimer's the way statins did for heart disease.



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Two Sides to Abeta

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Taking control of Alzheimer's through research.

At Cure Alzheimer's Fund's symposium in October, Tanzi and Moir discussed both the dangers and benefits of Abeta. Moir acknowledged the importance of CAF's funding in the work toward finding a cure.

"The public funding environment is so risk-averse that you can't get funding for critical, cutting-edge research, which is what we need to get to a cure," he says. Tanzi adds, "Without CAF support, we might never have known, or not known for a long time, that Abeta may be performing a beneficial or even vital role when its production and clearance are balanced effectively in the brain."

Tanzi adds that, "While CAF has provided tremendous support for research, we still need more. With the funding we have today, we can only tackle 2 to 5 percent of our top priorities. Alzheimer's disease is unique in that it's not science constrained, it's budget constrained."

One thing is certain.

The "two sides of Abeta" demonstrate clearly the importance of basic research for the development of truly effective therapies. Drugs based on just one understanding or the other will not work effectively and may even prove to be harmful. But finding a cure requires both time and money, neither of which there is enough of today.

Since we can't control time, the threat looming over the 71 million baby boomers headed toward the high-risk ages for Alzheimer's disease makes funding more critical than ever.

For more information on the pros and cons of Abeta, visit www.curealz.org/symposium. ■

CAF Symposium Recap

Thanks to a dynamic panel and more than 175 supporters, our Fall Symposium—*Taking Control of Alzheimer's Through Research*—was a huge success. Out-of-towners interested in the topic were able to watch it live on the Web.

"The goal of the symposium was to educate people about the latest breakthroughs in Alzheimer's research and to broaden our reach to raise awareness for Cure Alzheimer's Fund," says Tim Armour, president and CEO of Cure Alzheimer's Fund. "We accomplished both."

"It's clear that CAF is on to something, but it's also clear that the funding is simply not there at the government level to find a cure in the next decade."

The symposium was moderated by Robert Bazell, chief science and health correspondent, NBC News. Panel members included: Rudolph Tanzi, Ph.D., Harvard Medical School/Massachusetts General Hospital and chair, CAF Research Consortium; Robert Moir, Ph.D., Harvard Medical School/Massachusetts General Hospital; and



From left, Robert Moir, Rudy Tanzi, David Shenk and Robert Bazell at the symposium in October.

David Shenk, author of the national bestseller *The Forgetting, Alzheimer's: Portrait of an Epidemic*.

Attendees included caregivers and family members of those suffering from Alzheimer's disease as well as scientists and medical researchers. The audience was able to submit questions that were answered directly by the panel.

Judy Brand, an avid supporter of Cure Alzheimer's Fund, watched the webcast of the symposium. "It's clear that CAF is on to something, but it's also clear that the funding is simply not there at the government level to find a cure in the next decade," she says. "It's up to us in the private sector to make a difference and help raise the funds needed to stop the very onset of Alzheimer's disease."

The symposium can be viewed in its entirety on our website, and the questions and answers have been published at www.curealz.org. ■

**Don't Miss Our Upcoming Webinar:
Two Sides of Abeta for the Layperson**
Wednesday, Jan. 25, 2012, 1 p.m.

Join David Shenk, Rudy Tanzi, Ph.D., and Rob Moir, Ph.D., for a look at Abeta and its implications in the work toward a cure for Alzheimer's disease. Details of how to join will be posted on our website, www.curealz.org.

One Personal Story Goes Public

With a surge of baby boomers hitting retirement age, everyone seems to know someone who has been affected by Alzheimer's disease. But Bob DeMarco, a former Wall Street entrepreneur turned at-home Alzheimer's caregiver for his mother, has taken his experience one step further.

The Alzheimer's Reading Room.

In 2007, DeMarco created the Alzheimer's Reading Room—a blog about the challenges of being an Alzheimer's caregiver that offers insight, support and advice on tackling real issues around caregiving. Today, the blog has such a strong following it has become a top source of life news for the Alzheimer's community. This informative online hub culls the latest information on medical science, wellness and the art of Alzheimer's caregiving into one trusted resource.

Says DeMarco, "Alzheimer's caregivers are often thrust into their roles with little or no experience, training or education about the disease. As a result, they are often overwhelmed and suffer from feelings of helplessness. As I began acquiring valuable information about how to care for my mother, it occurred to me that I could help the 15 million Alzheimer's caregivers worldwide by personalizing my own experience and sharing what I had learned."

From entrepreneur to caregiver.

In 2003, with 20 years of working on Wall Street behind him, DeMarco was running a small software company in Reston, Va. That's also when his mother, Dorothy, at age 87, began to have health issues.

"I knew something was wrong, but I didn't know what," DeMarco says. "After spending about 10 days with her, I realized that she needed full-time care. So I quit my job, moved into her 1,250-square-foot condo in Florida with her, and dropped out of the world."

Together, DeMarco and his mother went to see four different doctors, and the first three told them the same thing. "She's just getting old," they said, but DeMarco knew it was something more. "Her behavior had changed," he explains. "She went from being a really nice, socialized person to

being mean and negative. She stopped having lunch with her friends and going to the pool, and she scraped her feet on the pavement when she walked. I knew this was more than just old age."

The fourth doctor gave his mother a prescription for Aricept, to slow down memory loss, and later on, Namenda, to help with her worsening dementia. Today, Dotty DeMarco uses a combination therapy, which DeMarco says helps.

"She doesn't always search around for things the way she used to, and she isn't as antsy. The medications, along with our routine, has improved her behavior and allowed us to live a 'fuller,' more productive life."

When DeMarco began taking care of his mother eight years ago, he started sharing his personal experiences on his blog. "Once I realized that most caregivers experience similar problems, I was able to make my blog more useful to my readers," he says. At first, he got an e-mail here and there, but soon he began receiving e-mails from Alzheimer's caregivers all over the world. In November 2011, the Alzheimer's Reading Room had more than 50,000 visitors—and awareness of the site continues to grow.

Dorothy at 95.

"My mother has improved dramatically since I moved here," says DeMarco. At 95, she still walks without a walker. DeMarco takes his mother to the gym to work out with weights and walk on the treadmill. "She is much more alert and happier now," he says.

"People living with Alzheimer's can do a lot more than most people can imagine," DeMarco says. He and his mother often go to Walmart, where she drives the cart around the store. "She has to use her hands in coordination with her brain and she can drive that cart perfectly," he says.

They also go to an outdoor bar and sit outside and eat, since "bright light helps tremendously." The staff has gotten to know Dotty DeMarco there and people often come up and talk to her. She can recognize them if she's known them for a long time, but she rarely remembers names.



Dotty DeMarco at her home in Florida.

"She used to be a pretty social lady," DeMarco says, "and that part of her is still there. She likes to tell stories that are loosely based on facts and her experience. Although she doesn't always get the facts straight, telling these tall tales is what's important."

Together, DeMarco and his mother took care of his father for 11 months before he died of brain cancer. "She and I became close friends during that period," he says. "From that moment, I decided that if something happened to my mother, I was going to take care of her. I didn't know anything about Alzheimer's in 2003 or what taking care of her entailed, I just went into action. I don't see taking care of my mother as a sacrifice. I chose to do this."

Cure Alzheimer's Fund.

A few years ago, DeMarco read something about Henry McCance, which led him to Cure Alzheimer's Fund. That's when he began following CAF's progress. "Cure Alzheimer's Fund gives me hope," says DeMarco. "Because of my background on Wall Street, I really believe in the venture philanthropy approach, and I think that Rudy Tanzi might just be the guy who hits the ball over the fence. If someone is looking to donate money toward Alzheimer's research, CAF is the number one place to give, since 100 percent of donations go toward finding a cure."

For more information on the Alzheimer's Reading Room, visit www.alzheimersreadingroom.com. ■

Every 69 seconds someone is diagnosed with Alzheimer's disease. If you haven't made a contribution recently, now's the time. Make an end-of-year, tax-deductible donation today. As the founders pay all overhead costs, 100 percent of your donation goes directly to Alzheimer's research.

Financial Update

	This Quarter	YTD*	Inception to date
Fundraising	\$872,123	\$2,143,197	\$21,192,559
Expenses paid for by the founders	\$259,189	\$828,298	\$4,388,467
Funded research	\$50,000	\$1,852,500	\$14,521,141

*These numbers as of Dec. 5, 2011

Research Update

Total Distributed to Research in 2011: **\$1,800,000**

At press time we have received six proposals for a total of \$1 million for the fourth quarter. These proposals are under review and will be reported on in our first quarter 2012 report.

For detailed information on our funded investigations, please refer to the "Research" section of our website at www.curealz.org.

Find Out More About Our Progress

Visit www.curealz.org for information on ordering a copy of our latest publication, *Alzheimer's Disease: The Science*, written by Jeff Morby and Rudy Tanzi of CAF. This piece discusses the latest state-of-the-art findings on Alzheimer's research, including scientific breakthroughs, potential new therapies and a vision for going forward. Copies are \$10 each and all proceeds go straight to research.



Cure Alzheimer's FUND

34 Washington Street, Suite 200
Wellesley Hills, Massachusetts 02481
Telephone: 877-CURE-ALZ (287-3259)
Fax: 781-658-2399
www.curealz.org

Henry W. Oliver Building
535 Smithfield Street, Suite 625
Pittsburgh, Pennsylvania 15222
Telephone: 412-261-2785

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
Virginia M.-Y. Lee, Ph.D., MBA, University of Pennsylvania
Robert C. Malenka, M.D., Ph.D., Stanford University
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Contributing Writer: Patty Bovie
Copy Editor: Colleen O'Neill
Design: Winking Fish

A Year to Reflect On

With his Seven Summits Climb for Alzheimer's: Memories Are Everything expedition now complete, Alan Arnette finally has his feet planted firmly on the ground.

In October, he summited Mount Kosciuszko in Australia and the Carstensz Pyramid in New Guinea, after scaling each of the highest peaks on the other continents. His goal was to honor the memory of his mother, whom he lost to Alzheimer's in 2009, and to raise money toward finding a cure.

Final two summits.

Of all Arnette's climbs this past year, the Carstensz Pyramid was the most technical. This 16,023-foot rock climb required him to hang upside down on a cable in mid-air. Arnette's biggest challenge was not the climb itself, but navigating the politics of thousands of miners who were on strike at the base of the mountain.

Kosciuszko is the base of a ski resort and the highest peak on the mainland of Australia at 7,000 feet. "Kosciuszko was a low-drama mountain and a tremendous amount of fun to climb," says Arnette.

Looking back.

"I feel gratified that the Seven Summits campaign accomplished the awareness and education objectives we set out to attain, including a message of hope, need and urgency," Arnette says. He is also deeply grateful to all of those who have contributed to the cause*, although the dollar amount is not yet where he hopes it will be. Arnette's journey has given him a deep sense of accomplishment in helping to get the frightening realities of Alzheimer's disease on people's radar.

*The Alzheimer's Immunotherapy Program of Janssen Alzheimer Immunotherapy and Pfizer Inc. funded Arnette's journey, which allowed him to dedicate 100 percent of the money raised directly to Cure Alzheimer's Fund, the National Family Caregivers Association and the Alzheimer's Association.

The future.

With mountain climbing in his blood, Arnette will continue to climb on a personal level. He also hopes to return to Denali (Mount McKinley) in Alaska, in an attempt to summit in order to honor the campaign. "I don't think it's OK just to give up on Denali just because the weather was bad. Like fighting Alzheimer's disease, you can't give up on something just because it's hard."

Seven Cities tour.

Arnette also plans to take his experiences on a Seven Cities speaking tour, in which he will share his experiences and continue to raise awareness and funds to fight Alzheimer's. "The fact that the financial equation is upside down—only one penny out of every dollar spent on Alzheimer's goes toward finding a cure—and the cost of caring for an Alzheimer's patient is going to devastate Medicare and Medicaid, brings a sense of urgency that I'm not sure people totally understand. It's important to get that message out."

Despite what Arnette has accomplished, he says, "there's a phenomenal amount of work ahead. My goal is to leverage the momentum we've built and continue to raise awareness and funds toward finding a cure. We still have a huge mountain to climb. I have been honored to work to raise money for CAF and will continue to do so. I thank them for their devotion and commitment to finding a cure." ■

Alan had to remember to drive on the left and look out for 'roos!



Alan preparing to cross a 50-foot gap 16,000 feet high on Carstensz Pyramid.



Alan with local kids at the remote Papua village of Bilogia.

The Numbers

12 million people reached
800,000 online supporters
85,000 feet climbed
120 time zones crossed
19 different airlines flown
8 summits climbed
7 months away from home
1 cause

Local Heroes

Supporting CAF and the Fight Against Alzheimer's

Softball On Oct. 16, members of both the Wellesley Police Department and the Wellesley/Weston Chabad Center joined forces for a charity softball game in Wellesley, Mass., CAF's headquarters. The event raised almost \$500 for CAF. We thank them for their contribution and commitment to our cause.



Participants in the charity softball game.

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Local Heroes Supporting CAF and the Fight Against Alzheimer's

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Hair Barbara Canty sees hundreds of clients weekly in her salon, The Color Studio, in Wellesley, Mass. Five years ago, her father was diagnosed with Alzheimer's disease, and her experience caring for him made her realize that education and funding are critical to finding a cure.

Putting the professional and the personal together, Canty thought of Colin Walsh, vice president of L'Oréal, and Dr. Lew Losoncy, who co-wrote *On*, an inspirational book that Canty says encouraged her to turn her life "on," when Alzheimer's patients are forced to live their lives in "off" mode. As a passionate advocate for finding a cure for Alzheimer's, Canty reached out to Walsh, who donated 100 copies of his book so Canty could sell them in her salon. Fellow hairdresser Karen Ricci, who also has a parent with Alzheimer's, has joined Canty in this effort. One hundred percent of the book sales go toward Cure Alzheimer's Fund, and the salon has raised \$370 to date. We thank The Color Studio for their support.

Barbara Canty with a copy of On at her salon.



Swim On Oct. 22, Jessica Wellman swam her second annual 5K in 2½ hours to support Cure Alzheimer's Fund.

"My decision to swim for CAF is both professional and personal," Wellman says. She spends most of her workday caring for elderly patients, helping them and their caregivers find ways to best remember their medicines and cope with their diseases. "On the personal side," says Wellman, "my mother and her siblings visit my grandmother, who has Alzheimer's, weekly. They have put their lives on hold to care for someone who at times forgets their names, and nearly always forgets that they were there in the first place."

While it's heartbreaking for Wellman to hear the stories, she does not endure it daily, since she lives 400 miles away. But she still wanted to do something to help. She chose to swim for CAF because "its sole purpose is to fund ongoing research for the prevention and cure of Alzheimer's disease." Wellman exceeded her goal and raised \$1,600 for CAF. We are very grateful to her for her support and congratulate her on her achievement. ■



Jessica Wellman and her grandmother.