



Cholesterol and Alzheimer's

A Big Step Forward

"Our hope is that one or more ACAT inhibitors currently in clinical trials for cardiovascular disease can be used for Alzheimer's disease in the near future," said Dr. Kovacs.

What is the relationship between cholesterol and Alzheimer's disease, and when might that connection lead to disease-limiting medications?

New research funded by Cure Alzheimer's Fund has helped advance these questions in a significant way.

For more than a decade now, researchers have been aware of important links between cholesterol and Alzheimer's disease. Studies have shown that cholesterol levels are a significant risk factor in developing the disease, and that cholesterol-limiting statins might lower this risk. Further investigation has revealed that cholesterol somehow regulates the production of the toxic protein fragment Abeta, a central player in Alzheimer's.

But researchers have been struggling to define the precise cholesterol-Alzheimer's relationship. How does cholesterol assist or instigate the production of Abeta?

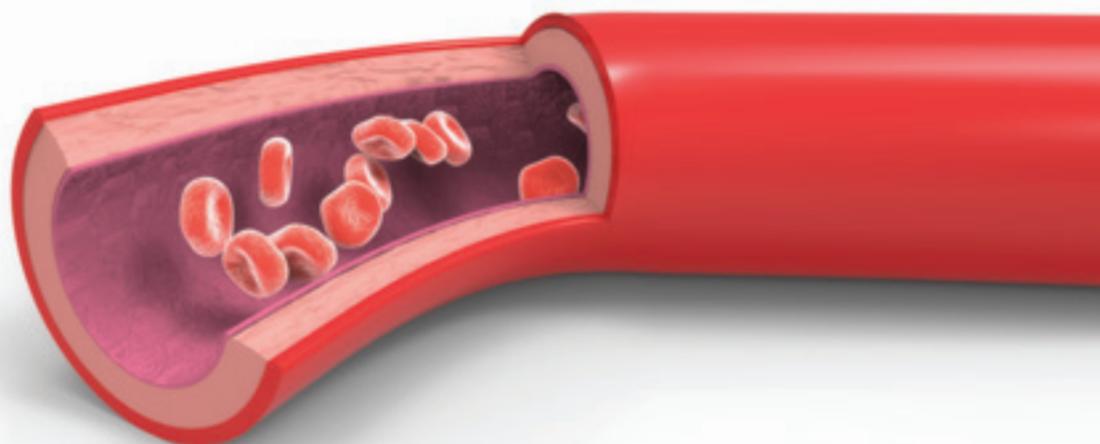
One step closer to a potential drug

A new study by Dora Kovacs, Ph.D., Raja Bhattacharyya, Ph.D., and Cory Barren, M.Sc., at Massachusetts General Hospital provides a specific answer, and brings us one step closer to a potential drug that might interrupt the disease process.

This is not the first important contribution to this issue by Dr. Kovacs and colleagues. In 2001, they identified a specific enzyme in the cholesterol pathway, abbreviated as ACAT, involved in the production of Abeta. By inhibiting ACAT, they demonstrated that Abeta production also can be reduced.

In a newly published **paper** in the *Journal of Neuroscience*, they identify a specific mechanism of action that accounts for this relationship between ACAT and Abeta production. The process, known as "palmitoylation," involves the attachment of fatty acids to pieces of a membrane protein.

continued on page 2 »



CHOLESTEROL AND ALZHEIMER'S A BIG STEP FORWARD

continued from page 1 »

The team also used two known ACAT inhibitors previously designed to reduce cholesterol to actually reduce Abeta production. They conclude that using these inhibitors “would appear to be a valid strategy for prevention and/or treatment of Alzheimer’s disease.”

This careful work points to more potential therapies for Alzheimer’s disease through the use of existing or future cholesterol-lowering drugs. “Our hope,” Dr. Kovacs said, “is that one or more ACAT inhibitors currently in clinical trials for cardiovascular disease can be used for Alzheimer’s disease in the near future.”

Breakthrough research

In recent decades, targeting cholesterol has helped to radically advance the prevention and treatment of heart disease. This accumulation of research suggests we might be on the cusp of achieving the same thing with Alzheimer’s.

“This is exactly the sort of groundbreaking research we set out to support,” said Cure Alzheimer’s Fund Chairman Jeff Morby. “In fact, Dr. Kovacs’ earlier cholesterol research was the very first project supported by Cure Alzheimer’s Fund. Alzheimer’s research is arduous, but having persevered and followed the facts, we’re now one important step closer to a useful treatment.” ■

FEATURED RESEARCHER

Dora M. Kovacs, Ph.D.



Associate Professor of Neurology, Harvard Medical School; Associate Neuroscientist, Massachusetts General Hospital; Director, Neurobiology of Disease Laboratory

Dr. Dora Kovacs didn’t always know she was going to end up on the forefront of Alzheimer’s research, but she always had a passion for science.

Born in communist Hungary in the city of Budapest, Kovacs’ mother was an entomologist who introduced Dora to the world of science at a young age. When Kovacs turned 12, her family moved to Bologna, Italy. “Everything was brighter there and the leather shoes were softer,” she says, but because she didn’t speak Italian, her parents wanted her to repeat a grade. That didn’t slow her down, though. She learned English as well and soon became trilingual.

Even in a different language, Kovacs was fascinated by the world of science. “When I first learned about DNA in high school, it wasn’t just a fleeting interest. To me, it was the key to life.” At age 16, a friend invited her to England for a three-week summer internship. “All my other friends in Italy were spending their time at the beach, but I felt lucky to be growing bacteria.”

Education

After high school, Kovacs went to the University of Bologna and graduated *summa cum laude* with a B.S./M.S. degree in biology. Coming from a long line of doctors and scientists, biology already was in her blood. Kovacs earned a Ph.D. in pharmacology and toxicology at the University of Padova, Italy, while performing research at Case Western Reserve University in Cleveland.

Her studies of the expression of the amyloid precursor protein (APP) gene in the central nervous system led to a breakthrough paper she co-authored in 1988 with Rudy Tanzi, Ph.D., now chairman of the Cure Alzheimer’s Fund Research Consortium. Kovacs then became a research fellow in molecular neurobiology and genetics at the University of Pittsburgh. “I later interviewed with Rudy in 1993 when I accepted a position at Massachusetts General Hospital

(MGH) in the Genetics and Aging Research Unit.” Little did Dora know then that years later, she and Rudy would get married.

Focus on Alzheimer’s

Twenty years later, Kovacs has co-authored more than 40 original articles and is a co-inventor on three patents. She has made significant headway in understanding the molecular mechanisms behind neurodegenerative diseases like Alzheimer’s and has been recognized for her discovery of a novel strategy for modifying Abeta generation via the cholesterol esterification pathway (the formation of insoluble cholesterol-esters from cholesterol and fatty acids).

“It was the first research project to be funded by Cure Alzheimer’s Fund,” she says. “In the late 1990s, my lab started collaborating with Dartmouth University. They sent us cell lines that overproduced cholesterol and by chance they sent us one without esters. At first we thought there was something wrong, because the line didn’t produce any Abeta, but it ultimately showed us how ACAT inhibitors can reduce Abeta.”

Most recently, Kovacs and her team at MGH published a paper on the connection between cholesterol and Alzheimer’s. “We’re now one step closer to understanding the mechanism, but there’s still so much more to learn,” Kovacs notes. “Because NIH only covers part of my research expenses, funding from Cure Alzheimer’s Fund is essential to my work.”

Kovacs and Tanzi were married in 2002 and have a daughter, Lyla, who is 5 years old. When asked if Lyla has a passion for science, Kovacs laughs. “She’s more interested in princesses right now than anything else,” she notes, but there’s still time. When Kovacs and Tanzi are not playing with their daughter, they are focused on their other greatest shared passion—finding a cure for Alzheimer’s disease. ■

Collaborating for a Cause

Service Above Self

At a chance meeting in 2010, Jeff Morby began a discussion with a member of the Martha's Vineyard Rotary Club. Little did either of them know this would be the start of a very important friendship—one that would fuel a worldwide effort to help eradicate Alzheimer's disease.

A few weeks later, Morby shared the facts regarding the threat of the disease at the Martha's Vineyard club. "Today, 5.4 million people in the United States and at least 50 million worldwide have Alzheimer's disease," Morby said. As the baby boomer generation and the world population overall ages, Alzheimer's is going to "wreak havoc on health care systems around the world. We need to be prepared for this onslaught and, more importantly, we need to stop the disease using the latest research techniques."

Because many Rotary members typically are middle-aged, Morby's talk really resonated with the audience. As a result, the Martha's Vineyard Rotary Club decided to focus its efforts on fighting Alzheimer's.

local Rotarians to get the word out about the threat of Alzheimer's. Afterward, Curren's Rotary Club in Reading, Mass., adopted the Alzheimer's cause as a district project. Curren then went out to clubs across Massachusetts and talked about the disease and the issues surrounding it.

In 2012, Morby spoke at the Rotary Club's annual meeting in Bangkok, Thailand. "Despite that fact that a high percentage of persons have been touched by the disease, many people don't really understand the degree of their personal or family risk," says Morby. "There has been passivity around Alzheimer's, and our society hasn't really been aware of the problem until recently." But in Bangkok, the room was filled to capacity and there were lines out the door. "There is such a hunger out there for information, and for hope," adds Curren.

At Rotary's 2013 annual meeting in Lisbon, Portugal, Morby, Curren and Dr. Rudy Tanzi, the chairman of the Cure Alzheimer's Fund Research Consortium, addressed a

Rotary Action Group

As concern for Alzheimer's grows around the world, Rotary has taken the next step. The Martha's Vineyard Rotary Group partnered with Cure Alzheimer's Fund to initiate a Rotary Action Group (RAG) to help fight Alzheimer's disease. RAGs focus on a single worthy cause and provide Rotary clubs worldwide with information about activities that have proven successful in supporting that cause.

This approach is illustrated by the Rotary Club's actions more than 40 years ago, when it set out to eradicate polio worldwide. "Rotary has been extremely successful," says Morby. "Polio is almost gone. Still, the organization is dedicated to completing that task. We hope to follow the lead of the foresighted polio organizers to accomplish the same outcome with Alzheimer's disease."

Mike Curren has played an important leadership role in working with a dedicated group of Rotarians to bring the Alzheimer's Rotary Action Group to fruition. "It was the first one to be approved in about five years," adds Morby, who is now a member of the Martha's Vineyard Rotary Club and who recently won Rotary's prestigious Paul Harris Award for Service Above Self, Rotary's motto. "We have also reached out to other Rotary-based Alzheimer's groups and are in the process of rolling out an action plan to enlist Rotarians around the world in this battle."

Now that the groundwork has been laid, the real work begins. ■

"With more than 1.2 million members in more than 100 countries, Rotary International is dedicated to improving the lives and health of people around the world. It's an ideal organization to help us with our quest to cure Alzheimer's disease."

—Jeff Morby, co-founder of Cure Alzheimer's Fund

Spreading the word

From the initial beginnings in Martha's Vineyard, Morby continued to speak at other Rotary gatherings, and each time he would ask the audience, *How many of you have been touched by Alzheimer's in some way?* "Consistently, 80 percent of people raised their hands," he says. "This disease is truly an epidemic."

In April 2011, Mike Curren, a Rotarian from Massachusetts, joined Cure Alzheimer's Fund as a senior executive. Curren was given the charge by Morby to work with

crowd of more than 500 Rotarians. Once again, the response was overwhelming. Hundreds signed up to be on a mailing list and pledged their support. Many had heartbreaking stories of family members, living and deceased, and the struggles their families went through to care for them.



Financial Update

	This Quarter	YTD*	Inception to Date
Fundraising	\$469,473	\$3,638,812	\$33,761,679
Expenses paid for by the founders	\$396,925	\$1,093,849	\$7,317,550
Funded research	\$600,000	\$3,126,000	\$21,179,008

*Numbers shown are preliminary for the period.

Research Update

Research funded during the third quarter of 2013

Project	Researcher	Distribution Amount
Continuation of Alzheimer's Genome Project™ (AGP)	Rudy Tanzi, Ph.D. Mass General/Harvard University	\$600,000
Total Distributed to Research for 3Q 2013		\$600,000

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.

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.

Join Our Mobile Community!



Scan this QR code or text ALZ to 50555 to join our mobile community.

SMS subscription service.

Up to 4msg/mo.
Msg&Data Rates May Apply. Text STOP to 50555 to STOP.

Full terms: mGive.com/E

Privacy policy: mGive.org/P

Cure Alzheimer's FUND

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

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

Mission

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

Research Consortium

Develops and updates a "roadmap for research" for the most effective and efficient route to slowing, stopping and/or reversing Alzheimer's disease. Members research their own projects and recruit others whose work will hasten development of effective therapies for and prevention of Alzheimer's disease.

Rudolph E. Tanzi, Ph.D., Chairman, Research Consortium; Harvard Medical School/Massachusetts General Hospital
Sam Gandy, M.D., Ph.D., Icahn School of Medicine at Mount Sinai
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
Roberto Malinow, M.D., Ph.D., University of California, San Diego
Sangram S. Sisodia, Ph.D., University of Chicago
Thomas C. Südhof, M.D., Stanford University
Robert Vassar, Ph.D., Northwestern University
Steven L. Wagner, Ph.D., University of California, San Diego
Berislav Zlokovic, M.D., Ph.D., University of Southern California

Scientific Advisory Board

Reviews individual grant proposals for science integrity and roadmap objectives. Provides advice and counsel to Cure Alzheimer's Fund regarding scientific soundness of the roadmap.

John C. Mazziotta, M.D., Ph.D., Chairman, Scientific Advisory Board; UCLA
Dennis Choi, M.D., Ph.D., Stony Brook University
Caleb Finch, Ph.D., University of Southern California
Paul Greengard, Ph.D., The Rockefeller University
Stephen Heinemann, Ph.D., The Salk Institute for Biological Studies
John S. Lazo, Ph.D., University of Virginia
Robert C. Malenka, M.D., Ph.D., Stanford University
Marc Tessier-Lavigne, Ph.D., The Rockefeller University

Board of Directors

Jeffrey L. Morby, Key Largo, Fla., Chairman*
Robert F. Greenhill, New York City
Henry F. McCance, Lake Wales, Fla.*
Jacqueline C. Morby, Key Largo, Fla.*
Phyllis Rappaport, Stuart, Fla.*
Tim Armour, Wellesley Hills, Mass., President
**Founder*

Administration

Tim Armour, President and CEO
Mike Curren, Senior Vice President
Sally Rosenfield, Senior Vice President
David Shenk, Senior Adviser
Laurel Lyle, Director of Fundraising Programs
Toni Carbone, Office Manager
Madeleine Adelson, Marketing Manager
Karen Robertson, Accountant
Jessica Mutch, Controller

Contributing Writer: Patty Bovie
Copy Editor: Colleen O'Neill
Design: Winking Fish

We thank all of you who devote time, energy and money to end Alzheimer's disease. Together you've raised more than \$250,000 so far this year! *To find out more about the events below, visit curealz.org/events.*

5th Grader Makes a Difference

At the Pine Hill School in Sherborn, Mass., they don't just teach reading, writing and arithmetic. At the end of the school year, each 5th grader participates in a project called "Citizenship in Action," where students choose an organization to research and help raise awareness for it. Nelson Everts selected Cure Alzheimer's Fund (CAF) and raised more than \$250 by asking relatives to donate (in lieu of birthday presents), holding a bake sale and selling "Silly String."



Nelson Everts

7th Annual Hay Harbor Tennis Tournament

Since 2007, Diana Fiske has organized a round robin tennis tournament at Fishers Island's Hay Harbor Club to raise money for CAF. Club member Alison McCance was diagnosed with early-onset Alzheimer's in 2004, and Fiske learned about CAF through Alison's husband and CAF co-founder Henry McCance.

Each July these dedicated women fill all 11 courts, playing to raise money for a cure—starting with the \$25 entry



Diana Fiske and Hay Harbor participants

fee. Every uttered "sorry" during a game costs \$1 and expletives cost \$10 each. "This year we had 44 players ranging in age from 20 to 84," Fiske notes. "Over the years, a remarkable 125 women have participated, and we've donated more than \$23,000."

Driving to Find a Cure

Founded in 2013 by Jake and Josh Akman in honor of their grandfather, Dr. Richard Hollander, The Dick Hollander Open™ is a charity golf tournament that raises money for Alzheimer's research. "Our grandfather has suffered for more than 15 years from Alzheimer's. He taught us both how to play the game of golf, so what better way to honor him than hosting a tournament in his name?" says Jake Akman, 24.

The tournament was held on July 21 at the Blue Mash Golf Course in Laytonsville, Md. Some 100 golfers participated and another 50 people came for lunch. The event netted more than \$60,000 for CAF. "We definitely plan to make this an annual event," says Josh Akman. "There's no stopping this train as long as Alzheimer's has no cure."



Josh, top, and Jake Akman

David K. Johnson (DKJ) Golf Tournament Brings a Community Together

In 1994, David K. Johnson was diagnosed with Alzheimer's disease at age 59. His wife and primary caregiver, Susan, passed away from a heart attack just five years into David's struggle. The responsibility then fell on their children—Gregg, Bruce and Laurel—to care for their father until his passing in 2004.

In 2001, Gregg and Bruce Johnson created the DKJ Foundation in their parents' honor. The foundation has held a charity golf tournament every summer since its inception, as well as other fundraisers throughout the year. All of the proceeds go to three nonprofits: Sanborn

Place & Home Care of Reading, Cure Alzheimer's Fund and to fund a scholarship at Reading Memorial High School. The 13th annual golf tournament, held on Aug. 19 at Four Oaks Country Club in Dracut, Mass., attracted 165 people, who collectively raised more than \$20,000.

"The tournament is my favorite day of the year," says Gregg Johnson. "My entire family, friends and my parents' friends join us each year and a whole lotta love is shared."

Swimming for a Cure

On Sept. 14, 2013, Greg Wellman Jr., 34, of Kingsport, Tenn., swam 440 pool lengths to help find a cure for Alzheimer's disease. Greg's grandmother, Grace Bosdell, is 87 years old and has been suffering from Alzheimer's for the last six years. "She's lived a vibrant life, but her final years have been defined by Alzheimer's," says Wellman.

"Swim for Them" is an annual charitable event in which swimmers raise funds for personal causes by conducting swim endurance challenges. To prepare for the event, Wellman swam three to four times per week until he could swim about two-thirds of his chosen event distance, a 10K. On Sept. 14, he was cheered on by his wife and three children, Grace (10), Ethan (8), and Samuel (6), and countless other supporters—and he completed his challenge in three hours and 22 minutes.



Greg Wellman Jr. and his grandmother



Bruce, top, and Gregg Johnson

And earlier this year...

"The Ups and Downs of Living with Alzheimer's," **Charlie Collier**, Hillsboro, Fla.; Wellesley, Mass.; Boston • **Boynton Beach Golf Tournament**, **Ellen Cohen and the Women's Golf League**, Boynton Beach, Fla. • **Benefit Concert**, **Ki Oh and band members**, Cleveland • **Marathon**, **Ann Bulson, Kristen Adrien and Travis Song**, Boston • **4th Annual Running 4 Answers Fun Run/Walk**, **Barbara Geiger and Carolyn Mastrangelo**, Roseland, N.J. • **Mountain Lake Golf Tournament**, **Jonathan Powell and members of Mountain Lake Golf Club**, Lake Wales, Fla. • **School Fundraiser**, **Nate Levine and Kyle Brown**, Fremont, N.H. • **Half-Marathon**, **Kim Chan**, Newport Beach, Calif. • **Branchburg Race Against Alzheimer's**, **Mike Napoli and friends**, Branchburg, N.J.



Cure Alzheimer's FUND

34 Washington St., Suite 200
Wellesley Hills, Mass. 02481

877-CURE-ALZ (287-3259)
www.curealz.org

Non-Profit Org
U.S. Postage
PAID
Washington, DC
Permit No. 13



Check out our Facebook page for our most recent posts, photos, videos and more!
Go to www.facebook.com/CureAlzheimers.

Record Turnout for 2013 Fall Symposium

Our 3rd Annual Fall Symposium—Taking Control of Alzheimer's Disease—was the best attended yet. Almost 500 people watched it live online and 180 gathered in Boston on Oct. 9 to hear leading researchers from the Cure Alzheimer's Fund Research Consortium discuss the latest research toward finding a cure. Sam Gandy, M.D., Ph.D., of the Icahn School of Medicine at Mount Sinai, and Chairman Rudy Tanzi, Ph.D., from Harvard Medical School/Massachusetts General Hospital, led the discussion.

Earlier that day, Banker White's award-winning documentary, "The Genius of Marian," was shown. The film is an honest portrayal of the filmmaker's mother in her struggles with Alzheimer's and takes place over three years. On display at the symposium was "Living with Alzheimer's," four short documentary films by world-class filmmakers that were produced by David Shenk and created in partnership with Cure Alzheimer's Fund, with funding from the MetLife Foundation.

For more information or to view the symposium presentations, please visit curealz.org/symposium.



L to R: Ed White and Devon Angelini (family of Banker White, "The Genius of Marian" director) and Cure Alzheimer's Fund co-founder Henry McCance.

Photo by Nir Landau