



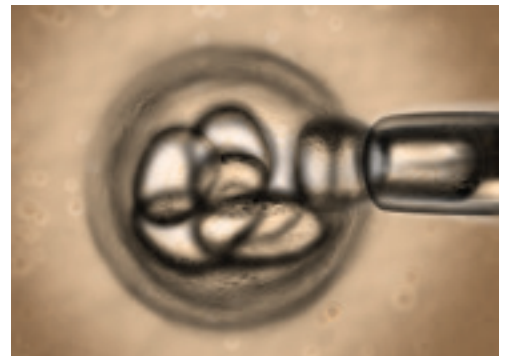
Launching the Stem Cell Consortium

Ordinary skin cells from Alzheimer's patients can be repurposed as nerve cells, allowing new modes of research and huge potential advances in drug testing.

Stem cells long have been the mythical *Excalibur* of Alzheimer's disease research—imbued with almost magical qualities that could allow us to conquer this nearly impossible disease. For decades, though, hope has outshone reality.

The Opportunity

Now, suddenly, stem cell researchers have created a very real opportunity. Ordinary skin cells from Alzheimer's patients can be repurposed as nerve cells, allowing new modes of research and huge potential advances in drug testing. This year, Cure Alzheimer's Fund responded to this genuine medical breakthrough by establishing a two-year, \$1.2 million Cure Alzheimer's Fund Stem Cell Consortium (CAFSCC). "This was too exciting not to jump into right away," explains Consortium Chair Rudy Tanzi. While the new project can't promise immediate results, it ultimately could alter the way scientists study and fight the disease.



This ambitious new project was funded by a generous group of individuals, foundations and trusts—without which exploring this new frontier would not be possible.

The Power of Stem Cells

Stem cells are different from all other human tissue in three important, unique ways. First, they are unspecialized. Second, they can renew themselves by cell division. Third, they can be directed under certain conditions to become a wide variety of permanently specialized cells. In 1981, scientists discovered how to isolate embryonic stem cells from mouse embryos; in 1998, they devised how to grow human embryonic stem cells in a laboratory.

The more recent breakthrough is the ability to genetically induce a specialized adult cell, such as a common skin cell, into reverting back to an unspecialized stem cell. Once generated, these pluripotent stem cells (iPS's) are able subsequently to be directed to become a specialized cell—such as a neuron.

Thus, an ordinary skin cell can now, in a lab, be converted into a neuron. From here, the hope is to create a new universe of Alzheimer's nerve cells living *outside* the human brain in order to study and test new drugs much faster than researchers currently are able. To get there, the seven-member stem cell consortium, assembled

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Launching the Stem Cell Consortium

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by Sam Gandy, M.D., Ph.D., at Mount Sinai Medical Center, will have to first complete a number of precise tasks:

- **Generate iPS cells and neurons from the skin cells of Alzheimer's patients.** This already has been accomplished by Scott Noggle, Ph.D., of the New York Stem Cell Foundation and Kevin Eggan, Ph.D., of the Harvard Stem Cell Institute. Mark Tessier-Lavigne, Ph.D., president of The Rockefeller University, also has done important Cure Alzheimer's Fund-funded work to determine the best method for obtaining these cells.
- **Perform molecular and biochemical analysis of new laboratory neurons.** The newly converted Alzheimer's neurons can be examined both in a laboratory dish and by transplanting them into the brains of host mice. Dr. Gandy already has discovered amyloid beta metabolism abnormalities in the Alzheimer's neurons. Future studies will examine how the neurons respond to various stresses.
- **Profile the Alzheimer's neurons.** Drs. Noggle, Eggan and Gandy will establish a baseline molecular characterization of nerve cells from Alzheimer's patients to determine the similarities and differences between those neurons and non-Alzheimer's neurons.
- **Generate human neurons with known Alzheimer's genes.** Dr. Doo Yeon Kim, Ph.D., will establish various Alzheimer's cell models designed to overexpress various known genetic mutations in order to enhance Alzheimer's pathology.
- **Plant the new human neurons in mouse brains.** Drs. Kim and Tanzi will establish a method to graft newly created neurons into mouse brains and analyze various disease markers in the months after cell injections. Tamir Ben-Hur, M.D., Ph.D., of Hadassah University Medical Center in Jerusalem will

help choose which genetically manipulated mice are most likely to accept a stem cell transplant, and will guide the manipulation of these substances using small molecules and drugs in order to determine how best to keep stem cells alive.

- **Identify functional properties of human Alzheimer's cells.** Ben-Hur will conduct various tests on lab-created Alzheimer's neurons inside and outside of mouse brains. He will gather new information on how Alzheimer's neurons survive and connect in the brain environment.
- **Create a new choline acetyltransferase (ChAT) human pluripotent reporter cell line.** Dr. Eggan will attempt to create a new cell line for studies into the *in vitro* generation of human cholinergic neurons.

Together the CAFSCC team will develop, study and maintain Alzheimer's neurons that will be used to screen for new drugs. In keeping with Cure Alzheimer's Fund's principle of openness, this stem cell "bank" also will be made available to other researchers throughout the world. "We have great expectations for this project," said Tanzi. "It could greatly accelerate the process of drug discovery."

Find Out More About Cure Alzheimer's Fund's Stem Cell Consortium—Wed., June 5, 1 p.m.

Sam Gandy, M.D., Ph.D., member of Cure Alzheimer's Fund Research Consortium and head of Cure Alzheimer's Fund Stem Cell Consortium; Scott Noggle, Ph.D., member of the Stem Cell Consortium; and David Shenk, author of the national bestseller *The Forgetting, Alzheimer's: Portrait of an Epidemic*, will moderate an "Alzstream," a live-streamed event about the new stem cell project, at www.curealz.org on Wednesday, June 5, at 1 p.m. The event will be available afterward on our website. ■

FEATURED RESEARCHER

Tamir Ben-Hur, 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. This quarter we are featuring Cure Alzheimer's Fund Stem Cell Consortium member Tamir Ben-Hur, M.D., Ph.D., professor of neurology, Israel S. Wechsler Chair in Neurology, chairman, Department of Neurology and Hadassah University Medical Center.

Background

Tamir Ben-Hur was born and raised in Jerusalem, Israel, where he still resides today. The younger of two boys, Ben-Hur developed an interest in life sciences when he was in high school. "My father was a surgeon and that might have influenced me, but I was so interested in biology that I read about it on my own, even though it wasn't one of my majors."

Ben-Hur had to put his interest on hold when he joined the army after graduation. "It's compulsory for all Israeli men to serve in the military after high school," explains Ben-Hur. "It's part of our culture and our country depends on it." Ben-Hur served in combat as a soldier for four years and worked his way up to the rank of major while serving in the reserve.

After the army, Ben-Hur was accepted to the Hebrew University—Hadassah Medical School in Jerusalem—where he eventually received his M.D. and Ph.D. degrees. In Israel, medical school is a seven-year program (six years of studies and a one-year internship), in lieu of college and university. As a first-year student, Ben-Hur wanted to better understand scientific research, so he began working in a lab. "That was 32 years ago," he says. "I still remember sitting with my professor and hearing about what they were doing in the

lab. I took it as a question that needed to be answered.” A couple of weeks later Ben-Hur went back to his professor with a suggestion for an experiment—to show how a virus has a predilection to invade nerve fibers and end up in the brain. “One experiment led to another and became the foundation for my Ph.D. thesis,” adds Ben-Hur. “That’s when I fell in love with neurology. I knew then that it was what I wanted to do for the rest of my life.”

After finishing medical school Ben-Hur began his residency at Hadassah University Hospital in the Department of Neurology. Nowadays, when he interviews candidates who are looking for a place to do their residency, he can tell who’s “hooked on neurology” by the way their eyes light up. “That’s how I feel, and those are the people I want to work with.” He describes neurology as the mystery of the brain and the nervous system. “Our feeling and thinking brain is who we are. It’s our identity. It’s the most important essence of life.”

Holistic Approach

Neurology also appeals to him for a different reason. “While clinical medicine has become more and more specialized, neurology is one of the last clinical fields left that takes a holistic approach to the patient—not only the medical aspects, but the mental aspects as well. This is the classical approach to medicine that I was raised on, and I try to teach it to the younger generation,” says Ben-Hur. He says science has advanced so much that you can put 15 brain scientists in one room and each one talks in a different language. “We need to rebuild bridges so that scientists and clinicians from different disciplines can talk to each other again and work together, because this is the only real way to find solutions for brain diseases like Alzheimer’s.”

In addition to being a researcher, Ben-Hur also has been a practicing physician with patients of his own for his entire career. “I wouldn’t give them up for anything. Moreover, the duality of medicine and science is very important, because it gives me perspective. As a physician you encounter the questions that need scientific solutions, so you understand the issues better, and as a scientist you get an important perspective on clinical medicine.”

“We need to rebuild bridges so that scientists and clinicians from different disciplines can talk to each other again and work together, because this is the only real way to find solutions for brain diseases like Alzheimer’s.”

Stem Cell Research

Ben-Hur did his post-doctoral fellowship in developmental neurobiology of neural stem cells at the Pasteur Institute in Paris. His goal was to learn more about cell biology by combining clinical medicine and research. Since then, Ben-Hur has focused on neural stem cell biology, transplantation of stem cells to the nervous system, neuroimmunology and neurovirology. Today he is chief physician in the Department of Neurology, professor in neurology and chairman of the Department of Neurology at Hadassah University Hospital in Jerusalem. “My work at Hadassah is to try to understand how stem cells from various sources can be used for therapeutic purposes,” says Ben-Hur.

Initially stem cells were seen only as types of cells that could replace missing cells and damaged tissue. But Ben-Hur and his colleagues found that both embryonic and adult stem cells have additional properties that may be very useful for therapy. “The brain is very limited in terms of regeneration,” explains Ben-Hur. His lab was the first in the world to discover that brain stem cells have properties that can inhibit inflammatory processes. His work also showed that stem cells protect their surrounding brain cells from injury and facilitate the repair process. “This was our basic rationale for developing stem cell therapy for multiple sclerosis (MS) that’s already in clinical trials. But stem cell research is not magic,” cautions Ben-Hur. “We need to better understand how they can be manipulated to increase the brain’s ability to protect itself from degeneration.”

Cure Alzheimer’s Fund

Ben-Hur was recruited by Cure Alzheimer’s Fund in 2012 to become part of the Stem Cell Consortium and collaborate on a project using stem cells derived from skin cells to better understand Alzheimer’s disease. His role is to help

members of the consortium identify the functional properties of neural stem cells, which may help to protect the brain from degeneration. He will compare these functions in cells derived from genetically manipulated mice and from human sources to determine whether loss of stem cell functional properties plays a role in perpetuating the degenerative brain process in Alzheimer’s disease. “My fellow scientists on this project are top-class and I was very enthusiastic about joining them. I just added my point of view on how to approach stem cells and Alzheimer’s disease and together we wrote a research proposal, Cure Alzheimer’s funded it, and each lab is working on its own part.”

The majority of Ben-Hur’s work had been on MS, but many of the questions the project addresses are related to various neurological diseases. “The people at Cure Alzheimer’s Fund are a wonderful, committed group of individuals who have contributed their own money to do what they can to help fight Alzheimer’s disease. For me, this is what I do. It’s my work. But what they’re doing is really special.”

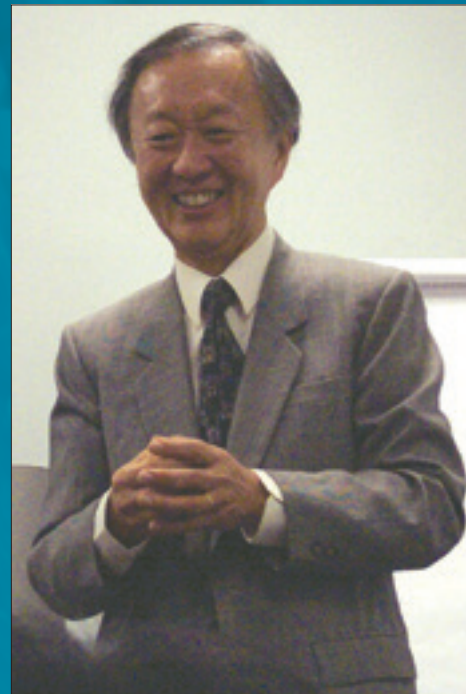
As a full-time physician who’s involved in full-time research, Ben-Hur made a life decision that leaves very little time left for much else. He is married and has three boys, ages 17, 23 and 25. But he also manages to find time for exercise, mixing in some culture and for reading, which he says provides peace and quiet and is “good for the mind.”

To learn more about the Cure Alzheimer’s Fund Stem Cell Consortium and how researchers are working toward finding a cure, visit www.curealz.org/projects/stem-cell-consortium. ■

When Alzheimer's Hits Home

In his heyday, Professor Charles K. Kao was a pioneer in the field of fiber optics. In 2009 he was honored with the Nobel Prize in Physics. Today, at age 79, Kao no longer is able to read or speak, because he suffers from Alzheimer's disease.

As hard as life is for Gwen Kao, his wife for more than 50 years and primary caregiver, she created The Charles K. Kao Foundation in his honor to raise awareness for the disease and educate the public about what can be done.



Early Symptoms

Known as the “father of fiber optics,” Charles Kao’s groundbreaking achievements in global telecommunication paved the way for the age of the Internet. Thirty-five years ago he worked at ITT Corp. and was at the top of his field. “We led a very exciting life then,” explains Gwen Kao. They traveled the world, since ITT Corp. had labs in Paris, the Netherlands, England and the United States. “But even then, when Charles was in his 50s, he used to misplace his keys all the time. Our two children and I used to tease him, saying he was the absent-minded professor.” It wasn’t obvious to Mrs. Kao that anything was wrong at the time—his symptoms were very subtle. “But as Charles got older he would forget where he was going. Once he took the tram the wrong way and got lost.” Then, at their monthly game of mah-jongg with friends, Professor Kao started playing the wrong cards. “My friend who was a nurse said, ‘something’s wrong.’ That’s what started it all,” explains Mrs. Kao.

That was about 10 years ago. “At the time, Alzheimer’s disease in Hong Kong was like cancer was in the early days. People didn’t talk about it. Doctors were unaware of it and ignored it as being just a sign of old age,” Mrs. Kao remarks. Their family doctor sent them to a neurologist, and then to a gerontologist. They both said Charles was “just getting old.” The Kaos decided to go to the United States to get an MRI, because Charles was well known in Hong Kong and the family wanted to keep his health situation private.

“Our son lives in San Francisco, and during a visit to him we made an appointment with a neurologist. He told us that Charles’ hippocampus had shrunk and that there were signs of amyloid plaques on his brain. He didn’t say it was Alzheimer’s, but he did say Charles had a degenerative brain disease,” says Mrs. Kao. A leading doctor in Hong Kong subsequently said Alzheimer’s disease was rare in the Asian population. “How wrong he was,” adds Mrs. Kao.

A decade ago Professor Kao was functioning pretty well, but over the last three years he began getting lost more often. “He wouldn’t know how to get back from his meetings and he would forget what he was buying at the grocery store,” says Mrs. Kao. The family moved to California for a while, where Charles went to day care about three times a week and stayed home with Mrs. Kao on the other days. But it wasn’t easy being a caregiver in the United States because of the high costs.

In 2010, the Kaos moved back to Hong Kong to a fanfare of publicity. “People were very proud to have a Nobel laureate here, but they also became aware of his illness. People would ask, ‘How can such a brainy person who isn’t poor get Alzheimer’s?’” There was so much ignorance around the disease,” she says. Mrs. Kao realized then she could use Charles’ fame to start a foundation to raise awareness for the disease.



Today more than **70,000** people in Hong Kong suffer from dementia and that number is expected to grow at a rate of **100%** every 10 years.

By 2036, it is estimated **280,000** people will be showing symptoms.



Photos (left to right): 1.) Promotional poster that ran in Hong Kong subways for the Charles K. Kao Foundation 2.) Sally Rosenfield, left, senior vice president, Cure Alzheimer's Fund, and Gwen Kao, chairman, Charles K. Kao Foundation, in Hong Kong.

The Charles K. Kao Foundation

Today more than 70,000 people in Hong Kong suffer from dementia and that number is expected to grow at a rate of 100 percent every 10 years. By 2036, it is estimated 280,000 people will be showing symptoms. But awareness around Alzheimer's disease in Hong Kong still is extremely low. The Charles K. Kao Foundation was established in 2010 to educate the general public on the disease and to provide brain health care strategies to help support Alzheimer's patients, their families and caregivers.

"Today we have facilities in more than 20 locations in Hong Kong run by various NGOs (nongovernment organizations) that provide respite care and training for tackling the problems of Alzheimer's," explains Mrs. Kao. "There's a lot more work to do to create more day care facilities. Exercises in social settings can help to elongate the early stage of this incurable disease. As a result of our efforts, our government is beginning to realize that a bombshell is coming and is thinking more about how to care for the elderly, since the life expectancy has increased so much."

Caregiving

"Unless you've been a caregiver, people find it very hard to understand how much of an emotional toll it takes on you," explains Mrs. Kao. "You lose the companionship of the person you're caring for. He's unable to entertain himself. He can't enjoy TV or read the newspaper. But if you look at Charles, you wouldn't think there was anything wrong. He is 79, but he looks like a 40-year-old. At least a cancer patient can tell you if he's hot or cold. He's still there as a person. But Charles has now forgotten how to do many of the tasks he used to do with his eyes shut. Someone has to be with him all the time."

Cure Alzheimer's Fund

"Over the years, Charles won many prizes and we felt like that money was money from Heaven, so we put it into the Fidelity Charitable Fund. Last year I discovered Cure Alzheimer's Fund and it said that all of its funds were used for research. So I took that money from Heaven and put it where it was needed—toward research and a cure," says Mrs. Kao.

We are grateful for the Kaos' generous contribution to our cause and for helping to raise awareness for the disease around the world. To learn more about the Charles K. Kao Foundation, visit www.charleskaofoundation.org. ■

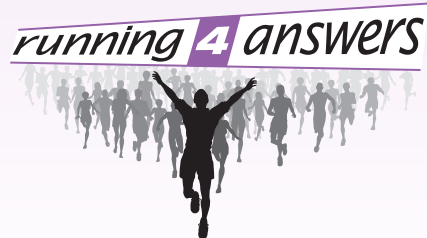
HEROES

We thank all of those who devote time, energy and money to end Alzheimer's disease. You are all heroes.

A Race Against Alzheimer's

For the fourth year in a row, co-founders Carolyn Mastrangelo and Barbara Geiger are holding their annual Running 4 Answers road race to fight Alzheimer's disease in Roseland, N.J. Mastrangelo's mother suffered from the disease, and together Mastrangelo and Geiger created this 5K road race (and 2-mile fun run) to bring families together to honor loved ones whom they have lost to Alzheimer's and to raise money for Cure Alzheimer's Fund.

"We are so thankful to our runners, sponsors and fundraisers that we wanted to do something fun this year," says Mastrangelo. For the first time, they are holding a fundraising contest. The first 10 people who raise \$250 win a Cure Alzheimer's Fund hat and anyone who raises \$500 or more wins a hat and shirt. In addition, the top three male and female finishers will take home prize money as an added incentive. Last year, Running 4 Answers raised \$40,000 for Cure Alzheimer's Fund. This year, organizers hope to raise even more. The race takes place on Saturday, April 27. To donate or for more information, visit www.running4answers.org. ■



Boynton Beach Golf Tournament

On Feb. 26 at Indian Spring Country Club in Boynton Beach, Fla., the Women's Golf League came together for a friendly round of golf and to raise money to fight Alzheimer's disease. Each year the women hold a fundraising tournament and pick a charity to benefit from entry fees. This year they chose Cure Alzheimer's Fund. "While none of us has Alzheimer's, it is one of those universal causes that we could all rally around," explains Ellen Cohen, one of the coordinators of the event. She said club members were "very pleased to know that 100 percent of the funds raised go directly to research." We thank Ellen and all the women for their generous donation. ■



Running for Memories—A Day of Celebration and Chaos

On April 15, 2013, The Boston Marathon experienced two explosions that shattered the celebration that symbolizes springtime, life and freedom in that city. This year three runners had stepped forward to run on our behalf and raise \$5,000 each for Cure Alzheimer's Fund. First-time marathon runner Kristen Adrien and her fiancé Travis Songer, who both work in the Biology Department at Boston College, joined our team in February. Meanwhile, Ann Bulson—who ran for Cure Alzheimer's Fund last year—says this year "a close friend of mine lost her mother in January after a lengthy battle with Alzheimer's. Seeing the effects of this horrible disease...has really shown me just how important it is to find a cure." The tragic events of the day were startling to all, including our team of runners, all of whom arrived at or near the finish line in time to avoid the explosions. We are so appreciative of their efforts, and for their safety. Thanks Ann, Kristen and Travis! There's still time to donate to our team—please visit www.curealz.org/events/2013/marathon-boston-2013. ■

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2013 Hero Events

Date	Event	Location
Jan. 24	Charlie Collier presentation	Hillsboro, Fla.
Feb. 26	Boynton Beach Golf Tournament	Boynton Beach, Fla.
March 24	Benefit concert	Cleveland
April 15	Marathon	Boston
April 27	Running 4 Answers	Roseland, N.J.
June 9	Branchburg Race Against Alzheimer's	Branchburg, N.J.
July 9	Charlie Collier presentation	Wellesley, Mass.

For more information about our Hero Events, please visit www.curealz.org/events.

Financial Update

	This Quarter	YTD*	Inception to date
Fundraising	\$1,512,000	\$1,512,000	\$31,634,867
Expenses paid for by the founders	\$338,598	338,598	\$6,333,624
Funded research	\$1,526,000	\$1,526,000	\$19,622,484

*Numbers shown are preliminary for the period.

Research Update

Research funded during the first quarter of 2013

Project	Researcher	Distribution Amount
Alzheimer's Genome Project™	Rudy Tanzi, Ph.D. Mass General/Harvard	\$600,000
Normalizing Abeta Synaptic Depression with Drugs Targeting PICK1	Roberto Malinow, M.D., Ph.D. University of California, San Diego	\$100,000
The Amylin Protein of Diabetes Mellitus is an Antimicrobial Peptide	Robert Moir, Ph.D., and Rudy Tanzi, Ph.D. Massachusetts General Hospital	\$300,000
Stem Cell Consortium	Sam Gandy, M.D., Ph.D. Icahn School of Medicine at Mount Sinai Tamir Ben-Hur, M.D., Ph.D. Hadassah University Medical Center Kevin Egan, Ph.D.* Harvard Stem Cell Institute Doo Yeon Kim, Ph.D. Harvard Medical School Scott Noggle, Ph.D. New York Stem Cell Foundation	\$400,000
Aβ Oligomers and the Pathogenic Spread of Tau Aggregation: Implications for Alzheimer's Disease Mechanism and Treatment	Dominic Walsh, Ph.D., and Dennis Selkoe, M.D. Brigham and Women's Hospital	\$126,000
Total Distributed to Research for 1Q 2013		\$1,526,000

*additional \$100,000 paid for by donor-directed grant to HSCI

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.

Cure Alzheimer's FUND

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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.

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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
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Robert Vassar, Ph.D., Northwestern University
Steven L. Wagner, Ph.D., University of California, San Diego
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HEROES

We thank all of those who devote time, energy and money to end Alzheimer's disease. You are all heroes.

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A Passionate Voice

Charlie Collier is a retired senior philanthropic adviser at Harvard University and a volunteer for Cure Alzheimer's Fund. Collier was diagnosed in 2008 with Alzheimer's disease. His illness has slowed his speech, but not his thinking. With the help of his sister, Debbie Zug, on Jan. 24 Collier presented "Alzheimer's, the Bad and the Good," at the Hillsboro Club in Hillsboro Beach, Fla., to educate attendees on the realities of Alzheimer's and what Cure Alzheimer's Fund is doing to get to a cure. Collier will repeat this presentation with Cure Alzheimer's Fund Senior Vice President Sally Rosenfield on July 9 in Massachusetts, in a program co-sponsored by the Wellesley Public Library. Our gratitude goes out to Charlie and Debbie for their efforts on our behalf. ■



Charlie Collier (right) with Cure Alzheimer's Fund founders Phyllis Rappaport (center) and Henry McCance (left).