



Targeting Tau's Tangles

Finding the correct arsenal for preventing plaques, tangle formation and neuroinflammation is the holy grail for scientists studying Alzheimer's disease. All three join together to disrupt communication between neurons—leading to an eventual complete loss of autonomy.

The Newfound Focus on Tau

Plaques are composed of amyloid protein and have been the major focus of Alzheimer's research for the past decade or so. In contrast, tangles, which are composed of the protein tau, have garnered much less attention. Clinical trials aimed at combating amyloid offer some hope, but results have been disappointing, and although there are many amyloid drugs still being developed and tested, scientists are widening their focus to include more investigations of tau. Some of this newfound excitement stems from newly marketed chemical compounds that, when injected by IV, attach to tau in the brain, allowing patterns of its accumulation to be imaged through positron emission tomography (PET) in living people. Analogous chemicals that bind to amyloid have been in use for several years and have greatly helped to improve the patient selection process for clinical trials. These brain imaging techniques that localize and quantify both amyloid and tau help fuel promising research. Tau imaging studies consistently report that the progression of tau closely tracks with the progression of cognitive decline, which is not the case for amyloid. Thus, investigating tau's properties, such as how tangles form and then spread, can inform drug discovery.

Tangles develop after amyloid builds up, and once tangles form, they seep into brain structures along a predictable path. They travel from their initial site in the medial temporal lobe (the brain's memory center), eventually ending up in the neocortex (the brain's outer layer), which is responsible for complex forms of cognition such as reasoning. Amyloid buildup sends an incompletely understood set of signals that encourage tau to change shape and to form tangles. These tangles, along with plaques, clog the system, leading to eventual cognitive decline.

Alzheimer's Disrupts Tau Clearing Process

In Alzheimer's disease, systems that promote clearance of extraneous proteins like amyloid and tau can malfunction. One such protein-clearing system is the ubiquitin-protease system (UPS)—the current focus of an investigation being led by Karen Duff, Ph.D., and Natura Myeku, Ph.D., at Columbia University through a grant provided by Cure Alzheimer's Fund. The UPS is responsible for maintaining proper protein balance within cells. Ubiquitin binds to proteins, tagging them for destruction. When the proteasomes within the UPS find the tags, they swallow the proteins. However, when this system is up against the likes of Alzheimer's disease, it can be overpowered, begin to fizzle out and lose its ability to clear unwanted tau protein. Once this deleterious sequence is set in motion, tau can spread.

continued on page 2 »



**Northbridge
Ride for a Cure**

2

State of the Mind Events

3

**Investment Firm
Gives Back**

3

Interns Pitch In

3

**Financial and Research
Updates**

4

'Tis the Season to Give

4

**Cure Alzheimer's Fund
Heroes**

5

**Jog Your Memory
Making Great Strides
for AD Research**

6



*Background: Microscopic view
of neurofibrillary tangles.*

Targeting Tau's Tangles

continued from page 1 »

Resurrecting Tau Clearance

Duff and Myeku now are investigating whether drug therapy aimed at resurrecting the UPS system by kickstarting proteasomes can bring tau spread to a halt. If Duff and Myeku find a drug effective at stopping tau spread in mice, the hope is that it can be harnessed for therapeutic development in humans.

How will they do it? They will invoke tangle formation by introducing a human form of tau into the entorhinal cortex—the initial site of tau formation. Using a fluorescent tracer that highlights proteins in the UPS, they will be able to visualize where in the brain the tau has traveled. Using other tissue-examination methods, they also

will be able to tell more specifically what compartments within the neuron (e.g., dendrite, axon) are contaminated with misfolded tau.

The next step is to try to prevent tau spread through drug therapy. They are pioneering a method in which a chemical compound will be injected locally, at the initial site of tau formation. Myeku explains that “The goal is to eventually use drugs in the synapse, where tau gets transferred from one neuron to another.” Duff adds, “Placing a drug in the precise place where tau is doing its damage will have the most impact.”

The compound Duff and Myeku are using works by restoring function to the proteasome to enable protein clearance. Additionally, its target is very specific, acting on just the portion of the neuron where tau initiates—where it can do the most good.

The very real possibility of being able to clear tangles raises the question of what symptoms will look like if the tau problem is solved before the amyloid one. “Finding a drug that can remove tangles, even if amyloid remains, will greatly decrease cognitive dysfunction and improve quality of life. There will still be cognitive problems, but they will be far reduced,” explains Duff.

Armed with a drug that can remove tau, techniques like PET imaging that visualize tau and amyloid in a human patient can be harnessed to tailor therapies that match the level of the individual patient’s disease. “PET imaging can show you where the amyloid and tau have traveled—and that information is critical, especially for tau, as its spread tracks so closely with disease symptoms. We are in very exciting times as we approach a point where we can position our drug toolbox to select the right treatment for the right patient,” concludes Duff.

Northbridge Ride for a Cure

This summer, Jim Coughlin and Wendy Nowokunski, co-founders of the New England-based senior living provider Northbridge Companies, rode their bicycles 350 miles to raise money for Alzheimer’s research. They left Brunswick, Maine, on July 7 and arrived in Plymouth, Massachusetts, on July 14, stopping at every Northbridge Community along the way to connect with residents and families, and to recharge. Coughlin and Nowokunski encouraged the teams of each of the 15 Northbridge locations to come up with their own creative “Ride for a Cure” welcome fundraiser and to spread the word about supporting Cure Alzheimer’s Fund to the greater communities they serve.

“As a senior living provider, we walk hand in hand with the families coping with Alzheimer’s disease and dementia, and we share in their desire to support the efforts of organizations working tirelessly to find a cure,” said Nowokunski.

“We believe in a world cured of Alzheimer’s disease, and we have the ability to effect change. We are honored to support Cure Alzheimer’s Fund.”

—Wendy Nowokunski and Jim Coughlin

They asked their supporters to donate through an online Crowdrise campaign and, along with a handful of generous sponsors, they raised more than \$50,000 for research.

Employees and residents gather at Avita of Wells, one of the stops along the route.



Nowokunski and Coughlin





John Slattery addresses the crowd in Duxbury.

STATE OF THE MIND EVENTS

In an effort to educate the public about the state of Alzheimer's disease and the urgent need for research funding, Cure Alzheimer's Fund has held more than a dozen *State of the Mind* presentations across the country this past year, each one featuring a leading scientist who has received a research grant. In some cases, generous supporters sponsor the event for friends and family.

On Sept. 7, Rick and Sharon Fownes of Duxbury, Massachusetts, hosted a State of the Mind presentation in their yard overlooking the ocean. Neighbors, friends and family gathered to learn about Alzheimer's research and what they can do to reduce risk. Sharon's father, a retired M.D., has been diagnosed with Alzheimer's, which inspired the Fowneses to host the event. The presentation featured Lisa Genova, Ph.D., neuroscientist and best-selling author of "Still Alice," and Rob Moir, Ph.D., Director of the Moir Lab, Massachusetts General Hospital Neurology Research. "The Fowneses

introduced CureAlz to so many wonderful, interested and generous friends, and the event exceeded all of our expectations," said John Slattery, Senior Vice President, Development, Cure Alzheimer's Fund.

CureAlz held two additional State of the Mind presentations late this summer. One was in Chicago at The Gage restaurant and featured Robert Vassar, Ph.D., from Northwestern University. The other event, held at The Mansion at Strathmore in Bethesda, Maryland, was supported by donors including the Akman, Hollander and Capon families. There, Jonathan Kipnis, Ph.D., from the University of Virginia presented his research related to his lab's discovery of the lymphatic system in the brain and its relationship to Alzheimer's disease.

With each State of the Mind presentation we continue to reach out to new audiences and build awareness for Alzheimer's disease and the need for a cure.



(L to R) John Slattery, Lisa Genova, Rick Fownes, Rob Moir and Sharon Fownes



Jonathan Kipnis presents in Bethesda.

Investment Firm Gives Back

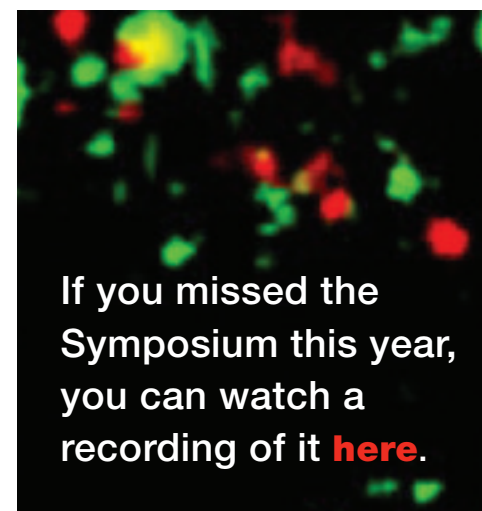
A Boston-based investment firm provided a \$20,000 grant in memory of **Janice Diperna** and in recognition of **Constance Bishop**, the loved ones of firm employees who were directly impacted by Alzheimer's disease.

Interns Pitch In

Ted Sirbaugh, a sophomore at Babson College, has joined us this fall to help with gift processing, communications and fundraising efforts. Ted will work alongside Katelyn Yuen, Boston University senior, and Lexi Goodhue, Boston College junior, who have been interning with us since the spring. We're lucky to have such a great team of interns on staff to help with day-to-day operations.



Ted Sirbaugh



If you missed the Symposium this year, you can watch a recording of it **here**.

Cure Alzheimer's FUND

34 Washington St.
Suite 200
Wellesley Hills, MA 02481
p: 877-CURE-ALZ (287-3259)
f: 781-658-2399
e: info@curealz.org
curealz.org

Centre City Tower
650 Smithfield St.
Suite 2015
Pittsburgh, PA 15222
p: 412-261-2785

Mission

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

Board of Directors

Henry F. McCance*
Lake Wales, Fla., Co-Chairman

Jeffrey L. Morby*
Key Largo, Fla., Co-Chairman

Phyllis Rappaport*
Stuart, Fla., Treasurer

Tim Armour
Wellesley Hills, Mass.,
President and CEO

Robert F. Greenhill
New York City

Jacqueline C. Morby*
Key Largo, Fla.

Sherry Sharp
Richmond, Va.

**Founder*

Fundraising Programs

Laurel Lyle
Vice President, Development Operations
and Fundraising Programs

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.

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

Financial Update

	This Quarter	YTD	Inception to Date
Fundraising	\$2.3M	\$7.8M	\$ 83.5M
Expenses paid for by the board	\$0.7M	\$2.4M	\$17.5M
Funded research	\$1.4M	\$6.1M	\$57.5M

Numbers shown are preliminary for the period and are rounded to the nearest \$100,000.

Research Update (Research approved for funding during the third quarter of 2017)

Project/Researcher	Distribution Amount
Inhibition of Tau Pathology in Human Neurons – Benjamin Wolozin, M.D., Ph.D, Boston University	\$100,000
Analytical and Statistical Tools for Sequence Analysis for Alzheimer's Disease – Christoph Lange, Ph.D., Harvard School of Public Health	\$250,000
A 3-D Human Neural Cell Culture System for Studying Neuron-Microglia Interaction in Alzheimer's Disease – Hansang Cho, Ph.D., UNC Charlotte	\$2,350
Early Role of Microglia in Synapse Loss in Alzheimer's Disease – Beth Stevens, Ph.D., Boston Children's Hospital	\$150,000
Activation of the 26S Proteasome for the Treatment of Alzheimer's Disease – Alfred Goldberg, Ph.D., Harvard Medical School	\$150,000
The Role of Meningeal Lymphatics in Cleansing the Brain: Implications for Alzheimer's Disease – Jonathan Kipnis, Ph.D., University of Virginia	\$150,000
Will Restoration of Normal Glymphatic Function Slow Progression of Cognitive Decline and Amyloid Plaques in a Murine Alzheimer Model? – Maiken Nedergaard, M.D., D.M.Sc., University of Rochester	\$150,000
Nanobodies to Cross the Blood-Brain Barrier – Bart De Strooper, M.D., Ph.D., and Maarten Dewilde, Ph.D., Vlaams Instituut voor Biotechnologie	\$150,000
Microglial TAM Receptors as Modulators of Alzheimer's Pathology – Greg Lemke, Ph.D., Salk Institute	\$150,000
Evaluation of Sleep and EEG in Transgenic Mice for Vassar G2T™ Project – Psychogenics	\$55,000
G2T™ Research Models and Materials – Taconic Biosciences	\$324,780
Total Approved Research for Q3 2017	\$1,632,130

For full abstracts of all funded projects, visit curealz.org/research/funded-research.

'Tis the Season to Give

Even a small gift can make a big difference to Alzheimer's research, and giving has never been easier.

You can donate directly from our website at curealz.org, text the word **RESEARCH** to **41444** to send a donation, or write a check made out to Cure Alzheimer's Fund and send it via snail mail.

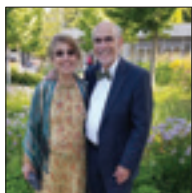
For gifts of securities or direct wire transfers, please contact
Laurel Lyle at **(781) 237-3800** for further information.

All donations are fully tax deductible. Thank you for your support!

"Your donations make a big difference in our progress toward finding a cure for Alzheimer's disease. Your passion, your energy and your generosity are an inspiration to all of us to work even harder to end this terrible disease. Thank you all for your leadership and support."

—Tim Armour, President and CEO, Cure Alzheimer's Fund

For the past several years, **Manny Reiser**, a financial adviser in New York City, has done something a little different around the holidays. Instead of sending holiday gifts to his clients as a thank you for their business, **The Reiser**



Rachel and Manny Reiser, founders of the Reiser Family Foundation.

Family Foundation, founded by Manny and his wife Rachel, made donations to CureAlz in his clients' names, which he communicated in a special holiday card.

Last July, **Whit Collier** of Wellesley, Massachusetts, kite-boarded across 100 miles of water near the Oregon coast to raise money for Cure Alzheimer's Fund and honor his father, Charlie Collier, 69, who was diagnosed with early-onset dementia and Alzheimer's several years ago.



Whit Collier

"I chose a small lake by the ocean where weather can be unpredictable—an appropriate metaphor for the transitions my father faces on his journey. This quest was a symbol of love and gratitude toward him, and a way to inspire others."
—Whit Collier

Known as the beloved "man on the corner" because he waved to everyone driving by, **John Ferrero Jr.** of Crystal Lake, Illinois, struggled with Alzheimer's; he died in March. To honor his memory, his **granddaughters and their friends** came together in August for a two-day bake sale, car wash and lemonade stand to raise money for research. They plan to do it again next year.



John's granddaughters and their friends

Located in the heart of Napa Valley, **ONEHOPE Wine's** mission is to bring people together to celebrate and serve the world. Each of the company's products supports a charitable cause. A portion of proceeds from its 2013 Joseph Jewell Russian River Valley Chardonnay will go directly to CureAlz (while supplies last).

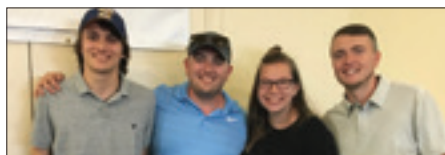


For the third year in a row, **Bob DiFilippo**, **Tom Bond** and **Jim Beers** held the Cure Alzheimer's Mid-Atlantic Charity Golf Tournament. This annual golf event and tennis tournament, held at the Bidermann Golf Course in Wilmington, Delaware, was established to raise money for, and awareness of, Cure Alzheimer's Fund. This year, **David Rosenblatt**, who lost his mom to Alzheimer's and whose family has sponsored the event for the last three years, won closest to the pin.



David

This past August, **Bruce and Gregg Johnson** of Reading, Massachusetts, held their 17th annual DKJ Foundation Golf Tournament at the Four Oaks Country Club in Dracut, Massachusetts, to honor the memory of their father, **David K. Johnson**, and to raise money toward finding a cure and support those affected by the disease.



(L to R) David Johnson's grandchildren: Drew Johnson, Eric Johnson, Madison Richards and Sam Johnson.

After watching his grandfather, once a dedicated runner, struggle with Alzheimer's, **Nico Ericksen-Deriso**, of Boulder, Colorado, and his three **Running Road Trip** teammates, **Charlie Watson**, **Bailee Mulholland** and **Sadie Witt**, ran 1,309 miles over 56 days in each of the 48 contiguous U.S. states, to further advance the battle against one of the world's most difficult diseases.



(L to R) Running Road Trip teammates Charlie, Bailee, Sadie and Nico

The Mongol Rally—a 10,000-mile road rally from Europe to Asia—is not for the faint of heart. Each team drives in a challenging, and sometimes treacherous, race across mountains, the desert and grasslands.

This summer, two teams supported CureAlz:

The Mongol Musketeers: **Brigitte Miller**, **Grady Northrop** and **Sam Bowers** of Santa Monica, California, and

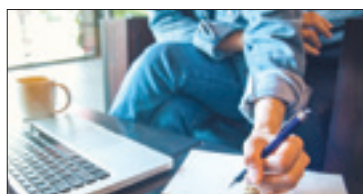
Team Wagonna: **Thomas Willkan** (Danish), **Constantin Wangenheim** (German/American), **Ioana Ilie** (Romanian) and **Oscar Parsley** (French/British).



(L to R) The Mongol Musketeers members Grady, Brigitte and Sam



(L to R) Team Wagonna members Thomas, Oscar, Constantin and Iona



When you work at a company with a dress code, wearing jeans to the office is a luxury. For the second year, **Ally Financial** encouraged its employees across six states to donate a minimum of \$5 each to CureAlz in exchange for the privilege of donning denim at its Jeans Day fundraiser.

Cure Alzheimer's FUND

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

877-CURE-ALZ (287-3259)
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 **facebook.com/CureAlzheimers**.

Jog Your Memory Making Great Strides for AD Research

In 2014, Jess and Bob Rice of Needham, Massachusetts, founded Jog Your Memory 5K Inc. An accredited 501(c)(3), JYM holds an annual USA Track and Field-certified 5K run and two-mile walk to support research aimed at ending Alzheimer's disease. Jess's mother, Carol Caley, was diagnosed with early-onset Alzheimer's in 2007, and the Caley and Rice families continue to be inspired by the strength Carol shows battling the disease.



(L to R) Dick Caley, Carol Caley and Jess Rice

On Sept. 17, the 4th Annual JYM event exceeded all expectations, attracting 560 participants of all ages and 325 donors, and raising more than \$185,000, to bring the event's four-year total to \$442,000. Jess and Bob Rice credit this success to caring friends and runners from the Northeast and throughout the United States, and especially the town of Needham. The hard work of board members, including Jess's father, Dick Caley, and Michelle Taranto, Michelle Schmidt and Harry Stants, has led this Needham-based race to become a community staple.

Part of the Needham Bank Race series, JYM is a fun family event that always keeps Alzheimer's disease and hope for a cure at the forefront. In addition to funding research



Jog Your Memory participants on race day

through CureAlz, JYM added a caregiver grant in 2016, giving families dealing with the disease access to geriatric consultation, respite care and temporary financial relief from lost incomes while caring for their loved ones. Today, 80 percent of the event's proceeds are directed to CureAlz, and 20 percent go to supporting caregivers.

"Cure Alzheimer's Fund supports the world's top research teams who are pursuing bold breakthrough ideas that are getting results and making headlines," said Jess. "Plus 100 percent of donations go directly to research, which is something we are proud to stand behind."