



# The Brain's Lymphatic System

Modern science has an incredibly thorough understanding of the human body. It is hard to imagine that any organ or system could exist within the body that has yet to be discovered. Yet this is exactly what happened in 2015, when researchers discovered lymphatic vessels around and within the brain.

The lymphatic system exists throughout the body. Part of the immune system, it consists of a network of channels (vessels) and glands called "nodes." Nodes create immune cells to help the body fight infection. The vessels carry fluid containing these immune cells, as well as pathogens and harmful cellular waste products, away from organs. Until recently, lymphatic vessels had never been observed in or around the brain. While there were other known ways—such as immune cells called macrophages—for waste products to be cleared from the brain, researchers had trouble explaining the volume of clearance they observed without a lymphatic system.

A recent study at the University of Virginia by Jonathan Kipnis, Ph.D., and his colleagues Antoine Louveau, Ph.D., and Tajie Harris, Ph.D., shed new light on this problem. Using a new method of examining the meninges, a membrane that covers the brain, they discovered there was in fact a network of lymphatic vessels surrounding the brain. Later research showed that the vessels extend within the brain as well. Even though these vessels are large enough to be seen with the human eye, they had never before been observed due to the way brains usually are removed from the skull for examination.

## The Link to Alzheimer's

"This discovery may have major implications for Alzheimer's," explains Kipnis, who is now working on a project, paid for by a grant from Cure Alzheimer's Fund, to investigate this system and its possible role in neurodegenerative disease. "One of the hallmarks of Alzheimer's is the buildup of proteins in the brain, namely amyloid beta and tau. Finding the lymphatic system for the brain opens up whole new avenues of research into how we might be able to facilitate clearance of these proteins and hopefully delay or ameliorate AD."

Kipnis is using fluorescent tracers to study the movement of particles in Alzheimer's mice from the brain to lymph nodes located elsewhere in the body, while also monitoring cognitive function. He hopes to gain a better understanding of how the brain's lymphatic system works in a healthy individual, and what might be going wrong in Alzheimer's. There are several possibilities: The vessels may become clogged with waste products as excess amyloid beta is produced. Inflammation also may play a role, preventing the proper flow of these harmful proteins from the brain. Or, another "upstream" factor may be involved, impairing the function of the lymphatic system around and within the brain. "Once we determine what's going wrong with the lymphatic system in Alzheimer's," Kipnis says, "we can start looking for drugs that might target that problem and reverse it." A therapy might be able to unclog the vessels, reduce inflammation or enhance lymphatic function overall.

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# The Brain's Lymphatic System

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## The Glymphatic System

Maiken Nedergaard, M.D., D.M.Sc., of the University of Rochester, is being supported by Cure Alzheimer's Fund for her research on lymphatic vessels within the brain itself. This portion is referred to as the "glymphatic system," the added "g" referring to glial cells, a type of neuron that makes up the brain's lymphatic vessels. Nedergaard, too, hopes to characterize the role of these vessels in both the healthy and the Alzheimer's brain. Her work focuses on the connection between the glymphatic system and sleep.

"The glymphatic system is like a 'dishwasher' for the brain," Nedergaard says. Though the glymphatic system is always active, it can process almost twice as much fluid during sleep as it does during wakefulness. "When we sleep, the brain cells actually become smaller," she explains, "forcing more fluid out through the glymphatic vessels. It's becoming clear that sleep is vitally important in removing toxic proteins, like amyloid beta, from the brain." Disrupted sleep and Alzheimer's long have been linked, but the direction of causality has not always been clear—lack of sleep may increase risk for Alzheimer's, but the disease itself also may cause sleep problems. Nedergaard hopes the glymphatic system will offer insight into the connection, and help to determine whether changing sleep habits or treating sleep disorders might reduce risk for Alzheimer's.

Tim Armour, President and CEO of Cure Alzheimer's Fund, is encouraged by the work of Kipnis and Nedergaard.

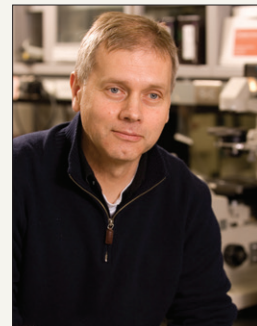
"The recent discovery of the glymphatic system demonstrates how much we still need to learn about the brain," Armour says. "Understanding how waste particles are cleared from the brain is vital to treating Alzheimer's. We're confident that the work of these two scientists will greatly enhance our knowledge of the brain, and take us one step closer to knowing how to stop Alzheimer's disease."



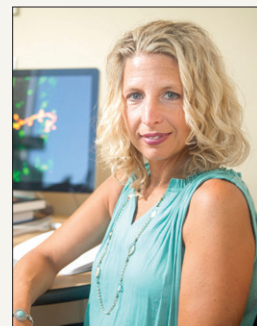
# Research Consortium Welcomes Three New Members

In May, three leading scientists joined our Research Consortium—Marco Colonna, M.D., Beth Stevens, Ph.D., and Stephen Wong, Ph.D. Each of these scientists has received a grant from Cure Alzheimer's Fund and brings new areas of expertise to the consortium.

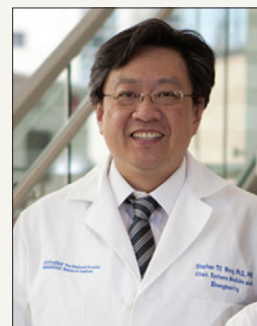
Born and educated in Italy, **Dr. Colonna** is Professor of Pathology & Immunology and Medicine at Washington University School of Medicine in St. Louis. He and the researchers in his laboratory study innate immunity. Together with his team, he discovered triggering receptors expressed on myeloid cells (TREM). Human deficiency in TREM2 causes a progressive, early-onset dementia known as Nasu-Hakola disease and recently, a TREM2 polymorphism was implicated as a genetic risk for Alzheimer's.



**Dr. Stevens**, an Associate Professor of Neurology at Harvard Medical School, established her independent laboratory in the FM Kirby Neurobiology Center at Boston Children's Hospital, Harvard Medical School in 2008. She is also a member of the Broad Institute and Stanley Center. Today, she is investigating the mechanisms that drive synapse loss and dysfunction in Alzheimer's and Huntington's disease, as well as neurodevelopmental disorders, such as autism and schizophrenia.



**Dr. Wong** is the Director of the Ting Tsung and Wei Fong Chao Center for Bioinformatics Research and Imaging for Neuroscience (BRAIN), the Chair of Systems Medicine and Bioengineering Department at Houston Methodist Research Institute, Chief Research Information Officer of Houston Methodist and a Professor of Radiology, Neurology, Neurosciences, Pathology and Laboratory Medicine at Weill Cornell Medicine. At Houston Methodist, Dr. Wong's work has focused on generation of disruptive technologies that seek to make disease cures faster and more efficient.



"It is exciting to bring researchers from across disciplines into the Research Consortium. Supporting collaboration and the exchange of ideas helps us to come closer to finding effective treatments for this disease," says Dr. Rudy Tanzi, Chair of Cure Alzheimer's Fund's Research Consortium. "I am looking forward to continuing to work with Marco, Beth and Stephen, and I know they will help us move our knowledge—and progress toward a cure—forward."



Check out  
our latest  
webinar with  
Dr. Sam Sisodia.

# ALZHEIMER'S AND THE GUT MICROBIOME

[curealz.org/webinar](http://curealz.org/webinar)

REGISTER FOR OUR 2017  
FALL SYMPOSIUM TODAY!

Thursday, Oct. 19  
Boston Public Library

2–3:30 p.m. **Film Screening – Rabb Hall**

4–5:30 p.m. **Scientific Presentation: “The Role  
of Infection in Alzheimer’s Disease” – Rabb Hall**

This event is free to the public, but registration is  
required. Sign up at [curealz.org/symposium](http://curealz.org/symposium).

## Phyllis Rappaport Updates Former College Classmates

In May, Phyllis Rappaport, Co-Founder, Director and Treasurer of Cure Alzheimer’s Fund, spoke about the organization to a self-selected subgroup of her Boston-area Smith College reunion class.

The group welcomed the opportunity to hear more about CureAlz’s latest research findings as part of a mini-reunion held at Rappaport’s home. Some of the women have personal connections to Alzheimer’s, and all are baby boomers who know they are entering the age of greatest risk—and they wanted to know more about the disease and the current state of research.

Rappaport distributed materials on women and Alzheimer’s, which note that two-thirds of all patients are

female. She told the group that little research has been done to date on the reasons for this discrepancy; historically, laboratory mice used in Alzheimer’s research have been male. Researchers do know that the difference in the rate of occurrence between the sexes is *not* due to the fact that women live longer than men. Rappaport also gave a comprehensive report on the state of research, emphasizing the many ways Cure Alzheimer’s Fund has changed the world’s understanding of this enormously complex disease.

“Thanks to our scientists’ work, we now know the different stages of the disease for purposes of

prevention or targeted therapies,” says Rappaport. “Most clinical trials for Alzheimer’s therapies have failed to date because they were based on an insufficient genetic and biological knowledge of the disease. Future clinical trials based on new scientific understandings may have a greater chance for success.”



*Phyllis Rappaport (front row, second from left)  
and her former Smith classmates*





**CureAlz thanks the Lord Foundation for its generosity and commitment to improving lives.**

As lifelong residents of Norwich, Connecticut, Ed and Mary Lord owned and operated many local theaters, several manufacturing companies and a real estate development company. They both were active philanthropists in their community, making many contributions to a variety of charities.

In 1997 they established the Edward and Mary Lord Foundation to provide charitable grants to 501(c)(3) nonprofit organizations. When Ed and Mary died at age 98 in 2009, within five months of each other, their remaining assets were used to fund the foundation. Grants are provided to help the poor, the elderly and children through health and education initiatives. In June, the foundation gave its largest grant to Cure Alzheimer's Fund.

## J. McLaughlin's 'Sip 'n Shop' Fundraiser

Janet Anthos, 58, store manager for fashion retailer J. McLaughlin in Wellesley, Massachusetts, has firsthand experience with Alzheimer's disease, having lived with her mother-in-law, who had it.



In an effort to raise money for Alzheimer's research, Janet approached Cure Alzheimer's Fund with an idea—an afternoon shopping spree with light refreshments to support Alzheimer's research. In June, a dozen Massachusetts J. McLaughlin stores, plus two New York City stores, donated 15 percent of their "Sip 'n Shop" sales to research, raising awareness for Alzheimer's disease among their clientele.

"We are so grateful to J. McLaughlin for its support," says Sally Rosenfield, Senior Vice President at Cure Alzheimer's Fund who attended several of the store events, along with seven of her CureAlz colleagues.



*Phyllis Rappaport, Cure Alzheimer's Fund Founding Board Member, at the J. McLaughlin's 'Sip 'n Shop' fundraiser in Nantucket, Massachusetts.*



The second annual Rick Sharp Classic (a reception, auction and golf tournament) has raised more than the record half-million dollars it brought in last year. Established in memory of Cure Alzheimer's Fund Board Member Sherry Sharp's husband, Rick, who lost his life to Alzheimer's in 2014, this year's classic was held on June 12 and 13 at the Independence Golf Club in Midlothian, Virginia. More than 350 people came out to support the uplifting and inspiring event. Sherry Sharp, along with Rick's former colleagues and friends, used the occasion to communicate the urgent need to find a cure.

The event benefited from a matching gift of \$300,000 from a generous donor, as well as support from other individuals and corporations, including the presenting sponsor CarMax, co-founded by Rick Sharp in 1993.



# Living with Alzheimer's FILM PROJECT

→ **Cure Alzheimer's FUND**  
targeting breakthrough research

## Living with Alzheimer's Film Screening

This past May at the Crosby Street Hotel in Manhattan, Cure Alzheimer's Fund—along with our Young Professionals Group, chaired by Lee and Allie Goldfarb—hosted a film festival featuring the four short films that won the 2015 Living With Alzheimer's Film Competition. The films were judged on three criteria: story merit, technical and artistic achievement, and conveying the challenges of dementia. "Don't You

Forget" by Thomas Bryan won the 2015 Young Filmmaker Prize for those younger than 25. "Crest Of The Hill" by Amanda Kowalski and Samantha Broun, and "Algo queda (Something remains)" by Ana Lorenz, both won a 2015 Jury Prize, while Eric Latek won the Grand Prize for his film "ANNA."

After the film screening, Latek joined John Hockenberry of WNYC's

"The Takeaway" and David Shenk, competition creator and senior adviser to Cure Alzheimer's Fund, for a talk-back where guests could ask questions about the films. Prizes also were awarded to the 2016 competitors: "Love, Zoë" by Zoë Smurr, "Undone" by Hayley Morris, and "Forgetful Not Forgotten" by Christopher Wynn. You can view all entries to the 2015 and 2016 competitions at [livingwithalz.org](http://livingwithalz.org).

## caringkind Alliance Update

It's been more than a year since Cure Alzheimer's Fund formed an unofficial "care and cure" alliance with CaringKind, a New York-based organization that focuses on caring for Alzheimer's patients and supporting their families. Since then we've continued to strengthen our relationship through a number of different activities and events.

In May, Karen Duff, Ph.D., of Columbia University, and a member of the Cure Alzheimer's Fund Research Consortium, spoke to the CaringKind Junior Committee about how the disease progresses. Also that month, the CaringKind Athletes for Alzheimer's Committee allocated \$20,000 to Dr. Duff's project on investigating tau—twisted protein fibers that cause tangles in the brain. And in June, Cure Alzheimer's Fund representatives attended CaringKind's annual gala to show support for the organization.

## Extra Sets of Hands

Cure Alzheimer's Fund has been fortunate enough to have the assistance of three hard-working interns in our office over the past few months. Katelyn Yuen, a 4th-year dual-degree student at Boston University; Lexi Goodhue, a rising junior at Boston College; and Gabrielle de Weck, a rising freshman at Tufts University, have been helping with fundraising, marketing/communications and gift processing. We're thrilled to have them on board!



L to R:  
Katelyn,  
Gabrielle  
and Lexi

*"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



Carolyn, left, and Barbara

For eight years **Carolyn Mastrangelo** and **Barbara Geiger**, both 48, have been holding the enormously successful Running 4 Answers fundraiser each April in Roseland, New Jersey, which has raised more than \$285,000 for research.

*"My mom suffered with early-onset Alzheimer's for 17 years before passing away. While she was the catalyst behind the creation of Running 4 Answers, we continue to hold it for all the attendees who have relatives with Alzheimer's. We believe in CureAlz's mission and feel honored to be a part of it."* —Carolyn Mastrangelo

After watching her mother-in-law suffer from Alzheimer's for eight years, **Stacy Hull**, 46, an independent director for India Hicks products in Richmond, Virginia, wanted to take action. On April 9 she donated 80 percent of her personal profits from that week to CureAlz for her company's *Get Together Give Together* week.



Stacy

For her Girl Scout Gold Award project **Grace Cunningham**, 18, from Glen Rock, New Jersey, distributed donated iPods

with customized music selections to patients suffering with Alzheimer's disease at an elder care facility, to help them spark memories.



Grace and one of her music lovers

**Gil Stubbs**, 89, and several of his fellow magicians put on a show in May at the Wellesley Community Center in Massachusetts to raise money and awareness for Cure Alzheimer's Fund. The idea for the show came after Gil's friend's wife died from Alzheimer's, and that friend asked for donations to CureAlz in lieu of flowers.



Gil

Each year, the **Freeburg High School girls and boys cross country teams** in Freeburg, Illinois, organize a 5K event to raise money for a selected charity. This year they chose Cure Alzheimer's Fund, because the disease has impacted some team members' families.

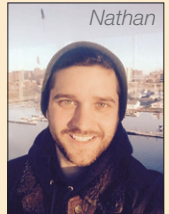


The Freeburg girls cross country team

Tattoo artist and author **Jess Scutella**, 26, and photographer **Nathan Sulecki**, 29, of Erie, Pennsylvania, are currently donating a portion of the proceeds from their work, as well as their time, to creating an understanding of Alzheimer's disease among a younger generation.



Jess



Nathan

## springbok

**Springbok Puzzles**, the oldest manufacturer of jigsaw puzzles in the United States, has created a line of puzzles for those suffering from Alzheimer's—and it's the fastest-growing line in the company. Springbok is donating \$3 of every Alzheimer's puzzle sold to Cure Alzheimer's Fund.

In April, vocalist **Morgan Middleton**, 24, of Springfield, Virginia, performed her one-woman musical as a fundraiser for Cure Alzheimer's Fund. The show was designed to harness the power of music in the treatment of Alzheimer's disease.



Morgan



## Cure Alzheimer's FUND

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f: 781-658-2399  
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**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.

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### 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 Bovie  
Copy Editor: Colleen O'Neill  
Design: Winking Fish

## Financial Update

	This Quarter	YTD	Inception to Date
<b>Fundraising</b>	\$2.2M	\$5.5M	\$81.2M
<b>Expenses paid for by the board</b>	\$0.9M	\$1.7M	\$16.8M
<b>Funded research</b>	\$2.7M	\$4.7M	\$56.1M

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

## Research Update (Research funded during the second quarter of 2017)

Project/Researcher	Distribution Amount
<b>A Combination of Anti-Amyloid Beta and Growth Factor Therapy for Alzheimer's Disease –</b> Mark H. Tuszynski, M.D., Ph.D., University of California, San Diego	\$125,000
<b>In Vitro and In Vivo Analysis of Amyloid Precursor Protein (APP) Variants –</b> Sangram S. Sisodia, Ph.D., University of Chicago	\$250,000
<b>Pathway Cross-talks Associated With Sex and Risk for Alzheimer's Disease –</b> P. Murali Doraiswamy, M.D., Duke University Medical Center	\$152,276
<b>Modeling Neuronal Aging in Specific Subtypes of Human Neurons by MicroRNA-Mediated Neuronal Reprogramming –</b> Andrew Yoo, Ph.D., Washington University School of Medicine, St. Louis	\$150,000
<b>Modeling DNA Methylation Changes in Alzheimer's Disease Using Human-Induced Pluripotent Stem (iPS) Cells –</b> Rudolf Jaenisch, M.D., Whitehead Institute	\$150,000
<b>The Role of APOE in Microglia Regulation in Neurodegeneration –</b> Oleg Butovsky, Ph.D., Brigham & Women's Hospital	\$250,000
<b>Effects of Peripheral APOE on Central Nervous System Functions and Alzheimer's Disease Pathogenesis –</b> Guojun Bu, Ph.D., Mayo Clinic Jacksonville	\$250,000
<b>Impact of APOE and Sex on Vulnerable Neuron-Specific Functional Network –</b> Paul Greengard, Ph.D., The Rockefeller University	\$250,000
<b>Using Human Bioengineered Cerebral Vessels to Explore How Native APOE Affects Cerebrovascular Properties Relevant to Alzheimer's Disease –</b> Cheryl Wellington, Ph.D., University of British Columbia	\$248,458
<b>APOE Proteoforms in the Human Central Nervous System and Validation of APOE Pharmacodynamic Translational Markers –</b> Randall J. Bateman, M.D., Washington University, St. Louis	\$250,000
<b>Understanding the Effect of APOE on Tau-Mediated Neurodegeneration –</b> David M. Holtzman, M.D., Washington University, St. Louis	\$300,000
<b>G2T™ Research Models and Materials –</b> Taconic Biosciences	\$340,475
<b>Total Distributed to Research for Q2 2017</b>	<b>\$2,716,209</b>

For full abstracts of all funded projects, visit [curealz.org/research/funded-research](http://curealz.org/research/funded-research).

# 100 percent of every donation goes directly to research.

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

Donations can be made through our websites, [CureAlz.org/donate](http://CureAlz.org/donate) or [WomenAndAlzheimers.org](http://WomenAndAlzheimers.org),  
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.

We'd love to get  
your feedback  
on our newsletters!

Help us out by taking  
a quick five-minute survey at  
[curealz.org/quarterly-newsletter-survey](http://curealz.org/quarterly-newsletter-survey).



Check out our Facebook page for our most recent posts, photos, videos and more! Go to [facebook.com/CureAlzheimers](https://facebook.com/CureAlzheimers).

## CureAlz Featured in O, The Oprah Magazine

The June issue of O,  
Oprah Winfrey's magazine,  
featured an in-depth special  
report about the human

brain. Writer Katherine  
Hobson reached out to Cure Alzheimer's Fund as  
a trusted source on women and Alzheimer's  
disease. In the article, she recognized our efforts  
to require our researchers to use both female and  
male mice in their labs.

The article helps educate readers about the  
higher risk for women, and clarifies the differences  
between Alzheimer's, senility and dementia. It also  
includes information provided by Ronald C. Peterson,  
M.D., Ph.D., a member of the Cure Alzheimer's Fund  
Science Advisory Board, and Rudy Tanzi, Ph.D., Chair  
of our Research Consortium. You can read the full  
article at [here](#).



## Jeff Morby Presents at Rotary Foundation's Centennial

In June, Cure Alzheimer's  
Fund Co-Chairman and  
Co-Founder Jeff Morby gave  
a presentation at the 100th  
anniversary convention of  
Rotary International titled  
"Fighting the Alzheimer's  
Tsunami." The presentation  
was attended by 400  
Rotarians from around the world interested in hearing  
about the progress being made in the fight against  
Alzheimer's disease.



Morby is a founder of the Alzheimer's/Dementia Rotarian  
Action Group (ADRAG, at [adrag.org](http://adrag.org)). The vision of this  
organization within Rotary is to leverage the experience  
and resources of Rotarians to support and promote  
Alzheimer's- and dementia-related projects. With  
33,000 Rotary clubs in more than 200 countries and a  
network of 1.2 million Rotarians who commit their time  
and talents to serving their communities and the world,  
there is great potential for raising global awareness of  
Alzheimer's and funding research.