Honoring Our Researchers

Tribute Edition

Cure Alzheimer's FUND

Often our greatest accomplishments begin with a tiny spark. A thought, a moment, a feeling, an experience—something small that inspired us to act. Motivated us to do something amazing—perhaps, even something that seemed impossible.

At Cure Alzheimer's Fund, we are inspired every day by the dedicated researchers and the scientific progress being made in the fight against Alzheimer's disease. We proudly fund their bold ideas, support their creative thinking and encourage them to collaborate, because that is what it will take to do what often seems impossible—prevent, slow or reverse Alzheimer's disease.

These scientists have dedicated their lives to the research that eventually will cure Alzheimer's disease. What has inspired them to make this their life's work? What was their tiny spark? What drives the CureAlz researcher?

We invite you to get to know some of the remarkable people working in laboratories around the world. It is our hope that their stories will inspire others to join us in finding a cure for Alzheimer's disease.

Dear Friends,

In October 2005, less than one short year after our founding, the first in-person meeting of our then-seven-member Research Consortium was held in Washington, D.C. At that meeting, the group developed an outline for our areas of scientific focus and agreed that collaboration was fundamental to success. Along with collaboration, an essential element for the future of Cure Alzheimer's Fund would be the continued identification and attraction of leading researchers in the field.

Back then, it was expected that, over time, we would learn a great deal about the causes and pathology of Alzheimer's disease. However, we have learned so much more from the 249 exceptional researchers who have been part of the Cure Alzheimer's Fund family.

- TENACITY — To be a researcher requires one to be tenacious—persistent—and to move forward when some may consider your ideas not worthy. Our researchers are the definition of tenacity.
- THE POWER OF POSITIVE THINKING — To be a researcher, one also must think positively. Imagine that, on a daily basis, your purpose—your life's work—is dedicated to solving problems. What could be more positive?
- GENEROSITY — Every day at Cure Alzheimer's Fund, we experience the unlimited generosity of so many who contribute to research. Our researchers also have provided great lessons in generosity with the sharing of their findings with other scientists, and with the leadership and mentoring qualities they exhibit each and every day.
- PATIENCE — Science is hard and often takes much longer than we would expect. To be a scientist and to take all of the necessary steps to see a project through from beginning to end requires great patience.
- GRACE — Our researchers are decent, thoughtful and kind.
- THERE ARE NO FAILURES — Finally, an important lesson—and one that may be hard to learn—is that there is no such thing as failure. Instead, each outcome that is not ideal or desired helps to inform and illuminate other paths.

Without question, it is the exceptional work, dedication and collaboration of our funded researchers, many profiled in this newsletter, that have contributed to significant advancements in the understanding of Alzheimer's disease. Their work has changed our world…and one day we will see a cure.

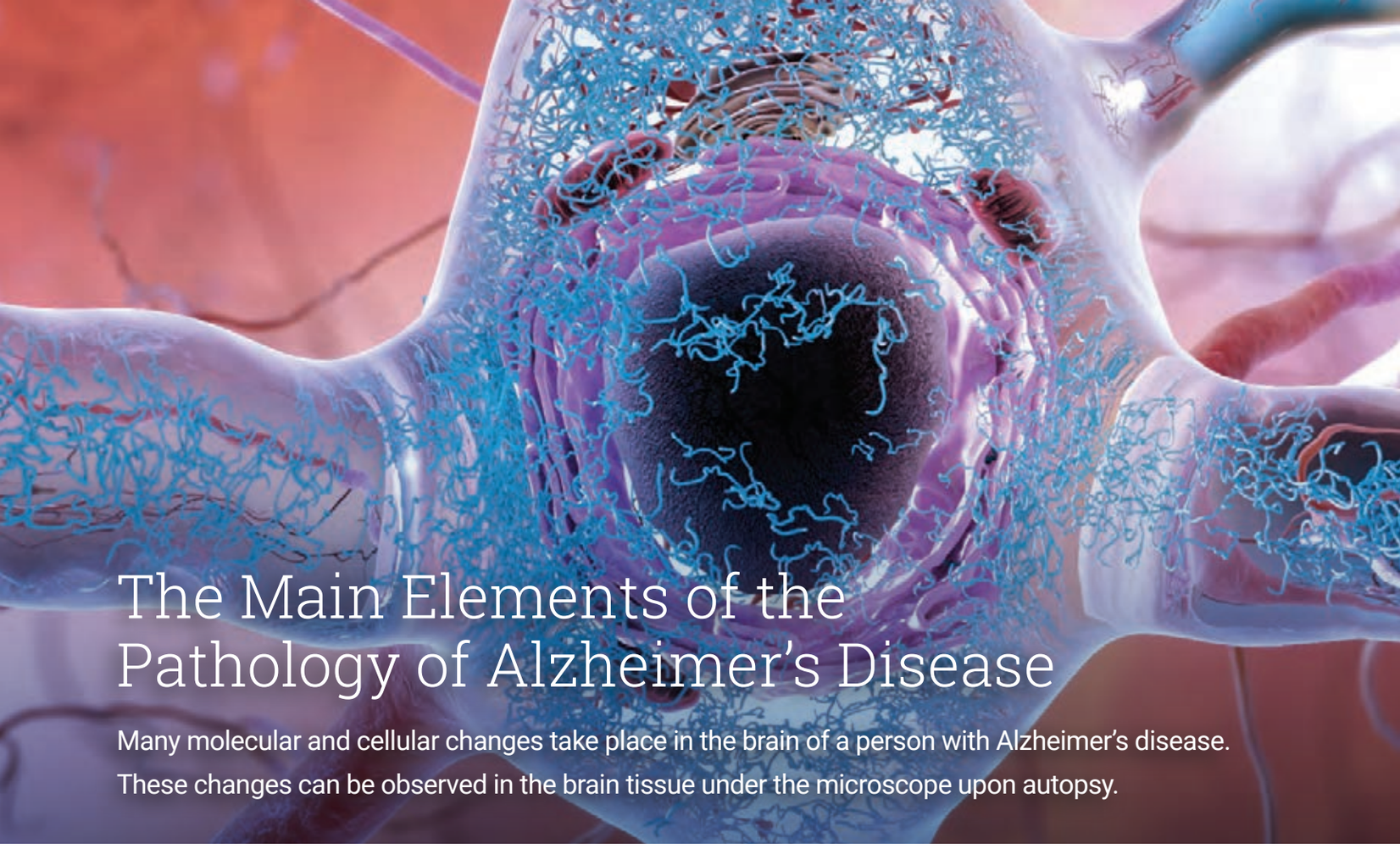
In this newsletter, we honor the exceptional scientists and the teams in their labs for the work they are doing to rid our world of Alzheimer's disease. Their contributions and commitment are vital to our future. They understand that 50 million people worldwide, and their friends and family, live with the burden and devastation of this fatal disease. Many of the researchers profiled have their own very personal experience with a friend or family member diagnosed with Alzheimer's disease, a motivating factor in their journey. For the 17 years I have been with Cure Alzheimer's Fund, I have admired and grown very fond of our researchers for their diligence, generosity and care. I can write with confidence that we are in great hands and, one day, there will be a cure for Alzheimer's disease.

I am honored to share their stories with you.

Gratefully,

Tim Armour
President and CEO
Cure Alzheimer's Fund

The first research group convened six months after the founding of Cure Alzheimer's Fund in Washington, D.C. Attendees included (front row, from left) Dr. Dora Kovacs, founders Jacqui Morby and Phyllis Rappaport, Dr. Virginia Lee; (back row, from left) Dr. John Mazziotta, founder Jeff Morby, Drs. David Holtzman, Sangram Sisodia, Charles Glabe, Steven Wagner and Rudy Tanzi, CEO Tim Armour.



The Main Elements of the Pathology of Alzheimer's Disease

Many molecular and cellular changes take place in the brain of a person with Alzheimer's disease. These changes can be observed in the brain tissue under the microscope upon autopsy.

AMYLOID PLAQUES

The amyloid plaques involved in Alzheimer's disease come in several different molecular forms that collect between neurons. Such plaques are formed from the breakdown of a larger protein, called amyloid precursor protein. In the Alzheimer's brain, abnormal levels of this naturally occurring protein clump together to form plaques that collect between neurons and disrupt cell function.

NEUROFIBRILLARY TANGLES

Neurofibrillary tangles are abnormal accumulations of a protein called tau that collect inside neurons. Healthy neurons, in part, are supported internally by structures called microtubules. In Alzheimer's disease, however, abnormal chemical changes cause tau to detach from microtubules and stick to other tau molecules, forming threads that eventually join to form tangles inside neurons. These tangles block the neuron's transport system, which harms the synaptic communication between neurons.

Emerging evidence suggests that Alzheimer's-related brain changes may result from a complex interplay among abnormal tau and amyloid plaque proteins and several other factors. It appears that abnormal tau accumulates in specific brain regions involved in memory. Amyloid clumps into plaques between neurons. As the level of amyloid plaques reaches a tipping point, there is a rapid spread of tau throughout the brain.

CHRONIC INFLAMMATION

Research suggests that chronic inflammation may be caused by the buildup of glial cells normally meant to help keep the brain free of debris. One type of glial cell, microglia, engulfs and destroys waste and toxins in a healthy brain. In Alzheimer's, microglia fail to clear away waste, debris and protein collections, including amyloid plaques.

LOSS OF NEURONAL CONNECTIONS AND CELL DEATH

In Alzheimer's disease, as neurons are injured and die throughout the brain, connections between networks of neurons may break down, and many brain regions begin to shrink. By the final stages of Alzheimer's, this process—called brain atrophy—is widespread, causing significant loss of brain volume.

Reprinted in part from information provided on the website of the National Institute of Aging/National Institutes of Health. *www.nia.nih.gov/health/what-happens-brain-alzheimers-disease*

Since our founding, Cure Alzheimer's Fund has provided grants to 249 of the world's leading researchers who have dedicated their lives to finding solutions for the disease.

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Rudolph E. Tanzi, Ph.D.

Vice Chair of Neurology, Massachusetts General Hospital; Joseph P. and Rose F. Kennedy Professor of Neurology, Harvard Medical School; Chair, Cure Alzheimer's Fund Research Leadership Group

"Few real nightmares on earth compare to the terror wrought by Alzheimer's disease. That this fatal brain disorder not only annihilates a person's mind, but starts doing so years before it takes their life, is surely its most insidious aspect. Its initial symptoms of forgetfulness and personality changes lie so close to normalcy that they typically go unnoticed; and, once noticed, too long unexplained. As the victim's grasp further slides, it can bring nothing but tormenting confusion for the patient and those close to him. What can be worse than watching someone you love cognitively flailing, until eventually they no longer recognize faces, surroundings, or even themselves?"

—Rudolph E. Tanzi, Ph.D., introduction to "Decoding Darkness," published in 2000

Early in 2004 Jeff and Jacqui Morby met with Dr. Rudy Tanzi, who was researching the causes of Alzheimer's disease (AD). During that meeting, the Morbys learned that the science of genetics offered opportunities to unravel the secrets of AD. Progress was slow because funding from the National Institutes of Health was extremely limited, even though the numbers of those diagnosed were expected to escalate with the aging of the baby boomers. In 2019, Jeff wrote, "In 2004, after learning about the funding issues, we made a deal with Rudy: We would fund Rudy and AD research if he would put together the finest group of Alzheimer's researchers in the world focused on curing the disease as soon as possible." Rudy agreed.

Rudy has a long family lineage in the sciences dating back to the early 1900s. Eugenio Tanzi is cited as an early pioneer in European neurology and is considered the father of long-term potentiation, the main form of synaptic plasticity providing the information storage processes of learning and memory. Later that century, as an undergraduate in a research lab, Rudy mapped genes in bacteria to their chromosome, work he enjoyed and that became the foundation for his love of genetics. In the early 1980s, Rudy discovered that common disorders affecting the human nervous system, Down syndrome and AD, involved genes on chromosome 21. To characterize Rudy as passionate about genetics is a tremendous understatement.

For 18 years, Rudy has been critical to all that has been accomplished through the grants provided by CureAlz. In addition to the great work in his lab, through Rudy and his role as Chairman of our Research Leadership Group, CureAlz has attracted leading researchers from around the world. Collectively, these researchers have made many groundbreaking discoveries and have truly changed our understanding of AD.

Thank you, Rudy, for leading our research, for being a strong advocate for Cure Alzheimer's Fund, and for your dedication to finding a cure for Alzheimer's disease.

Dr. Rudy Tanzi (center) pictured with Cure Alzheimer's Fund Co-Chairmen Jeff Morby (left) and Henry McCance (right).

George S. Bloom, Ph.D.

Professor of Biology, Cell Biology, and Neuroscience, University of Virginia

My Research

My lab is trying to understand what happens at the very beginning to convert normal healthy nerve cells (neurons) in the brain into Alzheimer's disease neurons, and how to leverage what we learn from a basic science approach to develop drugs that delay or prevent Alzheimer's disease symptom onset and slow disease progression.

Based on a study that my lab published a few years ago (Kodis, et al. 2018. Alzheimer's & Dementia 14: 1302–1312), my institution, the University of Virginia, recently began a pilot phase 2 clinical trial to repurpose memantine (Namenda®) as an Alzheimer's disease prophylactic by administering it to at-risk patients beginning years before expected symptom onset. Memantine already is approved by the FDA for modest and temporary symptom relief for moderate to severe Alzheimer's disease, and the research described in the Kodis paper was partially supported by Cure Alzheimer's Fund.

My Inspiration

The chance to make discoveries that will help control a devastating disease.

My Motivation to Research Alzheimer's Disease

I am a basic cell biologist by training and mindset, and until my lab began a very slow transition to Alzheimer's disease research about 25 years ago, we worked mainly on microtubules, intracellular transport, actin filaments, and cellular motility and morphogenesis. My initial interest in Alzheimer's disease was sparked by a desire to define the building blocks of paired helical filaments (PHFs), bundles of which form neurofibrillary tangles in Alzheimer's disease brain, and like microtubules and actin filaments are linear polymers of protein subunits. Of course, other labs figured out that PHFs are made from the microtubule-associated protein, tau, before I even got started, but I was already bitten by the Alzheimer's disease bug by then.

My Personal Connection to Alzheimer's Disease

Like most people, I have known and do know Alzheimer's disease patients, but I am not aware of any members of my extended family who had or have Alzheimer's disease.

Most Exciting Career Moment to Date

The award of a Zenith Fellowship from the Alzheimer's Association, which in my mind, at least, signaled my successful transition from a basic cell biologist to an internationally respected Alzheimer's disease researcher.

Biggest Unanswered Question in Alzheimer's Disease

How to prevent it, or at least halt or slow symptom progression. Advances in early detection are far ahead of efforts to treat presymptomatic individuals deemed to be at risk based on biomarkers.

What I Wish Most People Understood About Science

Cutting-edge science is, by its very nature, a journey into the unknown. It follows naturally that not all experiments will be successful, and that progress can take a long time to come to fruition.

Outside of Work, I Like...

To fly fish and bird watch.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

In the most general sense, the Cure Alzheimer's Fund support I have had over the years has enabled my lab to pursue research projects that probably would have been too risky to gain NIH support at the time. I am forever grateful.

The Bloom Lab team, clockwise from left: Anna Wasserman, Merci Best, Nutan Shivange, Lisa Post, Murat Koseoglu, Horst Wallrabe, George Bloom, Dora Bigler Wang, Victoria Sun, Andrés Norambuena.

Dr. Erin Kodis

Sandro Da Mesquita, Ph.D.

Assistant Professor, Meningeal Lymphatics and Neurological Disorders Lab, Mayo Clinic Jacksonville

My Research
We use animal models to better understand the cellular and molecular interactions that take place at the brain border tissues and underlie human neurodegenerative disorders. We are focusing on immune-related mechanisms that are dysregulated, and once normalized might delay or even prevent cognitive decay and other Alzheimer's disease symptoms.

My Inspiration
The capacity to generate novel experimental hypotheses based on the scientific advances promoted by the community.

My Motivation to Research Alzheimer's Disease
Scientific interest and the lack of therapies that efficiently arrest Alzheimer's disease-associated cognitive decline.

My Personal Connection to Alzheimer's Disease
I do not have family members that were diagnosed with the disease. I did, however, spend a summer in a retirement house when I was in college (back in Portugal), and had the chance to see with my own eyes the toll that this disease takes on patients and their families. Devastating. We need efficient treatments, fast!

Most Exciting Career Moment to Date
The discoveries generated as a postdoctoral researcher in the Kipnis Lab. Amazing years of research with a fantastic team of young researchers with whom I still maintain strong connections even now as an independent investigator.

Biggest Unanswered Question in Alzheimer's Disease
When to start the therapeutic interventions.

What I Wish Most People Understood About Science
How important basic scientific research is for the development of efficacious treatments, how costly it is and how little is being invested in research.

Outside of Work, I Like...
I am a soccer fan. I enjoy watching games on television and to play with colleagues on weekends.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
It was a game changer. During my postdoc, Dr. Kipnis was awarded a grant by the Cure Alzheimer's Fund that supported part of my training. Nowadays, Cure Alzheimer's Fund supports my laboratory at Mayo Clinic, where we continue to study the role of meningeal lymphatic drainage in Alzheimer's disease.

Da Mesquita Lab members, from left: Nickoleta Delivanoglou, Guadalupe Sanchez, Megan Barber, Shanon Rego, Sofia P. das Neves, Sandro Da Mesquita.

Christopher K. Glass, M.D., Ph.D.

Distinguished Professor of Medicine and Cellular and Molecular Medicine; Ben and Wanda Hildyard Chair of Hereditary Diseases, University of California, San Diego

My Research

I study how immune cells normally protect the body from infection, but also how they can cause tissue damage in chronic diseases of aging, such as Alzheimer's disease and atherosclerosis. We are particularly interested in brain immune cells called microglia, which can be both beneficial and harmful in Alzheimer's disease.

We are trying to understand the reasons that cause microglia to promote the development of Alzheimer's disease. This understanding would provide the basis for new therapies.

My Inspiration

Getting to the next step of solving a problem.

My Motivation to Research Alzheimer's Disease

I have a child with Down Syndrome who is at high risk for developing early-onset Alzheimer's disease.

Most Exciting Career Moment to Date

The discovery of a general mechanism by which the genome is decoded to specify the development of different types of immune cells.

Biggest Unanswered Question in Alzheimer's Disease

For me personally, it is the question of how immune cells contribute to the dysfunction and death of neurons.

What I Wish Most People Understood About Science

A major goal of science is to advance understanding of the natural world and, when possible, to use this understanding for human benefit. However, scientific advances can have unintended consequences or be used for inhumane purposes. It is thus important that scientists have an appreciation of the humanities and that people who are not scientists have a reciprocal interest in how science is carried out, so that these spheres of activity can be interconnected and work effectively for the common good.

Outside of Work, I Like...

I like to swim in the ocean.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund enabled us to develop new technologies to define regions of the genome that control the development of the different cell types in the human brain. This work was fundamental to linking genetic variation associated with Alzheimer's disease to regions of the genome that control the development and function of microglia.

Glass Lab members: Dr. Payam Saisan, Rick Zhenzhi Li, Christina Mora, Dr. Nathan Spann, Dr. Yohei Abe, Dr. Christian Nickl, Jana Collier, Dr. Bethany Fixen, Dr. Isidoro Cobo, Dr. Christopher Glass, Dr. Claudia Han, Dr. Martina Pasillas, Dr. Thomas Prohaska, Dr. Johannes Schlachetzki, Christopher Balak, Dr. Enchen Zhou, Dr. Lindsay Milich, Katelyn Griffith, Sydney O'Brien, Dr. Yi Zhou, collaborator Nicole Coufal.

Srdjan D. Antic, M.D.

Associate Professor of Neuroscience, University of Connecticut Health Center

My Research

Alzheimer's disease silently attacks the brain for many years before symptoms of the disease appear (memory loss, confusion and dementia). Once these classical symptoms of Alzheimer's disease are manifested in a patient, it is already too late; the amount of the brain structural damage is very high and it cannot be reversed. It is important to detect and stop the Alzheimer's disease cellular process before obvious behavioral changes. We think that behavioral changes (symptoms of the disease) are preceded with subtle physiological changes in cortical circuits, which only can be detected using electrical recordings. In our laboratory, we examine Alzheimer's disease model animals at this early age (before their brains develop strong Alzheimer's disease pathology). In these Alzheimer's disease model animals, we seek signs of functional impairment in the brain circuitry, or impairments in brain electrical signaling.

Knowing the silent physiological changes that occur prior to the manifestation of the obvious clinical symptoms of the disease will greatly improve the ability of researchers to direct therapy toward fixing these specific physiological deficits. It is believed that aberrant electrical activity causes or facilitates structural damage to the Alzheimer's disease brain. By removing physiological deficits in neuronal activity (aberrant activity), we may be able to significantly slow down the progress of the disease. Knowing these silent physiological changes also will greatly improve the ability of researchers to design diagnostic tools, which may be used for early detection of Alzheimer's disease.

My Inspiration

If I stayed in medicine (which is my original training), I would have spent my days seeing the same type of a patient, suffering from the same disease in which I had specialized. Today, I observe things in the brain that no one has ever seen before.

My Motivation to Research Alzheimer's Disease

Like everything else in my life, this decision was largely opportunistic. I had an experimental method for measuring physiological parameters in the brain, and my collaborator had Alzheimer's disease model animals and a strong background in Alzheimer's disease. We joined forces.

My Personal Connection to Alzheimer's Disease

First, I teach Alzheimer's disease in the UConn Health School of Medicine. I interact with neurologists and psychiatrists during these teaching sessions. Each year, I am reminded of many social and personal aspects of this disease.

Second, I have one semi-personal story to share. My best friend's grandfather succumbed to Alzheimer's disease. My best friend was 14 years old when his grandfather died. In the late stages of the disease, the entire family was having a nice Sunday breakfast. After the breakfast, while they were cleaning dishes, the grandfather suddenly slammed the breakfast table, made a huge noise (bang), and shouted, "When are we going to eat in this house?" So, the poor guy (grandfather) not only failed to record a family breakfast happening only 10 minutes prior, but also he did not get any information that his stomach was completely full with food. Furthermore, the grandfather was aggressive and rude to his beloved ones, those who cared for him over the weekend, and those who invited him to a Sunday breakfast.

Third, you could be a most wonderful and most productive person in the world, and, then one day you find yourself terminally ill from Alzheimer's disease. Is this how everyone will remember you? In my view, one of the most severe aspects of a personal tragedy called Alzheimer's disease is when family, friends and colleagues remember you by the events that occurred in the late course of your Alzheimer's disease.

Most Exciting Career Moment to Date

When I made my first electrical recording from a nerve cell. I provided a stimulus and I recorded the response in the form of electrical spikes (firing). What is the excitement? I was recording from a living nerve cell and reading its "state" and its "thoughts" in real time.

Biggest Unanswered Question in Alzheimer's Disease

Could doctors perform some form of screening in the population of 50-year-old people and determine with 95% accuracy (certainty) those individuals who will develop classical AD symptoms in the next 20 years? Why is this important? Such early diagnostics would provide clinicians and patients with a 20-year window to do something substantial (for example, design and explore novel therapeutic strategies, change food, change life habits).

Members of the Antic Lab team, from left: Darko Lovic, Srdjan Antic, Brianna Barbeau, Abigail Edelstein.

What I Wish Most People Understood About Science

Rejecting a research project-hypothesis (proving it wrong) is an excellent science, but [there is] no money there. We need to allow scientists to present their negative data, and apply for funding based on the negative data. At the same time, we should be careful of those researchers who have a constant stream of "positive data" confirming/approving all of their initial hypotheses.

Outside of Work, I Like...

I play electric bass guitar and I record "songs" on a desktop computer (amateur home studio) combining drums, keyboards and other digital instruments that come with the recording software. Strangely, my wife strictly prohibits the sound of my music when she is around. There is only one logical explanation to her behavior: she is jealous of my blooming musical talent.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

CureAlz allowed me to combine my basic science tools (e.g., electrophysiology and optical imaging) with the applied science questions (Alzheimer's disease). To a basic science researcher, the doors to translational and disease-oriented fields are often half-closed. Simply, many funding agencies think that only people who previously worked in the field of Alzheimer's disease should get Alzheimer's disease funding. Fortunately, CureAlz did not endorse that rule too strictly. With the CureAlz support, we developed a mouse line that combines two things. First, this mouse strain carries sick genes, resulting in the Alzheimer's disease pathology in brain. Second, this same mouse strain exhibits neurons with fluorescent indicators in their membranes. With this new mouse line in hand, we use optical imaging to measure neuronal activity in the brains of both the Alzheimer's disease model mice and their healthy littermates. This is the direct outcome of the CureAlz funding, and a huge positive impact to my work.

Nicola Allen, Ph.D.

Associate Professor, Salk Institute for Biological Studies

My Research

We study how the brain works in health and goes wrong in different disorders. We do this by studying all the cells in the brain, specifically a type of cell called an astrocyte. Astrocytes are essential for supporting neuronal function throughout our lives—indeed, if all astrocytes are removed, then the brain no longer functions, showing how important they are. In aging and in Alzheimer's disease, astrocytes change their properties in ways that can be damaging to neurons, so we want to know whether neuronal dysfunction can be rescued by targeting astrocytes.

We have identified specific signals made by astrocytes in the healthy brain that enable neurons to communicate with each other, and others that inhibit this communication. We are studying whether we can use these signals to stimulate new neuronal connections to form in Alzheimer's disease, or protect the connections that are there from being lost. If successful, this would provide new targets for therapeutic development.

My Motivation to Research Alzheimer's Disease

I want our work to have a positive impact on people's health, so developing ways to decrease the impact of different brain disorders on people's lives, including Alzheimer's disease, is a great motivator.

My Personal Connection to Alzheimer's Disease

My grandmother had Alzheimer's. Every few months my mum asks me if I've cured Alzheimer's yet, so that is pretty motivating.

What I Wish Most People Understood About Science

That science is constantly evolving. When new discoveries are made, this can lead us to update our conclusions on different topics. This doesn't mean the previous interpretation was wrong; rather, that science is often a work in progress.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

The support from Cure Alzheimer's Fund is essential for our work. It is supporting a project in its early stages, and will allow us to determine whether the pathway we are studying is important in Alzheimer's disease or not. If it is, then the support will have enabled us to generate enough data to apply for future funding.

Raja Bhattacharyya, Ph.D.

Assistant Professor of Neurology, Harvard Medical School; Genetics and Aging Research Unit, Massachusetts General Hospital

My Research

My research is dedicated to identifying the precise location of the production of neurotoxic beta-amyloid inside the nerve cells (neurons) in Alzheimer's disease brains.

Production of amyloid beta is one of the major hallmarks of Alzheimer's disease pathology. Our research revealed that a small pool of beta-amyloid precursor protein (APP) called palmitoylated APP (palAPP) inside special cholesterol-rich vessels called MAMs (mitochondria-associated ER-membranes) makes neurotoxic beta-amyloid. Identification of the precise location (e.g., MAMs) and/or the specific components (e.g., palAPP) for amyloid beta production inside the nerve cells or neurons would one day be used to develop targeted and effective therapeutics to prevent or cure this devastating neurodegenerative disease.

My Inspiration

One of the most inspiring aspects of my science career is to mentor young researchers into becoming seasoned scientists, because I believe that every scientist's goal is to prepare the next generation to carry on the mantle of scientific discovery.

My Motivation to Research Alzheimer's Disease

The human brain is probably the most mysterious object in our entire known universe. This roughly 3-pound jelly-like object makes us who we are by storing and restoring our memories. Alzheimer's disease incrementally and sometimes aggressively erases our memories and robs us from our senses of who we are. I believe that there is no other debilitating disease that could be more terrifying than Alzheimer's disease. This belief inspired me to pursue my scientific career in understanding and, if possible, curing this devastating disease.

Most Exciting Career Moment to Date

The most exciting moment of my scientific career is when I see that another scientist has validated my published work completely independently. Every time this happens, it gives me immense joy, primarily because it is the first step toward knowledge creation, which is the primary goal of every scientist, in my view.

Biggest Unanswered Question in Alzheimer's Disease

The biggest unanswered question in Alzheimer's disease research is: how is neurotoxic beta-amyloid, the key component of amyloid plaques in Alzheimer's disease brains, generated in neurons and cause neurotoxicity?

What I Wish Most People Understood About Science

As a scientist and as an avid believer of scientific method, I wish that the general public knew or understood that scientists all across the world are working at the frontier of science, stretching the boundary of our knowledge through breakthroughs and paradigm shifts following a rigorous scientific method of theorizing, experimentation, validation, scrutiny and peer review before their findings become established knowledge.

Outside of Work, I Like...

Outside work, I am passionate about reading nonfiction and watching fiction. My favorite pastime is to walk around the streets of crowded cities and eat local street food.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund has made an enormous difference in my research. The generous fund is instrumental for me to develop state-of-the-art biochemical and microscopic methods to advance our knowledge about the novel therapeutic target, namely MAM-associated palmitoylated APP against amyloid beta production in Alzheimer's disease. I have used the fund to synthesize a series of novel small molecules with a potential to lower both amyloid as well as tau pathologies, two of the hallmarks of Alzheimer's disease development.

→ RESEARCH MILESTONES

CRISPR EDITING OF APOE4 GENE

Using CRISPR gene editing technology, the harmful APOE4 gene was converted to the neutral APOE3 gene in the lab, alleviating Alzheimer's-related characteristics.
—Li-Huei Tsai, Ph.D. [bit.ly/3SqrIFj]

Staci D. Bilbo, Ph.D.

Haley Family Professor, Departments of Psychology & Neuroscience, Neurobiology, and Cell Biology; Associate Director of Graduate Studies, Psychology & Neuroscience, Duke University; Research Affiliate, Lurie Center for Autism, Massachusetts General Hospital

My Research

I study the way that our immune system talks to our brains, particularly during early development (for instance, during pregnancy or the early neonatal period). I am interested in the evidence that inflammation from infections, toxins or even stress can activate the developing immune system and therefore impact fetal brain development, and potentially lead to changes in brain and behavioral function throughout life.

There is evidence that altered brain-immune function is important in neurodegeneration, including Alzheimer's disease. In particular, we study cells called microglia, which are known as the primary immune cells of the brain. These cells are critical for pruning synapses in the developing brain. We are interested in the signals that neurons send to microglia for impacting their function (e.g., their pruning or elimination of synapses), and whether manipulation of these signals might be able to decrease the synapse loss that is observed early in Alzheimer's disease.

My Inspiration

Working with the fantastic students and other trainees in my lab is what inspires me the most and what makes me love my job. They are all smarter than me, so it also keeps me humble. 😉 I also love interacting with patient groups and advocates—this is what gets us up every morning for sure.

My Motivation to Research Alzheimer's Disease

I have been studying microglia in brain development for a long time. I have been aware of the growing recognition that microglia may be very important in Alzheimer's disease for some time, but never actively pursued it. At this point, the evidence is too strong to ignore, and I am excited to try to contribute meaningfully to this area. I also think I bring a novel perspective to the field, which I hope will be useful.

My Personal Connection to Alzheimer's Disease

A family member was diagnosed with dementia last year. I don't know if it is technically Alzheimer's disease or Frontotemporal Dementia (FTD) but the symptoms are very similar. It has progressed rapidly and it has been extremely painful to lose her little by little. It is heartbreaking.

Most Exciting Career Moment to Date

This is a hard question, as there have been many moments. I would say that, overall, it has been very exciting and rewarding to see the growing recognition for the role of microglia in brain function and in neuroimmune function more broadly in health and disease. When I started in this field it was very often ignored, but many have an appreciation for how these two beautiful systems (nervous and immune) interact now.

Biggest Unanswered Question in Alzheimer's Disease

For my field in particular, there is still a lot of controversy about whether microglial activity is helpful or harmful in Alzheimer's disease. We think it is likely both, depending on the stage of disease and other factors, including events occurring very early in life that may lead to lifelong changes in microglial function, and thus their contribution to Alzheimer's disease.

What I Wish Most People Understood About Science

I wish it was easier to convey nuance. What I mean by that is that often we make discoveries that are only part of the full picture, and then additional findings provide clarity or even overturn the previous findings. It is not that the previous work was wrong, but simply that we are acquiring more and more information all the time, and so the message necessarily changes. I think members of the general public understandably want very clear-cut answers to things, but it's not always that clear cut. It doesn't mean the early science is wrong! We just refine over time. It's a long process.

Outside of Work, I Like...

I enjoy painting, and spending time with my husband, cats and chickens!

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Our funding has only just begun in July 2022, but we are very excited to get started and extremely grateful for the support!

Front row, from left: Janai Williams, Kamryn Washington, Roshen Amin, Staci Bilbo, Benjamin Devlin, Danielle Rendina, Alexis Ceasrine, Julia Dziabis. Back row, from left: Caroline Smith, Irene Jonathan, Sarah Monroe, Madeline Clark, Lauren Burgett, Dang Nguyen.

Joel Blanchard, Ph.D.

Assistant Professor of Neuroscience at the Icahn School of Medicine at Mount Sinai

My Research

My lab engineers human brain tissue from patient stem cells to replay the events of Alzheimer's disease in the laboratory. This allows us to study how the cells and tissues of the brain change leading up to and during Alzheimer's, and identify ways to intervene.

Our research focuses on APOE4, the strongest risk for Alzheimer's disease. APOE4 is found in 40% to 50% of late-onset Alzheimer's disease cases. By understanding how APOE4 increases pathologies associated with Alzheimer's disease, such as neuroinflammation and vascular impairments, we aim to uncover pathological mechanisms that promote Alzheimer's disease, and then block these mechanisms with drugs. So far, our insights have revealed two FDA-approved drugs that we are currently trying to repurpose for APOE4-related Alzheimer's disease. We are currently studying whether similar mechanisms and drugs are involved and could be used in non-APOE4 Alzheimer's disease.

My Inspiration

Over the last decade, there have been major technological advances in genomics, gene editing, neuroscience and stem cell biology. Bringing these advances together will provide unprecedented insights that will transform our understanding and accelerate progress toward cures. Being a part of this multidisciplinary science that brings multiple approaches together to gain a deeper understanding of disease biology is truly exciting.

My Motivation to Research Alzheimer's Disease

I first became interested in aging research through watching my grandparents age. What struck me was that although their bodies seemed to age at similar rates, there was a considerable contrast between their minds. My grandfather's memory and mind remained clear and sharp until he died in his nineties. In contrast, my grandmother's memory started deteriorating in her seventies and she was eventually diagnosed with Alzheimer's disease. As a teenager, I wondered why these two people with shared experiences and lives had such different outcomes. During a high school AP biology course, I even wrote a paper on Alzheimer's disease. After many hours spent in the library, it was clear things went wrong in Alzheimer's disease—but why this happened in some people and not others still remained an enigma.

Years later, listening to the news I heard a story announcing that scientists had reprogrammed skin cells back to an embryonic stem cell state, which then could be used to create any cell in the body. Like many, I believed this would transform how we study and understand disease, by allowing the cells affected during a particular disease to be created from any individual and compared with another individual. As a result, I switched the focus of my training and then spent more than a decade studying embryonic stem cells and neurobiology. Today, my research uses personalized stem cells to recreate specific tissues found in the brain and examine how genetics and the environment promote healthy and unhealthy aging.

My Personal Connection to Alzheimer's Disease

Women on my mother's side of the family have a history of Alzheimer's disease that seems to be passed down from one generation to the next. My mother is currently in the early stages of dementia. Understanding this was a major inspiration for my work.

Most Exciting Career Moment to Date

To me, discovering something new is the most exciting moment in science. These moments are rare and often arrive after weeks or months of frustrations and failures. But, peering through a microscope or finally piecing together a dataset and knowing in that instant you've discovered something new and important is exhilarating. In these moments, I like to reflect on the impact and the road ahead, then get back to work. There is always the next breakthrough.

Biggest Unanswered Question in Alzheimer's Disease

Memory loss and impaired learning are the symptoms of Alzheimer's disease. But the causes of these symptoms remain largely unknown. Is it the same in every case, or are there multiple roads and pathogenic mechanisms that lead to Alzheimer's disease? Understanding these questions will point to new therapeutic opportunities and highlight whether therapies should be stratified based on genetics, sex or other factors.

Outside of Work, I Like...

Outside of work I enjoy spending time with my family. I have two active sons. We spend a lot of weekends at the soccer fields, on the ski slopes and playing in our yard.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund has been instrumental to my career. As a post-doc I was fortunate to work on Cure Alzheimer's Fund projects in Li-Huei's Tsai's lab at MIT. This introduced me to cutting-edge science and a network of the leading experts in Alzheimer's disease research. When I started my independent lab at Mount Sinai, Cure Alzheimer's Fund was one of the first foundations to invest in my new lab. This was instrumental to growing my lab and advancing our new technology to understand and target Alzheimer's disease. Cure Alzheimer's Fund's strong focus on patients is inspiring and motivates us every day.

Andreas R. Pfenning, Ph.D.

Assistant Professor, Department of Computational Biology, Carnegie Mellon University

My Research

Through a variety of research, including work from our collaborators in the Cure Alzheimer's CIRCUITs grant, we now know dozens of regions of the genome that are related to the likelihood of getting Alzheimer's disease. My laboratory is using artificial intelligence to predict what those regions of the genome are doing. Then, we're using genomic experiments to test those hypotheses.

There are so many different things that happen to the body during the progression of Alzheimer's disease. We think that understanding how certain mutations can decrease Alzheimer's predisposition can help us to understand which of those many things can actually influence the disease progression, rather than just being a consequence.

My Inspiration

The people that I work with inspire me the most. My lab has a diversity of backgrounds and perspectives. For example, one member has a Ph.D. in computer science from Stanford and another has skills that end with Excel spreadsheets. Some members of the lab have never done a bench experiment and others have worked on developing new genomic technologies. I'm inspired by how people in my lab with very different training can come together to work on big, important problems.

My Motivation to Research Alzheimer's Disease

Alzheimer's disease is such a complex disorder that it requires the type of advanced genomic and machine learning approaches that my lab works on developing.

My Personal Connection to Alzheimer's Disease

I think almost everyone does [have one]. At the time I started Alzheimer's research, my wife's grandmother was suffering from the disease. It added a human element to what I was studying.

Most Exciting Career Moment to Date

When I was still in training, I worked on a project to see how different parts of the human body were related to Alzheimer's disease predisposition. I thought for sure that parts of the brain would come up as the top hits, but the immune system came up instead as by far the strongest hit. I was excited to be wrong in a very interesting way.

Biggest Unanswered Question in Alzheimer's Disease

How to cure it.

What I Wish Most People Understood About Science

I think it is underappreciated how important basic scientific questions are, even to research that is translational. For example, the work that my lab is doing on Alzheimer's disease is based on the details of how levels of genes are controlled. Big discoveries in specific topics like Alzheimer's are often based on decades of work in things that might not seem related at first.

Outside of Work, I Like...

I like to spend time outdoors with my wife and two small children.

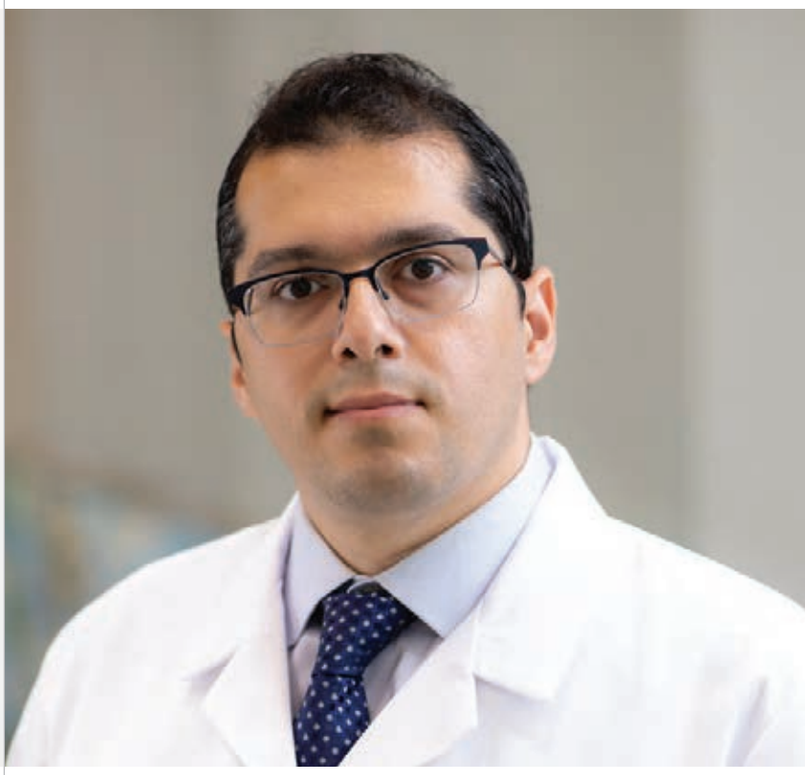
How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund has provided a wonderful platform for collaboration. Working with human genetics experts helps us better understand what goes into a strong genetic study and what types of regions to study. Working with collaborators on the translational side helps us to design studies in such a way that new drug candidates could emerge. I've learned so much from the team.

Pfenning Lab members: Back row, from left: Chaitanya Srinivasan, Andreas Pfenning, Mike Leone, Ruby Redlich. Middle row, from left: BaDoi Phan, Cathy Su, Ashley Brown, Irene Kaplow, Carson Sestilli, Amanda Kowalczyk. Front row, from left: Mike Franusich, Ziheng (Calvin) Chen.

Ali Ezzati, M.D.

Assistant Professor of Neurology,
Albert Einstein College of Medicine



My Research

We use data from large studies of Alzheimer's disease and advanced analytical methods, including artificial intelligence, to better understand what leads to cognitive impairment, what causes Alzheimer's disease, and how to improve diagnostic and therapeutic approaches.

Results from our research could be used for two major purposes: 1) Improving design and conduct of future Alzheimer's disease clinical trials. Improvement in design of trials increases the chance of successfully identifying effective therapies. 2) There are substantial individual differences between individuals at risk of Alzheimer's disease as well as patients who are already diagnosed with Alzheimer's disease. Therefore, each individual requires different preventive approaches—and once effective therapies become available, each person requires individualized therapeutic strategies. Results of our research can improve this individualized, patient-oriented approach to Alzheimer's disease prevention and therapy.

My Inspiration

Challenging myself to solve what has not been solved before. Conducting cutting-edge research that could make a huge difference in the lives of patients, families and the public.

My Motivation to Research Alzheimer's Disease

We are at a unique time in history. The population is aging and life expectancy is increasing. Concurrently, the number of people at risk of Alzheimer's disease and other dementia is increasing. Through contribution to Alzheimer's disease research, there is an opportunity to make meaningful change in the lives of millions of people worldwide.

My Personal Connection to Alzheimer's Disease

My grandfather suffered from Alzheimer's disease toward the end of his life. I was very young at the time and had limited understanding of what was happening to him. Inability to connect with a loved one due to Alzheimer's disease, while they are still alive, is an everlasting painful experience.

Most Exciting Career Moment to Date

It is hard to pinpoint a single moment, but receiving several grants over the last few years, which enabled me to continue the science that I'm most passionate about, is high on the list.

Biggest Unanswered Question in Alzheimer's Disease

What causes Alzheimer's disease? Are there multiple mechanisms involved? How can we develop treatments that target these mechanisms?

What I Wish Most People Understood About Science

Conducting scientific studies is time, labor and resource intensive. It takes many years and many trials and errors for scientists to move science forward. Without consistent support from both public and private industry, conducting meaningful, life-changing research is impossible.

Outside of Work, I Like...

I love playing with my kids, gardening and cooking for friends and family.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

My research field (artificial intelligence in Alzheimer's disease) is fairly new and it is still considered high risk by many grant organizations. Cure Alzheimer's Fund recognized the value of the project despite the risk. It was only through this support that I was able to substantially increase the speed and productivity of my projects.

Ali Ezzati in the arms of his grandfather, Abazar Esmaili, who suffered from Alzheimer's in his later years.

"Cure Alzheimer's Fund provides unparalleled flexibility and speed to put into practice good ideas that would otherwise take years to get funded and off the ground."

Karen Duff, Ph.D.

Centre Director, UK Dementia Research Institute at University College London; Professor Emerita, Columbia University Medical Center

My Research

I study what causes Alzheimer's disease at the molecular and cellular level using mouse and cell models. My goal is to be able to use this information to work out how, in the near future, we should make Alzheimer's disease less of a devastating disease and, in the long term, prevent it from being a problem.

I am developing state-of-the-art cell and animal models of Alzheimer's disease so we can test a wide range of therapies and have a really good feel for how well they will work in people. I am also applying newly developed techniques to understand how individual brain cells function in the healthy and Alzheimer's disease brain. I hope that this will help make it easier to target therapies to protect vulnerable brain cells, and strengthen resilient cells.

My Inspiration

That we are closer than ever to understanding Alzheimer's disease enough to be able to make a difference with the drugs we currently have, or are developing. Once we can match the right drug with the right patient at the right stage of their disease, we should be successful. Advancements in early and accurate diagnosis through fluid and brain imaging biomarkers are helping to identify the "right patient," coupled with a better understanding of what mechanisms to target; a larger, better understood and preclinically tested arsenal of therapeutic agents have rapidly improved our likelihood of making a meaningful impact on people with Alzheimer's disease.

My Motivation to Research Alzheimer's Disease

In high school I was taught there are 3 billion units of DNA, but an error in only one DNA unit can cause a devastating disease such as Alzheimer's disease. I was amazed by this and wanted to understand how one single DNA change can lead to a hugely complex disease. I chose to address the question by making the same DNA change in a mouse, using genetic engineering, and following what happens.

My Personal Connection to Alzheimer's Disease

Both my mother and father (now deceased) suffer from Lewy Body Dementia, a neurodegenerative disease that has many similarities to Alzheimer's disease.

Most Exciting Career Moment to Date

I feel the impact of my lab's work is more exciting every year as the momentum builds for the field to be truly impactful.

Biggest Unanswered Question in Alzheimer's Disease

What is happening in the brain of someone in the earliest stages of Alzheimer's disease, at the individual cell level, and how can we build resilience into each cell to prevent Alzheimer's disease?

What I Wish Most People Understood About Science

The human brain is extremely complex and there are many things that can go wrong, especially as the brain ages. When we look at the brain of someone who has died of Alzheimer's disease, it's like looking at the aftermath of a car wreck and trying to understand from the mangled wreckage what caused it. We have to understand the events that led to the wreckage, but we have to work backward, thinking of all the possible causes, developing tools to explore each possibility along the way.

Outside of Work, I Like...

To share life's ups and downs with my mother and my daughters.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

[It has been] absolutely fundamental and essential to my lab's continued success. In the past, Cure Alzheimer's Fund funding has helped bridge gaps in funding that would have been devasting to the continuity of my research, without which I might not have been able to get the bigger grants that allowed my lab to thrive. More recently, Cure Alzheimer's Fund funding has enabled me to start new projects, at an early stage, when they were still highly exploratory, for what are turning out to be highly impactful projects. Cure Alzheimer's Fund provides unparalleled flexibility and speed to put into practice good ideas that would otherwise take years to get funded and off the ground.

Bart De Strooper, M.D., Ph.D.

Director, Dementia Research institute of the UK, Professor and VIB researcher at KU Leuven, Belgium, and University College, London

My Research
I try to understand how genetic risk of Alzheimer's disease affects the response of your cells in the brain. Understanding the mechanism of disease is the first step toward precise and effective medication.

My Inspiration
Seeing results of new exciting experiments and to think what the implications are.

My Motivation to Research Alzheimer's Disease
When I started, we knew almost nothing about one of the most important diseases in the world. I felt that this was an important area of research and I was hoping that by understanding the molecular pathology, we would also find good targets for drug development.

My Personal Connection to Alzheimer's Disease
My mother has Alzheimer's disease.

Most Exciting Career Moment to Date
When I found that presenilin cuts amyloid precursor protein. This was a tremendous moment to understand how two major genes in the disease interacted with each other.

Biggest Unanswered Question in Alzheimer's Disease
What is the link between amyloid pathology and tau pathology?

What I Wish Most People Understood About Science
That scientists are human beings and make mistakes the whole time. It is by being critical for each other that we keep the science in check.

Outside of Work, I Like...
Running, my family, my garden.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Several times at very critical moments for my research, I could ask for extra support from Cure Alzheimer's Fund. This allowed me to generate data that brought me on course for more traditional grants.

Members of the De Strooper Lab.

Gilbert Gallardo, Ph.D.

Assistant Professor of Neurology, Washington University School of Medicine in St. Louis

My Research

Our lab studies brain inflammation, an emerging contributor to Alzheimer's disease regulated by a group of cells referred to as glial cells. In healthy individuals, the glial cells support normal brain function, but in Alzheimer's disease, the glial cells become inflamed, promoting brain inflammation. Two key questions we aim to answer include how might suppressing brain inflammation protect against Alzheimer's disease, and how do glial cells become inflamed?

Our research focuses on inflamed astrocytes, a type of glial cell that promotes brain inflammation in Alzheimer's disease. By investigating animal models of Alzheimer's disease, we have demonstrated that suppressing these inflamed astrocytes is beneficial and delays the progression of Alzheimer's disease-related pathologies. Perhaps someday our studies will lead to an effective therapeutic strategy that targets inflamed astrocytes that will slow the disease process.

My Inspiration

The biggest inspiration for my work is discovery. Having the opportunity to discover biological mechanisms that someday may contribute to understanding Alzheimer's disease and the development of a therapeutic strategy is my inspiration.

My Motivation to Research Alzheimer's Disease

One motivation to research Alzheimer's disease was the challenge of understanding one of the most complex biological mechanisms that leads to dementia, which is multifaceted in mechanisms and cell types.

Most Exciting Career Moment to Date

The most exciting moment of my scientific career is that I ever became a scientist addressing one of the most challenging diseases our generation needs to overcome. I could never have imagined the enthusiasm and passion would continuing growing each step of my career as a scientist.

Biggest Unanswered Question in Alzheimer's Disease

I think it is difficult to put one key question above another when so many unanswered questions from biology to health disparities need to be addressed before fully understanding Alzheimer's disease. However, as a biologist, perhaps the biggest question unanswered in Alzheimer's disease is how amyloid, tau and brain inflammation all come together at the crossroads in dementia development.

What I Wish Most People Understood About Science

Often the public believes effective therapies are developed in the clinic and/or the hospital, but the reality is they were created by years of research by multiple scientists in collaborative efforts.

Outside of Work, I Like...

I enjoy working in my garden, fishing and playing with my cats.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

The support from Cure Alzheimer's Fund has been invaluable in obtaining the right resources, tools and personnel, giving us little limits on expanding our scientific exploration of glial cells in Alzheimer's disease. Beyond the support, [being] part of the Cure Alzheimer's Fund community has put me in contact with leaders in field of Alzheimer's disease, enabling potential collaborative studies that will help advance our knowledge of Alzheimer's disease development.

From left: Postdoctoral student Shreedarshanee Shamulailatpam Devi, research assistant Alex Piasta.

Sam Gandy, M.D., Ph.D.

Mount Sinai Endowed Chair in Alzheimer's Disease Research; Professor of Neurology and of Psychiatry; Director, Mount Sinai Center for Wellness and Cognitive Health; Director, Mount Sinai NFL Center for Neurological Care, Icahn School of Medicine at Mount Sinai

My Research
I hope to understand enough about the risk(s) for and cause(s) of Alzheimer's to develop a meaningful intervention. The basic molecular pathogenesis is interesting but, for me, discovery of a meaningful intervention is the most important goal.

We are studying a drug that may mimic or potentiate the benefits of physical exercise on cognitive reserve and resilience. The drug shows memory benefits in models of amyloidosis, tauopathy and brain trauma.

My Inspiration
I would not say that this is exactly "inspiration," but I would like to be able to honestly tell each newly diagnosed dementia patient that I can recommend something that will show meaningful benefit for him or her.

My Motivation to Research Alzheimer's Disease
Lifelong exposure to affected family members and patients with dementia.

My Personal Connection to Alzheimer's Disease
Seven members of my extended family have died from Alzheimer's disease.

Most Exciting Career Moment to Date
The announcement of the cloning and chromosomal assignment of the APP gene.

Biggest Unanswered Question in Alzheimer's Disease
Is most cognitive decline attributable to a single disease pathology? Or do most patients with cognitive decline show multiple pathologies? In other words, will targeting any one single molecule or any one single pathology be sufficient to cause a meaningful benefit?

What I Wish Most People Understood About Science
That experiments and trials fail most of the time.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Cure Alzheimer's Fund funding allows our lab to pursue new leads, enabling us to accumulate enough data to prepare competitive funding proposals to more traditional federal and foundation funders.

Bradley T. Hyman, M.D., Ph.D.

John B. Penney, Jr., Professor of Neurology, Harvard Medical School; Director, MassGeneral Institute for Neurodegenerative Disease (MIND), Massachusetts General Hospital

My Research
We are trying to understand why the brain fails in Alzheimer's disease. If we can identify the elements that cause brain cells to not work, we can design therapies to counteract them.

My Inspiration
I still see patients.

My Motivation to Research Alzheimer's Disease
It's an awful disease.

My Personal Connection to Alzheimer's Disease
I see patients, and my own family has been affected by dementia.

Most Exciting Career Moment to Date
Seeing something new under the microscope—it never gets old!

Biggest Unanswered Question in Alzheimer's Disease
Why humans, but not other species, are susceptible? And why it takes decades to progress.

What I Wish Most People Understood About Science
Science is always evolving, with new ideas replacing old ones—always seeking the truth.

Outside of Work, I Like...
I love to play with my grandson!

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
We have the flexibility to explore new ideas.

David M. Gate, Ph.D.

Assistant Professor of Neurology, Northwestern University Feinberg School of Medicine

My Research

I study the intersection of the brain and the immune system. We are particularly interested in developing novel immune biomarkers or therapeutic targets for neurodegenerative disease.

We aim to identify immune genes that are risk factors for Alzheimer's disease, and to determine how these genes play a functional role in the disorder. If we can identify immune proteins that signal when a person is developing neurodegeneration, we can use this signal to treat their disease early.

My Inspiration

I enjoy teaching the next generation of scientists and passing on my knowledge.

My Motivation to Research Alzheimer's Disease

I recognized that Alzheimer's disease was an epidemic and that the disease would have dire consequences on society in the future. I think being a scientist is the best use of my skills and attributes.

My Personal Connection to Alzheimer's Disease

I have a close family member with dementia. I've seen firsthand how debilitating neurodegenerative disease can be for a patient.

Most Exciting Career Moment to Date

Receiving my first independent grant.

David and his wife hiking in Grand Teton National Park, Wyoming.

Biggest Unanswered Question in Alzheimer's Disease

What spurs the misaggregation of amyloid? How does amyloid accumulation lead to tau pathology in some patients, but not others?

What I Wish Most People Understood About Science

The amount of training that professors undergo is arduous. It takes a long time to develop expertise in a scientific subject.

Outside of Work, I Like...

I love exploring the outdoors. I am an avid hiker. My wife and I have visited over 25 national parks. I hope to see them all in my lifetime.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

CureAlz has allowed my lab to explore projects we otherwise would not explore. It has opened us up to new, creative avenues.

Gate Lab members at their annual summer party.

Maria Lehtinen, Ph.D.

Professor, Harvard Medical School, Department of Pathology, Boston Children's Hospital

My Research

We study the choroid plexus–cerebrospinal fluid (CSF) system. CSF is a fluid that essentially bathes the brain, and it is secreted by a structure called the choroid plexus. In addition to producing CSF, the choroid plexus also provides an important protective barrier that prevents harmful factors/signals distributed in the body's blood to enter the brain. We are studying how the choroid plexus produces and protects the CSF, which has the capacity to penetrate deep into the brain to affect brain function, and how this function is altered during inflammation—something that is emerging as a key aspect of Alzheimer's disease.

We have a unique opportunity to collaborate with Liisa Myllykangas, a neuropathologist who is also very interested in Alzheimer's disease and the choroid plexus. Thus, by comparing her observations in human specimens with our mouse studies, we anticipate that our work will expand our understanding of the conserved and important involvement of choroid plexus inflammation in Alzheimer's disease progression. We anticipate that our experimental approaches also will provide a critical real-time screening platform for future testing of Alzheimer's disease therapies on choroid plexus brain barrier integrity and brain inflammation. In the future, we hope to incorporate neurologists and pharmacologists to our team so that we can quickly pass the baton from one expert to another.

My Inspiration

There are several sources of inspiration in my work—the privilege of scientific discovery and possibility of finding something truly new that can be useful to neurology is at the top of the list. On a daily basis, I am continuously inspired by the talented scientists whose creativity and dedication allows our team to make new discoveries.

My Motivation to Research Alzheimer's Disease

Alzheimer's disease is a particularly challenging problem to solve. Even before I was motivated by personal experiences relating to Alzheimer's disease, I was very much drawn to thinking about how my research could be applied to the field of Alzheimer's disease research.

My Personal Connection to Alzheimer's Disease

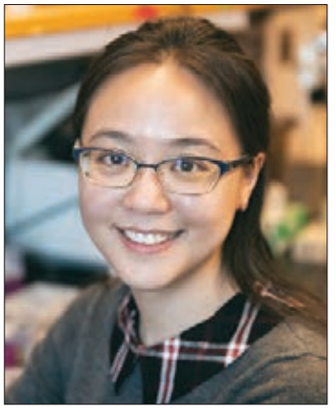
On a personal note, I have witnessed the devastation caused by Alzheimer's disease firsthand and am highly motivated to advance this line of research in my lab. Our ultimate goal is to collaboratively accelerate progress toward the development of effective therapies for Alzheimer's disease.

Most Exciting Career Moment to Date

There are certainly eureka moments that stand out, including realizing that the CSF confers benefits to the developing and mature brain, and observing cellular movements in real time through "sky lights" in the brain. It was also moving to receive news of the Presidential Early Career Award for Scientists and Engineers from the White House during the final days of the Obama administration. However, for me, persisting excitement comes from the inspiration that follows the discovery of something new, and applying/transferring that new knowledge to yet another challenge.

Biggest Unanswered Question in Alzheimer's Disease

There are so many questions that remain unanswered. In discussions with postdoc Huixin Xu, who is also very committed to Alzheimer's disease research, we think these questions will likely differ if looking through the lens of basic research vs. clinical research. For basic research, we think the biggest question is the challenge of identifying



Huixin Xu, Postdoctoral Research Fellow, Boston Children's Hospital

the earliest trigger of disease pathophysiology. While we have been looking under the lamppost of the brain, do we need to cast the net more widely to the brain and its barriers, or even beyond? And while the earliest event may not be the most amenable drug target, it is critical for the establishment of disease pathology, and will help identify which targets are the drivers of brain pathology.

From the perspective of developing a treatment, we think the biggest questions have to do with which part(s) of the disease-driving mechanism are targetable without interfering with normal body functions, and what time window is effective for intervention. Many current limitations to Alzheimer's disease clinical trials that target amyloid, including antibodies or BACE inhibitors, may be due to incorrect timing (too late) or safety issues (interference with normal functions). We need more people to sit at the table and "lean in" to collectively think about these issues in order to solve them.

What I Wish Most People Understood About Science
More discussions between scientists and the general public are needed. Often, it seems that a failed clinical trial or lack of treatment is interpreted to mean that scientists were basing their work on an entirely incorrect theory. It is important to understand that working in science and bringing a treatment to fruition involves multiple stages. Scientific theory and clinical outcomes rarely move in lockstep. It takes a lot of effort to fine-tune any scientific theory. Questions regarding timing of treatment, safety concerns and different responses from different individuals will only be revealed during the actual trial. Heterogeneity in response may lead to one trial failing, but this outcome can provide valuable information for the next attempt.

Overall, science involves many more failures than successes, and therefore achieving any success requires a certain kind of perseverance. The more shots on goal that are possible, the more likely everyone is to succeed. Similar to any sports team (nod to "Ted Lasso"), excellent teamwork within and across laboratories is critical to the success of this mission!

Outside of Work, I Like...
I started playing piano before turning 3 and then picked up the violin shortly thereafter. Despite my commitment to music while growing up, I opted for a more academic path. Fortunately, music and family now provide an enriching balance to my science life, and I often play piano and violin with my daughters. While I have played in a number of different ensembles and musical groups, including with lab members (!), I currently play with the Magic Bows chamber group.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
As a developmental neurobiologist, I have always hoped that my research could make a contribution to Alzheimer's disease. Support from Cure Alzheimer's Fund now makes this a possibility!

Vijay K. Kuchroo, D.V.M., Ph.D.

Samuel L. Wasserstrom Professor of Neurology at Harvard Medical School; Senior Scientist at Brigham and Women's Hospital; and Director of the Evergrande Center for Immunologic Diseases, Harvard Medical School and Brigham and Women's Hospital, Boston. Institute Member, Broad Institute of MIT and Harvard.

My Research
Our studies are beginning to identify how the innate immune system can regulate development of Alzheimer's disease. We have identified checkpoint molecule TIM-3 that regulates phagocytic function of microglia. The question is whether a TIM-3 blockade with either antibodies or small molecules will lead to a cure to development of Alzheimer's disease.

My Inspiration
Discoveries that might one day treat this devastating disease.

My Motivation to Research Alzheimer's Disease
Genetic linkage to immune molecules raising the issue of how the immune system regulates the development of the disease.

My Personal Connection to Alzheimer's Disease
My mother developed Alzheimer's disease as she got older and recently died.

Most Exciting Career Moment to Date
Discovery of a new set of immunoregulatory molecules called TIM family of genes, and discovery of a pro-inflammatory T-cell subset called Th17 cells.

Biggest Unanswered Question in Alzheimer's Disease
Although many genes in the immune system have been genetically linked to Alzheimer's disease, what is the mechanism by which the immune system regulates development of Alzheimer's disease?

What I Wish Most People Understood About Science
Identifying a target to develop a treatment for a disease takes a long time and effort. Sustained support is needed for a prolonged period of time to reach the goal.

Outside of Work, I Like...
To travel around the world, seeing historical places and listening to classical music.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Before the funding from the Cure Alzheimer's Fund, I had no funding for doing Alzheimer's disease work. The funding has enabled me to work in the field; otherwise, it would not have been possible.

Anna Greka, M.D., Ph.D.

Associate Professor of Medicine, Harvard Medical School, Brigham and Women's Hospital and Broad Institute of MIT and Harvard

My Research

My lab is broadly interested in how cells, the basic units of life, cope with challenges that disrupt their homeostasis, the mechanisms that keep them in balance. Our team of scientists specializes in deciphering how exactly these malfunctioning mechanisms lead to disease, and how this knowledge can be harnessed to gain deeper biological insights and develop new therapeutic strategies.

There are certain rules for how cells operate that are true across the human body, whether it is kidney cells or brain cells. My lab usually starts its problem solving by investigating a genetic mutation, an error in the DNA, that leads to an incurable disease. Recently, my lab focused on a mutation in a gene called Mucin 1 that causes the formation of a misfolded protein that toxically accumulates and kills kidney cells. We identified a compound that can discard the misfolded protein by dispatching it to the cell's trash can (the lysosome). This type of disease is called a toxic proteinopathy and it doesn't just affect the kidney. It also describes diseases affecting the brain, such as Parkinson's disease, ALS and some forms of Alzheimer's-like dementia. One arm of my laboratory is interested in investigating shared mechanisms across proteinopathies affecting different cells in the human body, including the brain.

Another area of investigation in my lab is how different lipids (fats) affect cells across the human body, from brain cells to immune cells to insulin-producing cells and beyond. We recently built a platform to study how environmental risk factors, like exposure to excess fats, exacerbates genetic risk for metabolic diseases, including Alzheimer's disease.

Our mission for our Cure Alzheimer's Fund-supported research is to determine how exposure to specific lipids (fats) exacerbates genetic risk for Alzheimer's disease. We are interested in why microglia, the brain's immune cells, are vulnerable to specific lipids called free fatty acids. We are using cutting-edge tools to prioritize genes that are susceptible to environmental triggers. We will use CRISPR gene editing to knock out genes of interest in microglia in order to identify potential new drug targets for Alzheimer's disease.

Most Exciting Career Moment to Date

One of the most exciting moments of my scientific career so far was making a discovery that both shifts our understanding about a fundamental biological process, such as the handling of misfolded proteins inside cells, and simultaneously changes the way we approach treatment for devastating diseases called proteinopathies. STAT news recently profiled the impact our research may have for rare kidney disease patients, and I am excited about its promise to ultimately make a difference for many more patients with devastating but understudied proteinopathies, including neurodegenerative diseases.

Biggest Unanswered Question in Alzheimer's Disease

I'm fascinated by the observation that the incidence of Alzheimer's disease is higher in type 2 diabetes patients and obese individuals. As a scientist, I think there is a lot of fascinating work to be done to uncover how insulin resistance and obesity could mechanistically contribute to Alzheimer's disease through impaired metabolism throughout the body, including the brain.

What I Wish Most People Understood About Science

While scientific investigations still take time and enormous effort, I hope everyone is as excited as I am about recent technological advances that have ushered in a new golden era in biomedicine. Using computer-controlled robotic systems, artificial intelligence, powerful screening tools and unprecedented capabilities in gene editing, we can now hope to achieve answers to pressing scientific questions at a remarkably fast pace. At the same time, we must never forget that patients are the most important stakeholders for everything we do. We, the scientists, must serve as responsible stewards of the awesome power of biomedicine, and make sure we partner closely with our patients and the general public at every step of this journey to cure human diseases.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund support sparked a collaboration between two investigators who on the surface appear to study two totally different topics: Beth Stevens, who studies immune cells in the brain, and my own lab, which has largely been working on fundamental mechanisms involving membrane proteins with a focus on kidney biology. Together we teamed up to think about Alzheimer's disease from a new perspective. We are so grateful for this flexible support from Cure Alzheimer's Fund that may allow us to gain new insights by bringing into the field investigators like myself who are not traditional neurodegenerative disease researchers.

Jaime Grutzendler, M.D.

Dr. Harry M. Zimmerman and Dr. Nicholas and Viola Spinelli Professor of Neurology and Neuroscience; Vice-Chair for Research, Neurology; Director, Center for Experimental Neuroimaging, Yale School of Medicine

My Research

The goal of our research is to uncover how the diverse cells in the brain interact and communicate with each other in health and neurodegeneration (Alzheimer's disease). We have a specific interest in interactions between glial cells, vasculature and neurons. We develop tools, methods and probes for live brain microscopy to understand cellular pathology in live mice. Finally, we have translational projects aimed at developing cell-type specific pharmacological agents to target glial-neuronal interactions to reduce neurodegeneration. We have exciting new findings uncovering mechanisms of axonal pathology in Alzheimer's disease and are currently developing small molecules and biologics aimed at reducing this pathology.

My Inspiration

The excitement of discovering highly reproducible biological principles by careful tissue visualization with modern microscopy tools combined with subtle and targeted manipulations of a highly complex organ like the brain. Finally, the most exciting part is to develop hypotheses based on our findings that one day could lead to innovative mechanistic discoveries and ultimately treatments for neurodegenerative conditions.

My Motivation to Research Alzheimer's Disease

I was always fascinated by the brain and initially trained as a clinical neurologist. During my clinical training I gradually acquired basic neuroscience research training. I became very interested in Alzheimer's disease because of its complexity, which required thinking at the interface of various neuroscience subscales, including cellular physiology, molecular/cell biology, neural circuits and ultimately behavior.

My Personal Connection to Alzheimer's Disease

I have had close relatives that developed dementia, and even though I see patients in my clinic with Alzheimer's disease on a regular basis, experiencing the gradual cognitive deterioration of loved relatives up close is extremely challenging.

Most Exciting Career Moment to Date

Without pointing to one specific finding, there have been many exciting moments—many of them the result of serendipitous discoveries that open our brain to completely unexplored areas.

Biggest Unanswered Question in Alzheimer's Disease

There are still major gaps in knowledge with regard to the earliest cell biological mechanisms that initiate the disease cascade. These gaps severely limit the rational design of therapies.

What I Wish Most People Understood About Science

Great discoveries are generally the product of many years of exploration, frequently with serendipitous findings, rather than goal-oriented research. Therefore, funding needs to be directed to the highest quality and reproducible science, regardless of supposed practical benefits. You cannot predict where cures—including those for Alzheimer's disease—will come from.

Outside of Work, I Like...

Doing simple things with family and friends.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

The Cure Alzheimer's Fund support has allowed us to take more risks in our research, something that I think is critical for obtaining unexpected and potentially impactful results.

RESEARCH MILESTONES

WHO KNEW? THE BRAIN HAS A DRAIN TO REMOVE DEBRIS

More than 200 years ago, it was speculated that the brain is protected by lymphatic vessels with the purpose of transporting bacteria and debris to the lymph nodes to be destroyed and eliminated from the body. In 2018 the hypothesis was confirmed using state-of-the-art imaging technology.
—Jony Kipnis, Ph.D. [bit.ly/3rkeyxB]

Christian Haass, Ph.D.

Chair, Metabolic Biochemistry, Ludwig-Maximilans-Universität, Munich; Speaker, German Center for Neurodegenerative Diseases (DZNE), Munich; Speaker of the DFG Excellence Cluster Systems Neurology

My Research
I try to find out what goes wrong in the brain of an Alzheimer's disease (AD) patient. If we understand the mechanisms, we may find ways to treat the disease. I hope that modulation of amyloid production and microglial activities will help to prevent or slow disease progression.

My Inspiration
Finding things nobody has seen before.

My Motivation to Research Alzheimer's Disease
The inaugural lecture of one of the founders of modern Alzheimer's research, Konrad Beyreuther at the University of Heidelberg, where I heard for the very first time about the extreme tragic fate of an AD patient and Konrad's exciting finding of the gene encoding the amyloid precursor.

Most Exciting Career Moment to Date
Seeing amyloid produced from simple kidney cells, a finding that provided the first model system to understand amyloid generation, production and modulation.

Biggest Unanswered Question in Alzheimer's Disease
How can we stop memory decline?

What I Wish Most People Understood About Science
Science is our future. We need research to solve the most important problems that challenge our society. These include dementia, climate change, loss of species diversity, generating environmental neutral energy resources, etc.

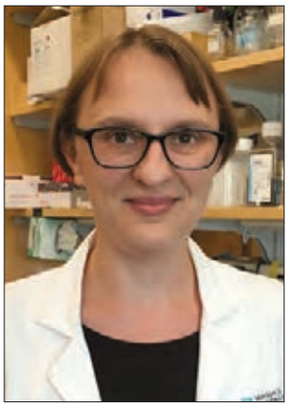
Outside of Work, I Like...
Watching and photographing birds and collecting modern art.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
The funds are fast, flexible and contain very little bureaucracy. It brings together some of the very best scientists in the field, and creates a very unique atmosphere for discussions. During Corona, we had a beautiful online meeting, where I felt "home" (for) the first time since more than a year.

Haass Lab team members (from left): Ignacio Paris, Michael Willem, Anja Capell, Christian Haass, Alice Suelzen, Beate Polke, Claudia Thiel, Maria Mühlhofer, Nicole Exner, Astrid Feiten, Ramona Rodde, Camila Giudici, Bettina Brunner, Lis DeWeerd, Marvin Reich, Georg Werner, Katrin Fellerer, Sophie Robinson, Sven Lammich, Ann-Katrin Bergmann.

Ana Griciuc, Ph.D.

Assistant Professor of Neurology, Massachusetts General Hospital



My Research

I work on neuroinflammation, with an emphasis on two microglial receptors: CD33 and TREM2. Microglia clear amyloid beta and dead or infected cells and prune excess synapses. However, microglia can be activated and become pro-inflammatory. CD33 is the "on" switch for neuroinflammation, while TREM2 acts like an "off" switch.

The microglial receptor CD33 modulates neuroinflammation and is a very interesting target for developing therapeutics for the prevention and treatment of Alzheimer's disease. Small molecule development of CD33 inhibitors, CD33-targeted gene therapy and immunotherapy could represent potential therapies for Alzheimer's disease.

My Inspiration

I hope to translate my research findings on neuroinflammation into clinical trials (from bench to bedside).

My Motivation to Research Alzheimer's Disease

I was fascinated by neuroscience during my undergraduate studies and became interested in protein misfolding and neurodegeneration, which later led me to neuroinflammation and Alzheimer's disease.

My Personal Connection to Alzheimer's Disease

My grandmother (maternal) has been diagnosed with Alzheimer's disease.

Most Exciting Career Moment to Date

My most exciting moment in my career was when AbbVie and Alector started clinical trials to test the safety and tolerability of the AL003 antibody to inhibit CD33 function as a potential therapeutic approach for Alzheimer's disease. This approach was based on our previous findings that CD33 inhibits microglia-mediated clearance of amyloid beta and promotes neuroinflammation in Alzheimer's disease.

Biggest Unanswered Question in Alzheimer's Disease

We need more research progress toward understanding the connection between peripheral inflammation, neuroinflammation and age-related neurodegeneration.

What I Wish Most People Understood About Science

Working in science includes asking the correct question at the right time, a decent amount of troubleshooting of experiments/techniques and exciting novel data, as well as repetitive actions.

Outside of Work, I Like...

I spend my time with my family, including my two children, and I do enjoy swimming when time allows.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

The support from Cure Alzheimer's Fund made a great difference for my research over the years. It allowed us to develop new projects, implement translational research (drug screening), generate novel animal models for neuroinflammation and Alzheimer's disease, as well as establish a gene therapy strategy targeting our gene of interest CD33.

Tamir Ben-Hur, M.D., Ph.D.

Chairman, Department of Neurology at Hadassah University Medical Center

Tamir Ben-Hur was born and raised in Jerusalem, Israel. The younger of two boys, Dr. Ben-Hur developed an interest in life sciences when he was in high school. After his mandatory time in the Israeli army, Dr. Ben-Hur was accepted to the Hebrew University—Hadassah Medical School in Jerusalem, where he received his M.D. and Ph.D. degrees. 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."

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 that takes a holistic approach to the patient—not only the medical aspects, but the mental aspects as well." In addition to being a researcher, Dr. Ben-Hur also is a physician with patients of his own. "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."

Dr. Ben-Hur has focused on neural stem cell biology, transplantation of stem cells to the nervous system, neuroimmunology and neurovirology. "The brain is very limited in terms of regeneration," he explains. His lab was the first in the world to discover that brain stem cells have properties that can inhibit inflammatory processes. His work showed that stem cells protect their surrounding brain cells from injury and facilitate the repair process. "We need to better understand how they can be manipulated to increase the brain's ability to protect itself from degeneration."

Giuseppina Tesco, M.D., Ph.D.

Professor of Neuroscience, Alzheimer's Disease Research Laboratory, Department of Neuroscience, Tufts University School of Medicine

My Research
I am a neurologist who studies Alzheimer's disease (AD) doing experiments in a laboratory. I am currently using patient-derived induced pluripotent stem cells (iPSCs) to model Alzheimer's disease in vitro. This approach can lead to the development of patient-specific therapies.

My Inspiration
The search for a cure.

My Motivation to Research Alzheimer's Disease
I realized that Alzheimer's disease is devastating for the patients and their families working as neurologist.

Most Exciting Career Moment to Date
I get excited every time we have some new data.

Biggest Unanswered Question in Alzheimer's Disease
Is it too late to treat AD patients when beta-amyloid depositions occur?

What I Wish Most People Understood About Science
Science requires innovation. Most of the time, to obtain NIH funding, we are required to propose projects that are already in progress and are low risk. We need to be able to have funding to explore high-risk, high-reward ideas.

Outside of Work, I Like...
Traveling and to enjoy nature.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
The support of Cure Alzheimer's Fund has been essential to support projects at very early stages. With such support I have been able to produce preliminary data to apply for NIH grants.

Patrik Verstreken, Ph.D.

Scientific Director & Group Leader, VIB Center for Brain & Disease Research, KU Leuven, Department of Neurosciences, Leuven Brain Institute, Laboratory for Neuronal Communication

My Research
One of the earliest and defining features of dementia is the loss of connections—synapses—between brain cells. Our goal is to find ways to preserve these synapses and even make them grow back. One of the reasons synapses fail and degenerate is because, during the early course of disease, a protein (tau) that is present in neurons ends up in the wrong place. It is normally localized to the long connecting cables in the cells of our brain, but in disease it invades these synapses and this abnormal localization causes havoc.

We found that at synapses tau can bind to the small vesicles that contain the messages brain cells send to one another to communicate (neurotransmitter-filled synaptic vesicles), and this causes these vesicles to be stuck. Hence, when tau invades synapses, it disturbs information transfer in the brain by clustering synaptic vesicles, and ultimately this leads to synaptic loss.

Our group identified a therapeutic inroad that prevents tau from associating with vesicles at synapses and we acquired excellent preliminary data using mouse Alzheimer's models. These mice suffer from tau-induced synaptic loss and cognitive decline. We now show that when we prevent tau from interacting with synaptic vesicles, synapses are preserved, and the mice are cognitively fine.

Based on this work we have now developed therapeutic tools that can be injected and that we are optimizing and testing in human cellular systems and in mouse models for efficacy.

My Inspiration
The people I work with. I am fortunate to be able to work with excellent students, postdocs and technicians, and every day is a joy to be able to interact with them and to define and sculpt ideas and experiments. In our work on Alzheimer's and Parkinson's disease, the patients are also an inspiration. Everyone has friends or family who come in contact with these diseases, so it becomes very personal very quickly.

My Motivation to Research Alzheimer's Disease
The connections with synaptic decline and synaptic dysfunction. I have worked my entire scientific life to understand how communication in our brain occurs, and seeing that it is exactly this that fails in early Alzheimer's stages sparked my interest. Now many years later, there is in addition to pathological evidence also ample genetic evidence.

Patrik Verstreken, Perrine Colla, Sabine Kuenen, lab manager. Lab technicians: Jef Swerts, Jeevanjot Singh, Sandra Fernández Gallego, Dries Chabot, Irka Van de Gaer, Alejandro González Gutiérrez. Postdocs: Uli Pech, Valerie Uytterhoeven, Natalie Kaempf, Roman Praschberger, Eliana Nachman, Nicolò Carrano. Ph.D.s: Marianna Decet, Pablo Largo Barrientos, Ayse Kilic, Lorenzo Ghezzi, Jacqueline Van Vierbergen, Gokhan Özturan, Esther Muñoz Pedrazo. Not pictured: Carles Calatayud Aristoy, Nils Schoovaerts.

My Personal Connection to Alzheimer's Disease

My grandmother passed away with Alzheimer's, as did my wife's grandmother.

Most Exciting Career Moment to Date

That's a difficult question. Historically, probably the very first paper I published as a graduate student defining the homologues of synaptic proteins across species. Since I started my own lab, we have made several discoveries, but the ones that stood out are: (1) that we were able to rescue a rare familial form of Parkinson's disease caused by mutations in pink1 by providing vitamin K2. Pink1 maintains mitochondrial function and vitamin K2 was known to act as an electron transfer molecule in the bacterial membrane. Given the evolutionary connections between bacteria and mitochondria, we were able to show that vitamin K2 also has such a function in mitochondria, i.e., it promotes energy production, and this alleviates the problems in pink1 mutants. And (2) we found that tau binds synaptic vesicles under pathological conditions and that we can undo the detrimental effects of this association by lowering the expression levels of synaptogyrin-3, a vesicle-associated protein.

Biggest Unanswered Question in Alzheimer's Disease

Alzheimer's disease is a very complex and multifactorial disorder. Our work focuses on synaptic decline, one of the defining early features seen in patients and animal models, but during the course of disease there are numerous intricate other cellular interactions that occur and that define how Alzheimer's disease progresses, including the neuroimmune system, brain support cells, the blood-brain barrier, etc. We will ultimately need (1) tools to identify which aspects are most affected in a given patient (i.e., synapses, support cells, neuro-vasculature, etc.) and (2) to define combinations of medication that target the relevant problems.

What I Wish Most People Understood About Science

That scientists can sometimes be wrong, too: we formulate hypotheses, i.e., think about how things could happen and then design experiments to test this. But as we learn more, sometimes our interpretations need to be adjusted.

Another item that I find important is to explain the value, and critical need, for animal experimentation, in particular in neuroscience. Unlike many other diseases that humans suffer from, scientists studying brain disease do not have (easy) access to living brain material, and when we do gain access when patients have perished; the areas of the brain we wanted to study have degenerated. This is an important problem in our field in general, and animals can be of great help. Furthermore, we still have an incomplete understanding of how the brain operates, and as long as we do not have this view it is not possible to accurately mimic brain function in vitro using cell-based systems. Finally, these cell-based systems do not display behavior, memory formation or thought—defining features in cognitive decline in Alzheimer's.

Outside of Work, I Like...

I looooove running and trail running and spending time with my kids and family, cooking a great meal and trying to involve my kids in helping.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

It has enabled us to move our work in vivo and is allowing us to assess whether the therapeutic modalities that we have developed to lower synaptogyrin-3 expression (and thus tau association with synaptic vesicles) have beneficial effects in mouse Alzheimer's models.

Oskar Hansson, M.D., Ph.D.

Professor of Neurology, Head of the Clinical Memory Research Unit, Vice Director of the Strategic Research Area of Neuroscience and Director of the Center for Neurodegenerative Diseases, Lund University, Sweden

Rik Ossenkoppele, Ph.D.

Associate Professor in Translational Neuroscience and Principal Investigator, the Alzheimer Center Amsterdam of the Amsterdam University Medical Centers and at Lund University, Sweden

Our Research

We use neuroimaging and biofluid biomarkers to 1) improve the diagnostic and prognostic process of Alzheimer's disease and other types of dementia in the clinic; 2) recognize Alzheimer's as early as possible; 3) advance our understanding of disease mechanisms; and 4) work toward a cure for Alzheimer's disease and other types of dementia.

Our studies might help in selecting the right participants for a specific trial; we have developed several markers that could be used to monitor the effects of therapeutic interventions, and we identified several targets that potentially could inform drug development teams.

Our Inspiration

We are inspired by teamwork, both nationally and internationally, where scientists with different backgrounds and expertise work together toward our scientific goals.

Our Motivation to Research Alzheimer's Disease

We are both motivated and attracted by the extreme complexity of Alzheimer's disease, and hope to eventually contribute to improving the quality of life of individuals living with Alzheimer's disease and their loved ones.

My Personal Connection to Alzheimer's Disease

Dr. Hansson: My grandmother had Alzheimer's disease for many years, and I have met many individuals with the disease at my memory clinic when practicing as a neurologist.

Most Exciting Career Moment to Date

The development of novel PET and blood-based biomarkers; both of them truly revolutionized the field.

Biggest Unanswered Question in Alzheimer's Disease

What is driving the enormous heterogeneity of Alzheimer's disease in terms of its pathological, neuroanatomical and functional manifestations?

What We Wish Most People Understood About Science

That science is an extremely time-consuming process because we demand extreme rigor in order to make a difference and really understand what is happening in the brain.

Outside of Work, I Like...

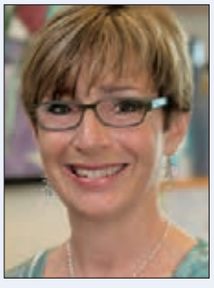
Dr. Ossenkoppele: Sports (soccer, running, high-intensity interval training), music, reading, traveling.
Dr. Hansson: Friends, reading books, running, music, hiking.

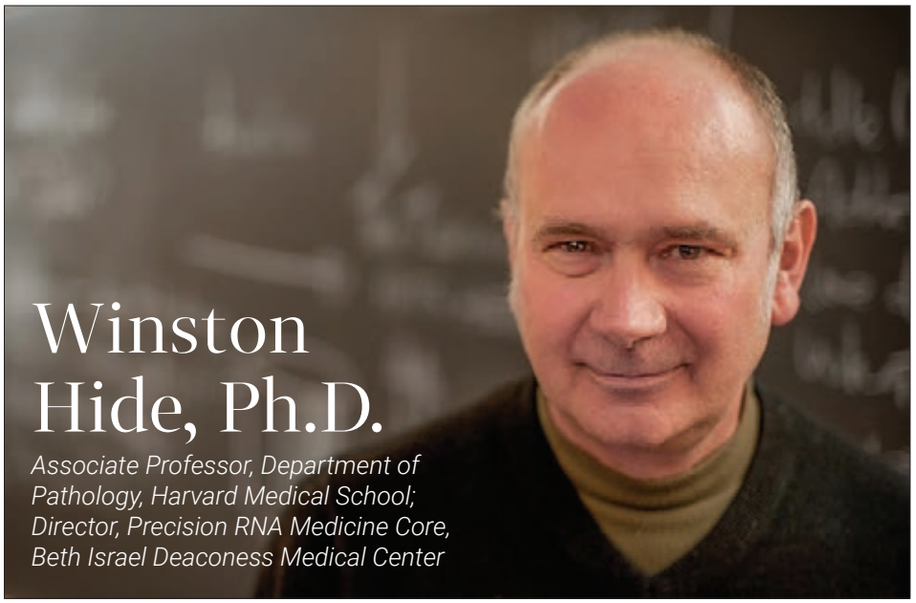
Alexandra C. Newton, Ph.D.

Professor of Pharmacology, University of California, San Diego

Dr. Alexandra Newton was born in Cape Town, South Africa. Although Dr. Newton had a strong aptitude for the arts, science was her true passion. "I was a data fanatic from a young age," admits Dr. Newton, who considers herself to be a "total nerd."

Dr. Newton attended Simon Fraser University, where she fell in love with chemistry, and earned a Ph.D. in chemistry from Stanford University. Dr. Newton did her postdoctoral work at the University of California, Berkeley, in the lab of renowned biochemist Dr. Dan Koshland, whose goal at the time was to better understand memory. Protein kinase C (PKC)—a critical enzyme that runs through our bodies and keeps our signaling pathways in check—had just been discovered, and Dr. Koshland believed it to be a memory molecule, since it was abundant in the brain and made imprints on other proteins. Since then, Dr. Newton has studied PKC to understand its molecular mechanisms and its role in disease. Dr. Newton eventually understood that PKC has to be exactly balanced in the body to be beneficial. "If your body has too much of it, cells die, leading to degenerative diseases such as Alzheimer's. If you don't have enough, it causes cancer," she says. In fact, Dr. Newton is so passionate about PKC she actually has had it displayed on her license plate for the past 20 years.





Winston Hide, Ph.D.

Associate Professor, Department of Pathology, Harvard Medical School; Director, Precision RNA Medicine Core, Beth Israel Deaconess Medical Center

My Research

Some older people get Alzheimer's disease (AD) in their brains but they don't lose their memory; in fact, they think like anyone else their age who doesn't have the disease. I am trying to find out how they ward off the pathology that accumulates in the brain so that their brain cells don't die. I do my research using computational biology—I literally use data to make discoveries.

I hope to find a drug that makes protecting the brain against Alzheimer's disease as simple as taking a pill. Our first clinical outcome will be a blood test that tells you exactly how well or not well you are coping with Alzheimer's disease in your brain. Maybe even a test to predict how well you can cope in the future.

My Inspiration

Growing the people I train, while hopefully improving what we know about Alzheimer's disease.

My Motivation to Research Alzheimer's Disease

I met up with an amazing set of Alzheimer's disease research scientists who really get it. I saw how they were being so good at learning new aspects of the disease by working synergistically but closely. I wanted to join them. The disease has a lot of data available—as a data person, this meant that I could do great science while living my passion for finding patterns in data.

Most Exciting Career Moment to Date

Getting the first paper I wrote in the respected journal Nature—I never understood until then the sheer breadth of the scientific community.

Biggest Unanswered Question in Alzheimer's Disease

Why do only some people suffer from memory loss when they get Alzheimer's disease-related brain pathology?

What I Wish Most People Understood About Science

Scientists often trust findings more if they use the tools that were used in the findings. So, they get biased to things they know. That means they can end up researching in the wrong direction—and if a lot of them do that, it keeps happening. Fortunately, constant discoveries, and the diversity of talent, people and geography that do science, means that good ideas do better than bad ideas.

Outside of Work, I Like...

I want to set up an international collaboration to photograph the caregivers for people who suffer from AD—the "AlzHeroes"—and create a multimedia exhibit that highlights the sacrifice and commitment of the unsung people who care for people living with Alzheimer's disease.

Isabel Castanho, Ph.D.
TEAM MEMBER

Pourya Naderi, Ph.D.
TEAM MEMBER

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

It's meant that I can do work I think is meaningful, innovative and translatable, far more rapidly than if I had never had the chance to get Cure Alzheimer's Fund funding.

RESEARCH MILESTONES

THE GUT-BRAIN CONNECTION

In a novel study of the relationship between the gut microbiome and the brain, it was determined that altering the composition of the gut microbiome in the lab could lead to lower levels of amyloid plaques in the brain.
—Sam Sisodia, Ph.D. [bit.ly/3CoB7HW]

Benjamin Y. Klein, M.D.

Senior Scientist, Biochemical Cellular Studies, Hebrew University

My Research

I am interested in studying the way vaccination with the anti-tuberculosis vaccine (called BCG) influences the metabolism of immune cells. Traditionally, immunologists are interested in the nature of immune cells responding to vaccine antigens, (specific molecular structures of disease-causing invaders). This immune response is by secretion of antibodies or developing T- cell receptors that specifically fit to bind (like a "key to its lock") invader antigens and neutralize them.

We have shown that the BCG vaccine reduces the risk of developing Alzheimer's disease (AD); however, subsequently other researchers found that vaccines against other infectious pathogens can also reduce the risk of AD. This means that secretion of specific antibodies or T-cells to the vaccines antigens are not directly relevant to prevent or postpone development of AD. Alzheimer's disease presents two characteristic features that may be relevant to what any vaccination would cause in immunized cells beyond the production of the specific "key to lock" neutralization effect. One feature is the fact that neurons are dependent on servant-cells (astrocytes and glia cells) for generating neuronal energy storage. Neurons are weak in initializing steps of breaking glucose into shorter molecules down to lactic acid, but they can absorb and use lactic acid secreted by astrocytes and take the "relay race baton" down the rest of the pathway to generate ATP (energy storing molecules). This is consistent with the knowledge that frequently neuronal death in AD is due to astrocytes' failure to support the neuronal energy metabolism.

We know that vaccination activates the energy metabolism of immune cells by intensification of the glucose breaking pathway in a sustainable manner. Sustainability is because this change is passed from stimulated cells to daughter cells, and thus help to supply lactic acid to neurons in assistance to failing astrocytes. A second feature of AD is the appearance of amyloid plaques in patients' brains that had been noticed in autopsies of AD patients—these consist of aggregates of fragments of a protein called amyloid precursor protein (APP). Amyloid plaques had been studied for decades and the benefit of their therapeutic removal has become a controversial issue. We now refer to amyloid plaques as a sign that something goes wrong in protein metabolism in either neurons or their supporting glia and astrocytes. If this is true, then we may identify changes in the metabolism of proteins that react to BCG vaccination.

Because we assume that the BCG effect on the brain is relayed via peripheral immunized cells, and because we cannot obtain brain tissue, we collect blood samples before and after BCG vaccine exposure, to isolate proper immune cells in search for changes induced by BCG. Cellular stress can be inflicted by several causes, such as UV irradiation, glucose, amino acid starvation or surplus, or oxidative stress; each will stop protein synthesis and set in motion a different cellular stress response integrated by a common effect on an mRNA-translation factor. We think that by analyzing the BCG impact on stress response pathways, we will get a clue regarding which steps in response pathways BCG impact is helpful in preventing AD, which can suggest ways alternative to vaccination to obtain AD prevention.

My Motivation to Research Alzheimer's Disease

We were asking ourselves why the BCG vaccine is given by the intradermal route instead of the oral route, as it was at the first decade after this vaccine was developed. Subsequently, Chuck Greenblatt found an ad where Leslie Norins, (a former figure in the Centers for Disease Control and Prevention) offered an award for authors who will advance the idea that Alzheimer's disease has an infectious background. We therefore went into the history of the neurologist that AD is named for (Dr. Alois Alzheimer), who operated a clinic in Germany. His famous iconic patient Auguste Deter, who died in her 50s with this dementia, demonstrated in her autopsy characteristic lesions in the brain. A contemporary neuropathologist, Dr. Oskar Fischer, has found traces of Actinobacteria in autopsies of demented patients. Because the genus Mycobacterium tuberculosis (Mtb) is a member of the same phylum of Actinobacteria, and because TB was a frequent infectious disease in Europe still during Alzheimer's carrier, we thought that Norins advertised his award for a good reason. If Auguste Deter's brain lesions were a sign of brain TB, and the antituberculosis BCG vaccine would have been developed 70 years earlier, perhaps she would never have become Dr. Alzheimer's patient.

To this end, we saw a paper that claimed that BCG improved cognition in an AD mouse model. This prompted the idea to BCG-vaccinate 100 people in their 60s and let our grandchildren become doctors and follow the vaccinated persons up to the age of 85 versus controls, just to establish that BCG indeed prevents/postpones AD. Subsequently, Chuck Greenblatt ran into Herve Bercovier, an expert on BCG strains, who suggested working with the Urology Clinic because they routinely treat noninvasive bladder cancer with an extended course of intra-vesical BCG instillations. The head of urology, Dr. Ofer Gofrit, decided to test this idea retrospectively on more than 1,340 patients treated with, versus without, BCG over more than two decades. The results showed an 80% reduction in the risk to develop AD for those treated with BCG compared with controls treated by other methods. At that time, work done in Massachusetts General Hospital has shown that BCG vaccination can spare the need for insulin in Type 1 diabetes by causing an increased intensity of glucose drown into immunized cells. This inspired me to review the normal biochemical cooperation between brain neurons and astrocytes that led me to the hypothesis that BCG activates peripheral immune cells' metabolism such to assist astrocytes and neuron metabolism to prevent their degeneration.

Most Exciting Career Moment to Date

There have been several moments:

When I found that among separated proteins of a malignant tumor model in mice there were proteins (immunogens) that stimulated immune cells that killed the tumor cells. However, among the separated molecules there also were proteins (suppressogens) that induced cells that killed the antitumor immunized cells. This was at a time when immunologists were skeptical about the existence of "suppressor" cells.

When I found in gut cells that oxytocin inhibits mRNA translation into proteins in conjunction with activation of the cellular stress response to unfolded proteins.

When I found that the incidence of Type 1 diabetes in females started to increase exactly from the year when BCG vaccination program of newborns was stopped nationally.

Biggest Unanswered Question in Alzheimer's Disease

Traditional vaccines like BCG, with a long-lasting prophylactic effect against their designated specific targeted-disease, turned out to have a nonspecific prophylactic effect against AD. This turns the spotlight from previous unanswered questions to a new big practical question: "Which of the nonspecific biological processes (taking place during immune cells activation) is responsible for this miraculous postponement of AD, and what mechanism is responsible for it"?

What I Wish Most People Understood About Science

That present civilization grew to the present size thanks to the invention of vaccination.

Outside of Work, I Like...

There are several things I have done outside work:

- When I trained in internal medicine, I took a painting course in the Brooklyn Museum.
- In a lot near our township, I planted the vine strain from which the Chianti wine is made, and went to Chianti Province in Italy to a ranch to learn how to make wine.
- I took refreshment courses in languages I had once spoken freely.
- I have collected leaves from wildly growing endemic vines in the Holy Land and, by extracting DNA, I have analyzed their strains' genetic signature.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund identified our thinking as out of the box.

Thomas C. Südhof, M.D., Nobel Laureate

Professor, Departments of Molecular & Cellular Physiology and of Neurosurgery, Stanford University School of Medicine; Avram Goldstein Professor Investigator, Howard Hughes Medical Institute (HHMI)

When Dr. Thomas Südhof first learned he had won the Nobel Prize, he could not have been more surprised. "Are you serious?" were the first words out of his mouth. "I was driving in the middle of Spain on my way to a conference and I was a little lost," he admits. "At first I was a little skeptical when I got the call," Dr. Südhof said, but he quickly realized the truth. "I was utterly surprised and, needless to say, delighted." Later he said, "Every scientist dreams of this. It's quite amazing." Dr. Südhof was awarded the prize for his work in synaptic transmission together with Randy Schekman, Ph.D., of the University of California, Berkeley, and James E. Rothman, Ph.D., of Yale University.

Dr. Südhof was born in Göttingen, Germany. As a child he had many different interests, including music. "My bassoon teacher taught me that the only way to do something right is to practice and listen for hours and hours. I believe that my training in classical music imbued me with a sense of focus and hard work that is a prerequisite for creativity," said Dr. Südhof. "I became interested in science as a serious endeavor when I was in medical school," he said. "I discovered how helpless we are as physicians in treating people because we don't actually understand how diseases arise. The brain is a very important organ and we really know very little about how it works. Brain diseases may not always be life threatening, but the most prevalent—schizophrenia, Parkinson's and Alzheimer's—impose an enormous burden on the population."

After medical school Dr. Südhof moved to the United States and eventually started his own lab at the University of Texas Southwestern Medical Center. In his work, Dr. Südhof revealed the role of presynaptic neurons in neuropsychiatric illnesses, and helped to advance knowledge of mechanisms behind such poorly understood diseases and conditions as Alzheimer's, schizophrenia and autism. In 2008, Dr. Südhof moved to Stanford University, where he has served as the Avram Goldstein Professor in the School of Medicine. As a neuroscientist, he continues to "work on how the brain works," he said. "It's quite an amazing organ with billions of nerve cells that constantly talk to each other. We have been trying to shed light on how the cells send information to each other at the synapse, which is like a little nano computer." He says, "I cannot tell you how much I enjoy what I do. I will always consider it an enormous privilege to be a scientist."

Shane Liddelow, Ph.D.

Assistant Professor, Neuroscience Institute; Assistant Professor, Department of Neuroscience and Physiology; Assistant Professor, Department of Ophthalmology; Neuroscience Institute at NYU Langone Health

My Research

We study the role of neuron-supporting "glial" cells called astrocytes. These bushy, star-shaped cells provide nutrients to neurons and ensure they function properly in the brain. In the context of diseases like Alzheimer's disease (AD), they lose many normal functions and can become toxic to neurons—driving degeneration in the brain.

Understanding the suite of molecules released by astrocytes that can keep neurons alive (nutrients) and cause them to die (toxins) provides novel targets for therapy. My lab investigates many "reactive" forms of astrocytes—one type that is toxic to neurons and present in many neurodegenerative diseases in addition to Alzheimer's disease. We think that reactive astrocytes are a fundamentally important common component of neuron death in the aged brain.

My Inspiration

I love seeing the success of my trainees—their excitement at the discovery of a new phenomenon, uncovering a new biological mechanism, or defining a new set of complex pathways and targets that we can use to begin development of new therapies. I love that every day we uncover something new about AD that was not known the day before.

My Motivation to Research Alzheimer's Disease

Like many people, I have a family history of Alzheimer's disease and have always been taken by such diseases that have no cure. What are we missing? What haven't we investigated yet? Why can we not crack this code? These are questions that I find fascinating about the biology and progression of Alzheimer's disease.

Most Exciting Career Moment to Date

The identification of a disease-agnostic driver of neuron death—that is, the release of toxic lipids from astrocytes that can kill neurons—has been incredibly exciting. Started in 2012 at Stanford, this work pulled from the expertise of dozens of excellent scientists across the globe, ultimately leading to the identification of a family of toxic lipid molecules and a single enzyme required for their production. This provides a first-in-class drug target that may be beneficial at preserving neurons in a whole range of neurodegenerative diseases—not just Alzheimer's disease.

What I Wish Most People Understood About Science

Science is both a rewarding profession and a lonely existence. Long hours sitting by one's self in the dark, looking down a microscope, delving into the data and agonizing over the interpretation of results, all the time working to make sure the benefit to patients is real and justified.

Dr. Liddelow (right) shares a light-hearted moment with team leaders.

Outside of Work, I Like...

I roast coffee beans each week for my lab. Several pounds—helping turn caffeine into results on a daily basis. This can often be an amusing endeavor in an NYC apartment!

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund has enabled us to take big risks on new ideas, speeding movement into new and novel spaces for research and accelerating science out of the lab and (ultimately) into the clinic. Even more importantly is the expansive network of Alzheimer's disease experts that are always on hand to provide insights, advice and support to push these discoveries ever further forward.

→ RESEARCH MILESTONES

AIR POLLUTION AND ALZHEIMER'S

Research revealed that nickel nanoparticles found in air pollution increased the amyloid levels in the brain that are also found at elevated levels in Alzheimer's disease. A separate study determined that air pollution might have a role in elevating the risk for Alzheimer's disease, citing nanoparticles emitted from vehicle exhaust as potential threats.
—Sam Gandy, M.D., Ph.D., and Caleb Finch, Ph.D.
[bit.ly/3dSBdht • bit.ly/3SA0lbG]

Se Hoon Choi, Ph.D.

Assistant Professor of Neurology, Genetics and Aging Research Unit, McCance Center for Brain Health, Affiliate of the Harvard Stem Cell Institute (HSCI), Massachusetts General Hospital and Harvard Medical School

My Research

Alzheimer's disease is the most common form of dementia among older people. Various animal and clinical studies have shown that exercise provides benefits against Alzheimer's disease. The mechanisms by which exercise protects the brain are diverse, complex and not yet fully understood. Exercise increases the generation of new neurons through a process called adult hippocampal neurogenesis, and also decreases the pathological lesions of the disease, such as the accumulation of amyloid-β (Aβ) proteins. Notably, adult neurogenesis is severely impaired in Alzheimer's disease patients. My research has focused on whether and how neurogenesis impairment affects Alzheimer's disease progression, and whether increasing neurogenesis (producing more neurons) can serve as a therapeutic target for resisting cognitive impairment and promoting synaptic resilience in Alzheimer's disease. I also have been studying whether and how secreted molecules during exercise decrease Aβ levels as well as developing human cell culture models of Alzheimer's disease to study the disease pathogenesis and to ultimately find drugs that can treat or prevent Alzheimer's disease.

My study will provide a better understanding of the molecular mechanisms whereby exercise provides neuroprotection in Alzheimer's disease and help identify novel drugs to restore brain function in Alzheimer's disease. It also will allow for a more physiologically relevant cellular Alzheimer's disease model that can be used for both basic mechanistic studies and drug discovery.

My Motivation to Research Alzheimer's Disease

The multifactorial and multicellular nature of Alzheimer's disease presents major challenges to understanding the disease and for drug development. This complex nature of the disease motivates me to think about and study diverse and combinational therapeutic approaches for hopefully solving the disease.

Most Exciting Career Moment to Date

The most exciting moments were when our papers got accepted into high-impact journals, and learning that our neurogenesis paper was positively discussed in an NIH symposium that led to new ideas for other colleagues to build up their research.

Biggest Unanswered Question in Alzheimer's Disease

We do not know why certain rare people who have amyloid plaque buildup don't end up getting dementia: what factors make them build up resilience to Alzheimer's disease through cognitive reserve?

What I Wish Most People Understood About Science

I wish the general public knew that the mission of scientists is not to prove that our hypotheses are true, but to disprove most of our hypotheses by experiments in order to find the best truth.

Outside of Work, I Like...

I like to watch science fiction (sci-fi)/mystery movies and documentaries. I also like to see musicals, such as "Phantom of the Opera" and "Jesus Christ Superstar."

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund provides me the opportunity for designing and carrying out high-risk, high-reward projects and brand-new projects. In addition to the generous financial support, Cure Alzheimer's Fund also importantly provides excellent research collaboration communities.

Frank J. Wolters, M.D., Ph.D.

Clinical Epidemiologist, Erasmus University Medical Center, Rotterdam

My Research
Many older people have some cognitive complaints. We strive to better predict in whom these complaints are a premonition of dementia, and in whom they are transient or stable and not too much reason for concern. Related to this, we're trying to disentangle which of the various types of brain injury is mainly responsible for further deterioration in individual people with cognitive complaints.

Better information about the course of complaints and disease helps to inform people more accurately. It also facilitates decision making for doctors and patients in terms of lifestyle advice and treatment choices. What can one expect from a certain treatment, and do the benefits outweigh the risks or side effects?

My Inspiration
I thoroughly enjoy the collaboration with people with different expertise and with different views, to create synergy and come to better solutions for dementia diagnosis and prevention. My work is on the verge between clinical neurology and geriatric medicine, radiology (brain imaging) and epidemiology (working on methods to promote sound research). Bringing ideas and people together I find very fulfilling.

My Motivation to Research Alzheimer's Disease
I saw the consequences of Alzheimer's disease for my grandmother. Her illness was aggravated by a stroke and vascular injury to the brain. She lived well into her 90s but the quality of life in her final years I would not wish for anyone. I hope I can prevent that for others so that they may live more healthily and independently into old age.

My Personal Connection to Alzheimer's Disease
My grandmother, Maria J.G.C. (Rie) Nollen-Oonk.

Most Exciting Career Moment to Date
Difficult question! Obtaining my Ph.D. in front of my parents and close friends was a really memorable moment, but I get excited also when I notice I can inspire people or fellow clinicians with insights on dementia prevention and care from our work.

Biggest Unanswered Question in Alzheimer's Disease
Of course, the precise causes of dementia need to be unraveled for optimal treatment. I think an important first step to tailored treatment, in practice, is better detection and acknowledgement of the various causes of cognitive decline that often reside within a single person. In most older people with cognitive complaints there's not just a single cause, but multiple types of brain pathology playing part. We need to find ways to better determine what their predominant problem is.

What I Wish Most People Understood About Science
That most scientists have a very strong intrinsic motivation to make the world a slightly better place, and are truly grateful for the societal support that allows them to passionately pursue these goals. At least for me that's most certainly the case!

Outside of Work, I Like...
I love to read, go hiking or cycling, and I've recently started an art course to develop some skills in portrait drawing!

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Thanks to Cure Alzheimer's Fund, we have recently been able to start a—I believe—very promising project to determine how vascular brain injury (calcification to the brain vessels) influences Alzheimer's disease and vice versa. Both conditions are very common causes of cognitive decline, but the interplay is relatively unexplored.

"I saw the consequences of Alzheimer's disease for my grandmother. ...I hope I can prevent that for others so that they may live more healthily and independently into old age."

Frank and his grandmother, Maria Nollen-Oonk, who had Alzheimer's disease.

Stephen T.C. Wong, Ph.D.

John S. Dunn, Sr. Presidential Distinguished Endowed Chair in Biomedical Engineering; Associate Director of Shared Resources, Houston Methodist Neal Cancer Center; Chief Research Information Officer, Houston Methodist Hospital; Founding Director, the T. T. & W. F. Chao Center for BRAIN; Houston Methodist Research Institute; Professor of Radiology, Neurosciences, Pathology and Laboratory Medicine, Weill Cornell Medicine

My Research

I apply technology and engineering science to find cures and improve safety and quality of life for those with Alzheimer's disease (AD), cancer and related disorders. We would like to reposition known drugs for faster track to clinics; identify biomarkers for early detection and prognosis; and apply artificial intelligence to improve disease management and care, e.g., predicting in-hospital demented geriatric patient risks to avoid poor hospitalization outcomes, and tracking progress of virtual physical therapy of Alzheimer's disease patients with physical disability.

My Inspiration

Solving disease problems, notably AD and related disorders.

My Motivation to Research Alzheimer's Disease

I came back from industry to work on disease and health problems in the second half of my life. It so happens that I started my academic career in brain imaging and neurological research at UCSF, and later on ran the Center for Bioinformatics for Harvard Center for Neurogeneration and Repairs at Harvard Medical School, and the Center for Functional and Molecular Imaging Center at Brigham and Women's Hospital. I found Alzheimer's disease fascinating and challenging.

Most Exciting Career Moment to Date

I helped develop the first hospital-wide picture archiving and communication system (PACS) in the nation while a faculty member at UCSF that realized digital radiology departments and changed the clinical practice of radiologists and cardiologists. This got me hooked in medical research and I came back to academia medicine after many years in private industries, including semiconductors, finance and health care.

Biggest Unanswered Question in Alzheimer's Disease

Causes and subtyping of Alzheimer's disease as it has been done in other devastating diseases like cancer.

What I Wish Most People Understood About Science

A scientific hypothesis is similar to a business strategy. It is data driven, not based on opinions alone. As in business strategy, it may fail in execution. But we learn in due process and get closer to the truth.

Outside of Work, I Like...

Tennis, reading, traveling the world and mentoring young people.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

It helps me to work with the bright Alzheimer's disease neuroscientists of Cure Alzheimer's Fund.

Wilma Wasco, Ph.D.

Senior Science Advisor, Cure Alzheimer's Fund; Associate Professor of Neurology, Harvard Medical School; Genetics and Aging Research Unit, MassGeneral Institute for Neurodegenerative Disease, McCance Center for Brain Health, Massachusetts General Hospital

Born and raised in Fairfield, Connecticut, Dr. Wilma Wasco was always a promising student. As part of her education, she took honors chemistry without the prerequisite course, demonstrating her aptitude—and passion—for science. But when she accidentally cloned an amyloid precursor-like protein as a post-doctorate fellow, she began her lifelong career studying Alzheimer's disease.

Dr. Wasco graduated from Albert Einstein College of Medicine with a Ph.D. in molecular pharmacology and become a research fellow at Massachusetts Institute of Technology. While at MIT, she accidentally cloned something that was similar to the amyloid precursor protein (APP). "At the time, almost 30 years ago, APP had just been discovered," said Dr. Wasco. "It was a precursor to amyloid and my post-doctoral adviser and I met with Dr. Rudy Tanzi to determine if my APP-like clone was worth characterizing."

After completing her post-doctoral work, Dr. Wasco joined Massachusetts General Hospital investigating the genetics and cell biology of Alzheimer's disease. "I was almost 30 years old at the time, and looking for an opportunity to focus my research on something that could have a direct impact."

Dr. Wasco was part of an international effort that identified the familial Alzheimer's disease-associated presenilin 1 (PS1) and presenilin 2 (PS2) genes. Her laboratory also identified genes that encode the two amyloid precursor-like proteins (APLP1 and APLP2) and calsenilin, a calcium-binding protein that interacts with the presenilin proteins. Her research has been focused on understanding the biological role that each of these AD-linked proteins plays in the normal, aging and diseased brain. More recently, Dr. Wasco has also worked on Genes to Therapies™.

Dr. Wasco is a Pew Biomedical Scholar and a member of the Genetics and Aging Research Unit at MassGeneral Institute for Neurodegenerative Disease (MIND), led by Dr. Rudy Tanzi. She has been honored with the National Research Service Award, the Becton-Dickson Research Fellowship Award and the MGH Women's Career Faculty Development Award.

Charles L. Greenblatt, M.D.

Professor Emeritus, Hebrew University, Faculty of Medicine

My Research

Our group is interested in how the immune system can be brought to bear against neurodegenerative diseases such as Alzheimer's and Parkinson's disease. Our emphasis is on a 100-year-old vaccine for the control of tuberculosis, BCG. The vaccine is an attenuated bacterium derived from the causal agent of bovine TB. This vaccine is used in the treatment of superficial bladder cancer in patients older than 60. A long follow-up of these patients indicated 80% less Alzheimer's in the treated group compared with the controls treated by other methods. CureAlz is funding us in investigating the mechanism of this protective action. The work has been independently confirmed and other vaccines are also beneficial, but less so. We consider these vaccine effects to be "proof of concept" that adult vaccination can prevent Alzheimer's disease.

We need to put into the agenda of every medical practitioner the promotion of his patients' routine vaccinations. With further research as we discover the general mechanism an oral vaccine, similar to a probiotic, should be developed. Whether BCG will be the bacterium of choice, perhaps genetically engineered somewhat, it is early to tell. At the same time, as the physician reviews his patient's vaccine history, of course, he is pushing a program of nutrition, exercise, stress management, anti-smoking, etc.

My Inspiration

It is doable. The costs of Alzheimer's to the health systems will become apparent after our present pandemic quiets down. Even a small reduction in dementia, in costs and suffering, will be a blessing.

My Motivation to Research Alzheimer's Disease

After years thinking about specificity in vaccination, I discovered the nonspecific effects of BCG in juvenile diabetes and multiple sclerosis. If it works there, why not try in Alzheimer's?

My Personal Connection to Alzheimer's Disease

Not directly in the family. I am 91, and my two sisters and mother have died at over 95, clear mentally to the last. But as a physician I have been in close touch with friends and patients who have suffered. It's a terrible disease.

Most Exciting Career Moment to Date

I am the father of "ancient DNA" of pathogens. Preliminary to the ancient microbial studies, we began on the feasibility of retrieving DNA from any ancient material. So, we did the DNA of the Dead Sea Scrolls. Wow!

Biggest Unanswered Question in Alzheimer's Disease

What the effect of inflammation somewhere, anywhere in the body does to promote amyloid in the brain. A boxer's head injury at 25 leads to dementia at 60???

What I Wish Most People Understood About Science

Try to make decisions on evidence. Anti-vaxxers, look at the evidence for vaccine protection against COVID-19, then carry this over to prevention in general. Cure is OK; prevention is better.

Outside of Work, I Like...

Reading mostly history and archaeology. Being in Israel and being a Zionist, this mostly deals with Jewish history and literature.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Without it, we could not have begun our lab studies.

Berislav V. Zlokovic, M.D., Ph.D.

Mary Hayley and Selim Zilkha Chair in Alzheimer's Disease Research Director, Zilkha Neurogenetic Institute Professor and Chair, Department of Physiology and Biophysics, University of Southern California

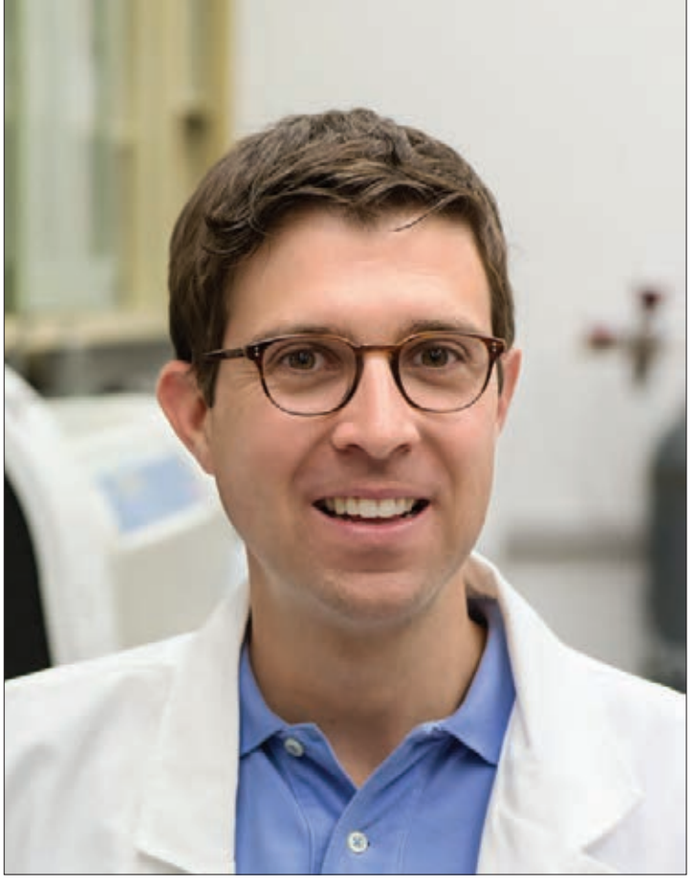
Born in Belgrade, Serbia, Dr. Berislav "Betza" Zlokovic grew up an only child with a passion for the arts. As a child he played violin, learned four languages and loved to sing. By age 19, he had performed several Italian operas. He also had a passion for science and earned his M.D. and Ph.D. from the University of Belgrade. While at medical school, he met his wife, Zora Mihailovich, a concert pianist who had been a child prodigy. Dr. Zlokovic did his postdoctoral fellowship with Dr. Hugh Davson, the renowned physiologist and co-developer of the Davson-Danielle "protein sandwich" cell membrane model. With Dr. Davson as his mentor, Dr. Zlokovic developed an interest in the blood-brain barrier and eventually moved to the United States to become an associate professor at the University of Southern California.

In 2011, Dr. Zlokovic was invited to join the Cure Alzheimer's Fund Research Consortium. He studies the role of blood vessels in the pathogenesis of Alzheimer's disease and neurological disorders. He also studies the blood-brain barrier cellular and molecular mechanisms that can lead to neuronal injury and degeneration. His most recent investigations seek a better understanding of the underlying mechanisms by which genes that influence the risk for Alzheimer's affect the brain's vascular system.

Dr. Zlokovic has won numerous honors and awards for his contributions to Alzheimer's disease research. In an interview, he stated, "I love Cure Alzheimer's Fund—it lets you test your ideas quickly and ask risky questions. It's really a first-class organization and it has been essential for helping my colleagues and me generate preliminary data."

John R. Lukens, Ph.D.

Associate Professor, Department of Neuroscience and the Center for Brain Immunology and Glia (BIG), University of Virginia



My Research

We study microglia, which are the immune cells of the brain. Microglia are specially equipped to safely dispose of potentially damaging agents that can incite loss of brain cells and defects in cognitive function, motor control and mental stability. Microglia can become dysfunctional with aging and in response to various environmental and genetic factors. We seek to identify molecular players that can be therapeutically targeted to rejuvenate beneficial microglial responses as a strategy to prevent and/or reverse brain damage and dysfunction.

We have recently identified new molecular players that, when targeted, are effective in boosting beneficial microglial responses and limiting the neuropathology that underlies Alzheimer's disease.

My Inspiration

Coming up with new ideas that may hold the promise of helping people who are suffering from neurological disease.

My Motivation to Research Alzheimer's Disease

Frustration with the lack of disease-modifying therapies to treat Alzheimer's disease as well as the opportunity to inject new ideas into this research area as an outsider of this field who trained as an immunologist.

My Personal Connection to Alzheimer's Disease

My grandmother.

Most Exciting Career Moment to Date

Seeing the effects that the immune molecule SYK has on microglial responses, brain cell death and cognitive function.

Biggest Unanswered Question in Alzheimer's Disease

Why does amyloid beta deposition cause brain damage in some individuals but not others?

What I Wish Most People Understood About Science

The role of the immune system in many neurological disorders, including Alzheimer's disease, has only been studied in great detail within the last 10 years or so. Moreover, the potential of targeting the immune system to treat neurological disease has not been extensively tested in comparison to other approaches over the last few decades. As a result, immunomodulatory treatments could hold great promise for the treatment of Alzheimer's disease and other neurological disorders.

Outside of Work, I Like...

Running, skiing and playing soccer with my two little boys.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

The support from Cure Alzheimer's Fund has enabled us to explore high-risk, high-reward topics that would not be funded by more traditional funding mechanisms, but hold the potential to make a transformative difference in both our understanding as well as the treatment of Alzheimer's disease.

Luken Lab team members (from left): Kristine Zengeler, Aman Mangalmurti, Katherine Bruch, Ashley Bolte, Ana Royo Marco, Jess Thanos, Josh Samuels, Addie Walsh, Lexi Johnson, Hannah Ennerfelt.

Richard Daneman, Ph.D.

Associate Professor, Departments of Neurosciences and Pharmacology, University of California, San Diego

My Research

We study the blood vessels in the brain, and how problems with these blood vessels may contribute to Alzheimer's disease.

Blood vessels bring blood, containing oxygen and nutrients, to every part of the body, including the brain. The blood vessels in the brain have a unique property that we call the blood-brain barrier, which is very important to control the brain's environment and protect the brain from potential harm. Dysfunction of this barrier has been observed in patients with Alzheimer's disease, and it has been suggested that this may be important for the onset and/or progression of this devastating disease. We aim to understand the role of the blood-brain barrier in Alzheimer's disease and determine whether targeting therapeutics to make the barrier healthier will be beneficial for Alzheimer's treatment. We would like to determine whether targeting the therapeutics to normalize the blood vessels may be beneficial to prevent or attenuate Alzheimer's disease.

My Inspiration

Training the next generation of scientists.

My Motivation to Research Alzheimer's Disease

I watched my grandfather experience Alzheimer's disease and saw how devastating this disease was, and how important it is to find a way to prevent or treat this terrible disease.

My Personal Connection to Alzheimer's Disease

My grandfather had Alzheimer's disease.

Most Exciting Career Moment to Date

Watching my trainees get excited about their work!

Biggest Unanswered Question in Alzheimer's Disease

What causes Alzheimer's disease?

What I Wish Most People Understood About Science

How important the work can be to their lives and the lives of their loved ones.

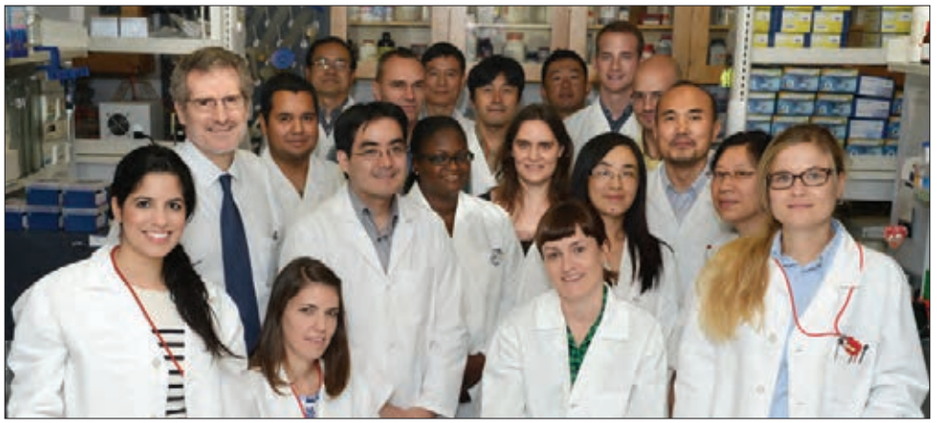
Outside of Work, I Like...

I like to travel, especially adventure travel and eco travel, play and watch sports, grow exotic fruits and cook.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund has made a huge difference to my work in two ways: First, the funding has allowed me to greatly expand my work on Alzheimer's disease and examine many potential pathways for therapeutics than I would have without the funding. Second, it has put me in touch with amazing collaborators, whom we now work with on a regular basis, providing amazing synergy.

Members of the Daneman Lab enjoy the latest craze, axe throwing. From left: Tony Zhang, Nicole Lummis, Tamara Chan, Iris Garcia-Pak, Stephanie Liaw, Mario Malfavon, Richard Daneman, Kaja Bajc, Roeben Munji, Robert Pulido, Cayce Dorrier, Ryan Sheehy, Caterina Profaci.



Iadecola Lab members.

Costantino Iadecola, M.D.

Giuseppe Faraco, M.D., Ph.D.
TEAM MEMBER

Antoine Anfray, Ph.D.
TEAM MEMBER

Costantino Iadecola, M.D.

Director and Chair, Feil Family Brain & Mind Research Institute; Anne Parrish Titzell Professor of Neurology and Neuroscience; Weill Cornell Medicine

My Research

We are interested in the contributions of the blood vessels of the brain to the health of the brain. In particular, we strive to understand how, in the normal state, the vessels work to keep the brain healthy and how, in neurodegenerative diseases like Alzheimer's disease, they contribute to impair cognitive function, eventually resulting in permanent brain damage.

The involvement of the blood vessels in Alzheimer's disease occurs early in the disease course and could serve as a much-needed biomarker of early disease, and help initiate treatments targeting blood vessel function as well as the neurodegenerative process (accumulation of amyloid, tau, etc.)

My Inspiration

As a clinician, the patients and their families, especially in the initial phases of the disease when they do not know what to expect. As a scientist, it's the thrill of scientific discovery combined with the hope of, one day, improving the lives of the patients we see in our clinics.

My Motivation to Research Alzheimer's Disease

Alzheimer's disease and related dementias are the major challenge facing the aging world population and a worthwhile cause to be involved in.

My Personal Connection to Alzheimer's Disease

My connection to Alzheimer's disease comes mainly from patients in the clinic.

Most Exciting Career Moment to Date

When I discovered that a mouse model of Alzheimer's disease had a profound dysfunction in the vessels of the brain very early in the disease process, which was then confirmed in patients at risk for Alzheimer's disease.

Biggest Unanswered Question in Alzheimer's Disease

The initial factors driving the diverse pathological processes underlying sporadic Alzheimer's disease (Abeta, tau, TDP43, synuclein, vascular factors, etc.) and their interaction with the aging brain.

What I Wish Most People Understood About Science

The development of treatments for Alzheimer's disease requires major investments not only in the scientific bases of the disease, but also in the development of a social infrastructure to assure that patients, their families and caregivers are best cared for.

Outside of Work, I Like...

While I grew up with rock-and-roll music and played electric guitar in several bands, I also enjoy early music and I am seriously studying the renaissance lute (the "prince" of instruments from the 1400s to the 1700s).

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund has allowed us to jumpstart new research projects on how gut immunity also can compromise cognitive function. The Cure Alzheimer's Fund support allowed us to then garner additional funding to expand these projects to a fuller scale.

Jonathan Kipnis, Ph.D.

BJC Investigator; Alan A. and Edith L. Wolff Distinguished Professor of Pathology and Immunology; Professor of Neurology, Neuroscience and Neurosurgery; Director, Center for Brain Immunology and Glia (BIG); Washington University School of Medicine in St. Louis

My Research

We work on the interface between the immune system and the brain, and also on how brain cleansing via the lymphatic system takes place.

We hope that we could harness the power of the immune system to fight neurodegeneration and ameliorate or slow down Alzheimer's disease (AD) progression. We also hope that improving brain cleansing via enhancement of meningeal lymphatic vessels may be a promising therapeutic approach in delaying the onset of AD.

My Inspiration

Unraveling the truth that nobody before us knew!

My Motivation to Research Alzheimer's Disease

It is a fascinating disease linked to the immune system, and it is a disease of "dirt" accumulation in the brain, so the systems we are interested in must be playing a role in Alzheimer's disease.

My Personal Connection to Alzheimer's Disease

Don't we all have one? My grandmother passed away from Frontotemporal Dementia and Alzheimer's disease (FTD/AD).

Kipnis Lab members on a hike in October 2021.

Most Exciting Career Moment to Date

Probably the discovery of meningeal lymphatic vessels, but I think every time we get an interesting result I'm experiencing "the most exciting moment." 😉

Biggest Unanswered Question in Alzheimer's Disease

From my perspective, we are still missing a better insight into the role of immunity and meningeal lymphatics in Alzheimer's disease in humans.

What I Wish Most People Understood About Science

Science is like Legos. One cannot build a castle without having the building blocks. Basic science is the building blocks that make up the castles (therapies). Some basic science is "boring" (or even unexplainable) to nonspecialists, but it is fundamentally important! Without a foundation, one cannot build a building.

Outside of Work, I Like...

I do not work. I live my science. 😉 But outside of science, I enjoy books, wine and chess (for amateurs).

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

This is simple! I do not think we would be working on Alzheimer's disease without Cure Alzheimer's Fund's support. They invested in us super early when nobody believed our work had anything to do with Alzheimer's disease.

Lab members, back row, from left: Erwin Dreesen, Paul Declerck, Maarten Dewilde, Nick Geukens, Rani Soenen, Griet Compernolle. Middle row, from left: Nada Dia, Vesna Krapež, Elien De Smidt, Els Brouwers, Rita Vleugels, Marie-Lynn Cuypers, Liesl Jacobs, Miet Peeters, Pieterjan Van Maele. Front row, from left: Zhigang Wang, Wannee Kantasiripitak, Maya Imbrechts, Louanne Ampofo, Dina Rodrigues Martins, Debby Thomas, Sophie Tops, Nathalie Van den Berghe. Not pictured: Tom Jaspers, Zhongyao Zhang.

Maarten Dewilde, Ph.D.

Assistant Professor in the Laboratory for Therapeutic and Diagnostic Antibodies, KU Leuven, Belgium

My Research

Currently, there are limited options to treat patients with brain-related disorders like Alzheimer's disease. There are multiple reasons for that, one important one being that potential promising drug candidates can't reach the brain. This is because the brain has a special protective barrier that controls what is transported from the blood to the brain (blood-brain barrier). Although highly effective to protect itself, it causes a serious problem for drug delivery. Our research is focused on how to facilitate transport over this barrier to allow efficient drug delivery.

Several drugs are currently proposed to treat Alzheimer's disease, but simply can't reach the disease brain cells due to the blood-brain barrier. With our research we hope to overcome this barrier, allowing more efficient drug delivery.

My Inspiration

Seeing patients and their families and relatives in need.

My Motivation to Research Alzheimer's Disease

The big unmet need and the complexity of the disease.

Most Exciting Career Moment to Date

When we first had unambiguous proof we could shuttle drugs into the brain at therapeutically relevant concentrations.

Biggest Unanswered Question in Alzheimer's Disease

If drugs would become available, how can we make it affordable for patients and public health care?

What I Wish Most People Understood About Science

That we try to unravel how nature works, do experiments to do so, make the best theories based on the facts we collect, inherently make mistakes—but above all, we're driven by the truth.

Outside of Work, I Like...

Spending time with my family and traveling.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Our project is a typical high-risk, high-gain project. Many other granting bodies are reluctant to support such projects, as the risk to fail is high. The support of Cure Alzheimer's Fund allowed us to de-risk our project by generating preliminary data. Based on these data, we could secure additional funding and could make major steps forward in our research.

Daniel Bos, M.D., Ph.D.

Clinical Epidemiologist and Associate Professor, Department of Radiology and Nuclear Medicine and the Department of Epidemiology of the Erasmus University Medical Center

"Given that Alzheimer's disease is one of the most devastating brain pathologies, it would be great to contribute to its cure/prevention through this internal motivation/interest."

My Research
I investigate the causes and consequences of vascular disease in the brain. My specific focus is on the role of vascular disease in the development of dementia (including Alzheimer's). If vascular disease proves to be an important player in the development of Alzheimer's disease, a whole new avenue with respect to therapy and prevention will be opened.

My Inspiration
Curiosity, collaboration and teaching young researchers how to become a good researcher.

My Motivation to Research Alzheimer's Disease
For many years I have been fascinated about the blood vessels and the brain, and how these two interact in the brain. Given that Alzheimer's disease is one of the most devastating brain pathologies, It would be great to contribute to its cure/prevention through this internal motivation/interest.

My Personal Connection to Alzheimer's Disease
My grandmother suffers from Alzheimer's disease.

Most Exciting Career Moment to Date
Proving for the first time that vascular calcification in the brain increases the risk of dementia.

Biggest Unanswered Question in Alzheimer's Disease
What are the driving causes of Alzheimer's disease and how can we intervene on these to prevent Alzheimer's disease?

What I Wish Most People Understood About Science
Being a scientist is one of the most beautiful jobs, as it gives you unique opportunities to answer questions with respect to health that no other field of work can.

Outside of Work, I Like...
I love to spend time with my wife and 2-year-old son, and I really enjoy playing tennis and working out.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Through this support I can further pursue this somewhat unexplored terrain on the link between vascular disease in the arteries of the brain and the risk of Alzheimer's disease.

Dr. Bos presents at the annual Dementia Delta Plan, a Dutch initiative designed to alleviate the effects of dementia.

Paola Bovolenta, Ph.D.

Research Professor and Chair of the Program "Homeostasis of Tissue and Organs," Center for Molecular Biology Severo Ochoa, CSIC-UAM, Madrid, Spain

My Research

I am investigating the contribution of a small molecule, known as SFRP1, as a potential therapeutic target to fight the progression of Alzheimer's disease. Alzheimer's disease is a complex condition in which several of the mechanisms that sustain basic brain functions start to go wrong. These initial alterations establish a feedback loop that worsens the progression of the disease. In previous studies, we obtained evidence that a secreted molecule, known as SFRP1, is involved in different aspects of Alzheimer's disease pathogenesis. In the brain, SFRP1 is produced mainly by astrocytes, a type of glial cell that has an intense communication with both neurons and microglial cells (the main immunological defense of the brain against insults). Astrocyte-derived SFRP1 is involved in at least three pathological Alzheimer's disease traits: the generation of toxic Aβ peptides, the loss of synaptic components and the maintenance of a pernicious neuroinflammatory state.

Its biochemical characteristics and multiple functions make SFRP1 a potentially promising therapeutic target for neurodegenerative diseases. We believe that neutralizing its activity would help to break the feedback loop that worsens Alzheimer's disease progression. On the basis of quite encouraging initial data, we are now validating the use of an antibody against this protein as a possible treatment that may, at least, slow down disease progression. We also are working on alternative therapeutic approaches based on "ad hoc" drugs with SFRP1 inhibitory activity.

My Inspiration

Reading and discussing with colleagues and lab members are key factors for inspiration.

My Motivation to Research Alzheimer's Disease

Our stepping into Alzheimer's disease research was motivated by an unexpected finding while we were studying how neurons in the retina become specified. We immediately realized that our discovery could be of potential interest for Alzheimer's disease and followed the path. In other words, serendipity and curiosity have been our main motivations.

My Personal Connection to Alzheimer's Disease

My personal connection is with age-related dementia, which, I believe, is no different from Alzheimer's disease from an emotional point of view.

Most Exciting Career Moment to Date

Indeed, the first evidence that inactivating SFRP1 function from the brain of Alzheimer's disease-like mouse models was sufficient to decrease amyloid plaque formation! It was a special moment.

Biggest Unanswered Question in Alzheimer's Disease

We have learned a great deal of what goes wrong in the brain of Alzheimer's disease patients in the last decades. However, we do not yet know what really triggers the onset of the disease. Nor we know whether Alzheimer's disease is a "brain only" disease or a systemic disease, in which the brain is the most affected organ.

What I Wish Most People Understood About Science

Solutions to complex problems may come from the most unexpected findings or from research that was performed in other contexts. It is thus important to foster research broadly.

Outside of Work, I Like...

Swimming, walking in the mountains, gardening, cooking, reading novels, knitting...in no specific order, it depends on the moment.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund is giving us the opportunity to explore whether SFRP1 is a valuable target for Alzheimer's disease treatment. The financial support is certainly very important, but the real difference has been the idea that "someone" was "trusting and believing" in what we were proposing. This has been way more important than the money, at least to me, especially because we are newcomers in the field of Alzheimer's disease.

Bovolenta Lab members, from left: Polynikis Kaimakis, Elena Sanchez, Cristina Vico, Carlos Camacho, Guadalupe Pereyra, Noemi Tabenera, Paola Bovolenta, Pablo Miaja, M. Jesus Martin, Marcos Martinez, Pilar Esteve, Marcos Cardozo.

Tsuneya Ikezu, M.D., Ph.D.

Professor, Department of Neuroscience; Director, Molecular NeuroTherapeutics Laboratory; Associate Director, Regenerative Science Graduate Program; Mayo Clinic, Jacksonville

My Research

My laboratory is discovering the target mechanism for ameliorating the development of Alzheimer's disease at an early stage. We are focused on brain immune cells—microglia—and small particles released from the brain cells. These play important roles for disease spread in the brain.

We believe identification of druggable targets may ameliorate or prevent the onset of Alzheimer's disease.

My Motivation to Research Alzheimer's Disease

This is one of the most prevalent diseases in humans without a cure, and it is also very difficult to prevent. I believe we can provide significant contributions through Alzheimer's disease research and therapeutic development.

My Personal Connection to Alzheimer's Disease

I have met with so many friends, benefactors and colleagues whose parents or grandparents had Alzheimer's disease.

Most Exciting Career Moment to Date

Discovery of tau-tubulin kinase 1 as neuron-specific tau kinase, microglia and extracellular vesicle-mediated spread of tau pathology, and identification of neuronal subtypes responsible for the spread of tau pathology into the hippocampus.

Biggest Unanswered Question in Alzheimer's Disease

We still don't know how the immune system is involved in the prevention of Alzheimer's disease and how the aging process compromises the prevention. This is an important question aside from amyloid beta and tau protein.

What I Wish Most People Understood About Science

I wish the public is aware that science is one of the core intelligences of human beings, along with language and culture. There is no technical advancement without scientific discoveries.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund has made a significant difference by funding our high-risk/high-impact research on Alzheimer's disease.

Ikezu Lab members, from left: Victor Santos, Navi Watanabe, Mo Abdullah, Marissa Russo, Alyssa Elliott, Katrina Rae Bueser, Margaret Rushman, Zhi Ruan and his family, Seiko Ikezu, Tsuneya Ikezu.

Rudolf Jaenisch, M.D.

Professor of Biology; Member, Whitehead Institute; Member, Institute of Medicine; National Medal of Science recipient, Massachusetts Institute of Technology

My Research
We are trying to understand the causes of Alzheimer's disease and how to treat it using stem cell models. Once we understand the causes of the disease, we can devise therapeutic strategies.

My Inspiration
The opportunity to learn new principles of normal development and disease.

My Motivation to Research Alzheimer's Disease
It is a major health issue and it is exciting and satisfying to be able to contribute to understanding the disease.

Most Exciting Career Moment to Date
Several moments: (i) the generation of the first transgenic animal; (ii) generation of a mutant mouse that was DNA methylation deficient; and (iii) generation of induced pluripotent stem cells to study human diseases.

Biggest Unanswered Question in Alzheimer's Disease
What causes neurons to degenerate, and how to slow or prevent progression.

What I Wish Most People Understood About Science
Scientific work is complex and results are not easy to predict. But experimental research to understand the causes of the disease is the basis for eventual treatment.

Outside of Work, I Like...
Kayaking, playing an instrument.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
The support from Cure Alzheimer's Fund enabled groups with diverse expertise to join forces and enabled us to use complementary approaches to understand Alzheimer's disease.

Hui Zheng, Ph.D.

Huffington Foundation Endowed Chair in Aging; Director, Huffington Center on Aging; Professor, Departments of Molecular and Human Genetics and Neuroscience, Baylor College of Medicine

My Research
We are interested in understanding how cells in our brain clear unwanted materials, and how this clearance system declines with aging to contribute to Alzheimer's disease (AD).

In other words, we are looking for ways to elevate the cells' garbage disposal system and, more specifically, ways to clear the protein aggregrates that accumulate in brains of Alzheimer's disease individuals. Learning more about the system will help us to develop therapies that are effective and safe.

My Inspiration
Every day is a learning process.

My Motivation to Research Alzheimer's Disease
Alzheimer's disease affects the brain. There is so much that we still do not know about how the brain works in normal and disease conditions. Learning more about the brain keeps me motivated.

My Personal Connection to Alzheimer's Disease
My best friend's mother died from AD. Her sister developed AD in her early 60s. She is at that age and is very concerned.

Most Exciting Career Moment to Date
Getting my first NIH grant.

Biggest Unanswered Question in Alzheimer's Disease
Why AD is so age-dependent? Despite the genetic and environmental factors, aging is the greatest risk factor. Understanding how the brain changes with aging will help in developing therapeutic interventions.

What I Wish Most People Understood About Science
The general public is mostly interested in therapy. However, fundamental and curiosity-driven research is critically important to developing breakthrough therapy.

Outside of Work, I Like...
To run and hike.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Cure Alzheimer's Fund allows us to initiate a new project related to lipid signaling in immune system regulation. We have been able to generate some exciting data in the past year, and we are expanding the project to both investigating the mechanisms and exploring therapeutic targeting.

RESEARCH MILESTONES

GET MORE SLEEP!

Separate areas of study have confirmed the important roles of sleep and the circadian rhythm to the health of our brains. For example, one study detailed how the natural cleaning system of the brain goes into action while we sleep, removing debris and toxic particles.
—David Holtzman, M.D., Erik Musiek, M.D., Ph.D., Geraldine Kress, Ph.D., and Matthew Walker, Ph.D. [bit.ly/3E2vbFC]

Alison Goate, D.Phil.

Jean C. and James W. Crystal Professor and Chair; Director, Ronald M. Loeb Center for Alzheimer's Disease; Department of Genetics and Genomic Sciences, Icahn Genomics Institute, Icahn School of Medicine at Mount Sinai

My Research
The goal of our research is to use human genetics to understand the mechanisms underlying Alzheimer's disease, and apply this knowledge to develop novel therapeutics. Through our genetic studies we expect to identify molecules that are likely therapeutic targets. We then use computational and experimental approaches to find drugs directed toward these targets.

My Inspiration
I love collaborative, team science and working on something that I think can positively contribute to public health and wellbeing. I love working with students and trainees.

My Motivation to Research Alzheimer's Disease
Alzheimer's disease is an interesting scientific problem, but also a huge public health problem that has affected my family personally.

My Personal Connection to Alzheimer's Disease
I have worked on Alzheimer's disease for more than 30 years. My mother-in-law, Kitty Ashall, died from Alzheimer's disease, and my mother had mild dementia when she died of other causes. My paternal grandmother also died with dementia most likely resulting from strokes.

Most Exciting Career Moment to Date
I have been fortunate to be part of several successful gene-finding projects, including identifying the first mutations to cause Alzheimer's disease and Frontotemporal Dementia. These were true eureka moments that changed both fields forever.

Biggest Unanswered Question in Alzheimer's Disease
How does genetically regulated microglial function contribute to risk of developing Alzheimer's disease?

What I Wish Most People Understood About Science
There are few eureka moments in science. Generally, progress occurs by incremental steps, and through replication and extension of this knowledge we make progress. The media likes eureka moments, but these are rare and often false starts. On the positive side, we have made great progress in understanding Alzheimer's disease in the last 30 years.

Outside of Work, I Like...
I am a great tennis fan and enjoy attending the U.S. Open every year. I also enjoy great food—both eating and cooking it. Hiking is a favorite hobby.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Cure Alzheimer's Fund support has enabled us to begin a new project that incorporates computational approaches to drug repurposing. A very talented senior postdoc is leading this work. I hope that this will lead to a successful project for her future career. In recent years I have tried to develop a more directly translational program. This grant is one step in that direction.

Dr. Goate (in green) hiking the Samaria Gorge in Crete with her extended family.

Goate Lab summer BBQ, July 2022: Front row: Manon Herbinet, Sarah Neuner, Alison Goate, Tulsi Patel, Yiyuan Liu, Jo-Anne Elikann, Kam-Meng Tchou-Wong, Chiara Pedicone, Rose Temizer. Middle row: Kim Soesbergen, Rozhan Khaleghi, Sanya Marcora, Kathryn Bowles, Brian Fulton-Howard, Shea Andrews, Alan Renton, Carmen Romero-Molina, Aleisha Aristel, Marcelina Ryszawiec, Bianca Esposito. Back row: Nadia Harerimana, Edoardo Marcora, Travyse Edwards, Woojin Jung.

Kitty Ashall with her granddaughters.

Lance A. Johnson, Ph.D.

Director of Graduate Studies, Department of Physiology; Associate Professor, Sanders Brown Center on Aging, University of Kentucky

Left to right: Nick Devanney (Ph.D. student), Lesley Golden (Ph.D. student), Cassi Friday (Ph.D. student), Dr. Sangderk Lee (data scientist), Lance Johnson, Nick L'Italien (lab manager), Gabriella Morillo-Segovia (visiting student), Steve MacLean (Ph.D. student), Katy Smith (lab manager), Diksha Satish (undergraduate student). Not pictured: Dahlia Siano (undergraduate student). Photo credit: James Haggie

My Research

Our lab studies a strong genetic risk factor for Alzheimer's disease, a gene called APOE. While everyone has this gene, we have inherited different versions of it from our parents. There are three common versions, or variants, of APOE (E2, E3 and E4), and depending on which you inherited, you may have a much higher risk (E4) or a much lower risk (E2). Our lab is particularly interested in how these different variants of APOE affect brain metabolism and inflammation—and whether these two things may be linked.

Our hope is that by figuring out how the "good" variant of APOE affords its protection, we can design treatments that can help protect individuals who have inherited the variant that increases their risk of Alzheimer's disease.

I am grateful to collaborate with Drs. Josh Morganti and Ramon Sun on this important work.

My Motivation to Research Alzheimer's Disease

I actually started my career studying this same gene (APOE) in the background of heart disease. But just a few months into my Ph.D., I read a paper describing the differences in risk of Alzheimer's disease associated with the different variants of APOE. I was blown away by both the strength of that association and the fact that there was absolutely nothing we could offer patients suffering from the disease. I decided that day that I wanted to run my own lab, and that this is what we would study.

What I Wish Most People Understood About Science

I think some people think of scientists having a genius idea that solves a problem with a single eureka moment. I absolutely love my job, but science is hard, takes a lot of work and is full of failure. It takes perseverance—even a bit of a stubborn streak—to hammer away at a problem for weeks, months or even years, and progress is often incremental and sometimes difficult to see.

Outside of Work, I Like...

I love spending time with my family (wife, two young children—8 and 5—and dog), traveling and exploring new places, and cooking (and I hardly ever follow recipes because I've had my fill of following protocols in the lab).

Above: Diksha Satish and Cassi Friday work in the lab. Photo credit: James Haggie

Left: Lesley Golden. Photo credit: James Haggie

The lab team pictured at a regular drop-in gathering at Dr. Kamm's home.

Roger D. Kamm, Ph.D.

Cecil and Ida Green Distinguished Professor of Biological and Mechanical Engineering, Massachusetts Institute of Technology

My Research

We create models of healthy and diseased organs that we can use in the lab to better understand the causes of disease and test therapies that might prevent it or alleviate the symptoms. Among the advantages of the models we generate is that they are made entirely from human cells, so they better mimic what happens in patients, and also that they reduce the need for animal experiments.

The models we create and use in our lab can recapitulate many of the diseases we suffer from. Alzheimer's disease is currently a major focus of our efforts, so we generate models of the brain that include the blood supply and other brain tissues. We can use these models to discover better ways of getting therapeutic molecules into the brain to treat Alzheimer's disease. We also can use cells from Alzheimer's disease patients to produce the models that pharmaceutical companies can use to screen for entirely new treatments.

My Inspiration

Even in the short time that we've been working on Alzheimer's disease, we already can capture using our laboratory models many of the same features one sees in the Alzheimer's disease brain. As the models become more refined, they should tell us even more. That's what inspires us and drives us to do more.

My Motivation to Research Alzheimer's Disease

My lab is relatively new to the Alzheimer's field, having worked for much of the past 15 years on metastatic cancer. At one point, we wanted to study how cancer metastasizes to the brain, and why the brain is such a common site of metastasis. In the process of developing those models, we realized that we could use a similar approach, and many of the same cells and tissues, to generate a model in which we could study various neurological diseases such as Alzheimer's disease.

My Personal Connection to Alzheimer's Disease

Unfortunately, I do have a close personal connection to the disease. My mother, Betty Kamm, died of Alzheimer's disease after a 10-year decline. Her Alzheimer's began soon after she had been the primary caretaker for her sister-in-law, who also suffered from Alzheimer's disease for many years. Today, one of my closest relatives, a cousin with whom we lived for some years, has Alzheimer's disease.

Most Exciting Career Moment to Date

There have been many, but perhaps the most exciting moment came when we realized that we could simply mix together some of the key cell types in the brain, and that they would self-organize and self-assemble into structures that look and function in a way that mimics what happens in the human brain. The cells form the right structures, they organize in a way that enables them to interact, and they do this all on their own. Order "emerges" from disorder, leading to incredibly beautiful structures, the organs of our body.

continued >

Biggest Unanswered Question in Alzheimer's Disease
The most unfortunate aspect of Alzheimer's disease is that we have no proven way to prevent it. And once a person develops Alzheimer's disease, we can only treat the symptoms, not the disease.

What I Wish Most People Understood About Science
That despite the currently bleak picture regarding potential treatments for Alzheimer's disease, the methods that we and others are developing hold genuine promise for identifying new and effective treatments. We already understand a great deal about the disease and the factors that contribute to it. We now need to put that understanding to use in developing new strategies for treatment.

Outside of Work, I Like...
Bicycling has become my main mode of transportation and exercise these days. I love being outdoors and having the freedom to explore new places, either by bike or on foot.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Soon after we started working on Alzheimer's disease, we heard that the brain has a drainage system that clears unwanted molecules, such as the proteins that lead to Alzheimer's disease, called the meningeal lymphatic system. We had wanted to include this in our models, but didn't have the resources to until we linked up with Cure Alzheimer's Fund and started to collaborate with the research team that first discovered the new pathway.

In the lab: From left, Roger Kamm, Georgios Pavlou, Clare Ko and Marie Floryan.

Dr. Kamm's mother, Betty, succumbed to Alzheimer's disease after a 10-year battle with it.

Beth Stevens, Ph.D.

Associate Professor of Neurology, Harvard Medical School; Research Associate, F. M. Kirby Neurobiology Center, Boston Children's Hospital; Investigator, Howard Hughes Medical Institute (HHMI); Member, Broad Institute

In 2016, award-winning developmental neurologist Beth Stevens, Ph.D., published a groundbreaking study identifying a pathway that may be responsible for synapse loss in the Alzheimer's brain, which is closely correlated with cognitive decline.

In the developing brain—from birth to early adolescence—synapse loss occurs normally and frequently. "It's a 'use it or lose it' system," Dr. Stevens explains. "The brain figures out which connections are important and which ones aren't, based on experience. It prunes the ones it doesn't need so that it can strengthen the more useful connections." Synapses transmit signals throughout the brain, facilitating the formation of thought, memory recall, motor skill function and more. Dr. Stevens, along with her mentor, the late Ben Barres, M.D., Ph.D., published a paper showing that a protein named ***complement*** mediates healthy synapse loss by tagging unnecessary synapses for destruction. In much the same way macrophages devour invading pathogens like bacteria throughout the body, brain cells called microglia devour the complement-marked synapses. This tag-and-destroy activity is important to healthy brain development as part of the brain's innate immune system. In healthy adults, this complement-pruning pathway is largely dormant. While microglia and complement still play other important roles, they're no longer trimming synapses on a large scale.

Dr. Stevens and her colleagues also found that by disabling or blocking the creation of complement, they could preserve synapses. These protected mice experienced less synapse loss. "Complement shows real potential as a therapeutic target," Dr. Stevens explains. "It's especially exciting because it's involved at a very early point in the disease. If we could stop synapse loss early, we might be able to stop cognitive decline, or at least stave it off for several years."

Eng H. Lo, Ph.D.

Professor of Neurology and Radiology, Harvard Medical School, Massachusetts General Hospital

My Research

The 24-hour cycles of sleep and wakefulness are part of a biologic process called circadian rhythm. Sleep disturbances and problems with this circadian rhythm are an important part of Alzheimer's disease. It is increasingly suspected that disruptions in circadian rhythm may arise very early on, and may play some unknown role in Alzheimer's disease progression. Our research will study how circadian disruptions alter gene expression within small blood vessels of the Alzheimer's disease brain. These interactions may be especially important because up to 75% to 80% of all Alzheimer's disease patients also suffer from some problems in blood flow to the brain.

If our ideas are correct, then we may be able to eventually find ways to renormalize circadian rhythms in blood vessels of the brain, and prevent or slow down disease progression.

My Inspiration

The best part of my job is the opportunity to work with the best and the brightest—the new generation of young scientists with their new ideas and their brilliant trajectories.

Most Exciting Career Moment to Date

Hard to say. I started my lab in Massachusetts General Hospital in 1991. Thirty years later, every day is still new, and every experiment still excites me.

Biggest Unanswered Question in Alzheimer's Disease

Amyloid and tau are the two major "standard" components of the Alzheimer's disease process. But they are not the only ones. In fact, it has been difficult to find success in clinical trials that solely target amyloid and tau. We hope that our research can reveal how mechanisms in circadian biology feed into and worsen "standard" Alzheimer's disease mechanisms, and thus allow us to find novel therapeutic approaches.

What I Wish Most People Understood About Science

I am excited to do science. I am hopeful that I can do something for society. Mostly I am just grateful—it is a privilege.

Outside of Work, I Like...

I like to eat! My wife likes to cook. So it kinda works. 😊

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

NIH grants are difficult to get because, counterintuitively, NIH is actually very conservative and it is hard for new "slightly different" ideas to get funded. CureAlz is a blessing. Without CureAlz, we would never have gotten this chance to pursue our new circadian ideas for Alzheimer's disease.

"NIH grants are difficult to get because, counterintuitively, NIH is actually very conservative and it is hard for new 'slightly different' ideas to get funded. CureAlz is a blessing. Without CureAlz, we would never have gotten this chance to pursue our new circadian ideas for Alzheimer's disease."

→ DID YOU KNOW?

Knowledge gained from CureAlz-funded projects focused on Alzheimer's disease was utilized in 2020 by CureAlz investigators who shared their findings to advance treatments for COVID-19.

Erik S. Musiek, M.D., Ph.D.

Charlotte & Paul Hagemann Professor of Neurology and Co-Director, Center On Biological Rhythms And Sleep (COBRAS), Washington University School of Medicine in St. Louis

My Research

We study how our internal circadian clock, which regulates our sleep-wake cycle and the 24-hour rhythms of our body, impacts risk for Alzheimer's disease. Our data suggests that disrupting the circadian rhythm, as occurs when we are exposed to light late at night or when we fly across time zones, can accelerate pathology related to Alzheimer's disease through multiple mechanisms. We are trying to understand this and combat it.

We think that certain drugs that improve our sleep or our circadian rhythms might be able to prevent the accumulation of amyloid plaques and tau tangles that lead to Alzheimer's disease.

My Inspiration

Discovering new things that I'm always surprised have not already been discovered. As if they are just sitting there under our nose for years. Perhaps the cure to Alzheimer's disease is the same.

My Motivation to Research Alzheimer's Disease

Such an important problem, and still such a mystery.

Biggest Unanswered Question in Alzheimer's Disease

People with Alzheimer's disease have amyloid plaques for years with little problem. Then, for some reason, a switch flips and their tau starts to accumulate, leading to neurodegeneration and memory loss. What is this switch? How can we stop this?

What I Wish Most People Understood About Science

Actual scientific discoveries are always much more complicated and multifaceted than they are portrayed in the media!

Outside of Work, I Like...

I'm a runner, but spend most of my time traveling around the country for my kids' soccer games.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Funding from Cure Alzheimer's Fund helped my lab make some important discoveries that have now launched a major area of research for us and led to several NIH grants, as well as a new drug discovery effort. So, the impact has been huge.

Musiek Lab members. Back row, from left: Adya Dhuler, Pat Sheehan, Jen Lawrence, Ashish Sharma, Melvin King. Middle row, from left: Collin Nadarajah, Julie Dimitry, Jiyeon Lee, Celia McKee, Erik Musiek. Front row, from left: Asha Patel, Cynthia Chen.

Krista L. Moulder, Ph.D.

Executive Director, Charles F. and Joanne Knight Alzheimer Disease Research Center, Professor of Neurology, Washington University School of Medicine in St. Louis

My Research

Too much of the research that has been done about Alzheimer's disease has been done with White research participants. Work from our group here at Washington University in St. Louis and others has shown that certain markers of Alzheimer's disease are different between people who identify as Black versus these White individuals, but we need more data from Black research participants to truly understand these differences. Our Cure Alzheimer's Fund grant is allowing us to collaborate with Emory University to share tissue samples from Black participants, and ask harder, more specific questions.

If it is true that levels of some Alzheimer's markers are different in people who identify as Black, then clinical trials or prevention studies will need to incorporate racially distinct inclusion criteria and endpoints for their trials.

My Inspiration

Our research volunteers are so inspiring. They give of their time with no real benefit directly to themselves, but only with the hope that they will make things better for the next generation.

My Motivation to Research Alzheimer's Disease

I have long been fascinated by the brain. The fact that our brain cells use electrical signals to communicate with each other to guide what we do and to make memories is pretty amazing.

My Personal Connection to Alzheimer's Disease

My paternal grandmother, Helen Moulder, died with Alzheimer's disease. I will never forget how she thought that my cousin's wedding was her own daughter's (my aunt's) wedding instead.

Biggest Unanswered Question in Alzheimer's Disease

The field needs definitive evidence in humans that removing amyloid from the brain, if done early enough, has a downstream beneficial effect on memory and thinking.

What I Wish Most People Understood About Science

We are always learning in science. If we find new data that shows an old idea is wrong, we are still working toward the goal of understanding more and more. Like with the COVID-19 pandemic, some ideas from early in the pandemic may not have been quite right, but scientists keep looking at all of the data so that, overall, we know more now than we did in the beginning.

Outside of Work, I Like...

I am an avid runner and have run marathons in 15 states!

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Our Cure Alzheimer's Fund grant has allowed us here at Washington University in St. Louis to ask harder, more specific questions about racial effects on Alzheimer's markers because we are able to collaborate with investigators at Emory University and combine our precious tissue samples from Black research volunteers. It is very gratifying that the Cure Alzheimer's Fund supports our goal of understanding the contributing factors for Alzheimer's disease in people of all races.

Dr. Krista Moulder is an avid runner and marathoner. She's pictured here, second from left, with fellow CureAlz-funded researcher, Dr. Erik Musiek, second from right, and other investigators at Washington University.

Marc Diamond, M.D.

Founding Director, Center for Alzheimer's and Neurodegenerative Diseases; Distinguished Chair in Basic Brain Injury and Repair, University of Texas Southwestern Medical Center

My Research

I work on the molecular mechanisms that underlie the initiation and progression of Alzheimer's disease, focusing on the tau protein, which accumulates in Alzheimer's disease and other dementias to cause neurodegeneration. We are working on better ways to diagnose and treat Alzheimer's disease.

Our work is directly focused on how we can intervene to block fundamental disease mechanisms in Alzheimer's disease, and to create tools for improved diagnosis.

My Inspiration

I love working with and inspiring others, and figuring out the mechanistic basis of human disease.

My Motivation to Research Alzheimer's Disease

When I was a neurology resident in the 1990s, I became interested in neurodegenerative diseases because they are devastating and untreatable, and at the time we had very little idea about how they worked.

My Personal Connection to Alzheimer's Disease

My grandparents had this disorder.

Most Exciting Career Moment to Date

I don't know if there is one moment that stands out; however, I can say that the progressive development of an understanding about fundamental mechanisms by which tau initiates and underlies progression of Alzheimer's disease and other tau-related disorders has been unbelievably exciting.

Biggest Unanswered Question in Alzheimer's Disease

We don't know what will be the best way to intervene to stop initiation and progression of disease.

What I Wish Most People Understood About Science

Science is an intensely rewarding, collaborative job that is great for people who are fundamentally curious. The goal is to understand the world around us through rigorous testing of ideas about what we think is going on. We don't "prove" anything. We just try to develop an understanding of the natural world with higher and higher levels of certainty. Science isn't facts. Science is a way of knowing about the natural world in all its forms: physical, chemical or biological.

Outside of Work, I Like...

I am an avid tennis player and study guitar.

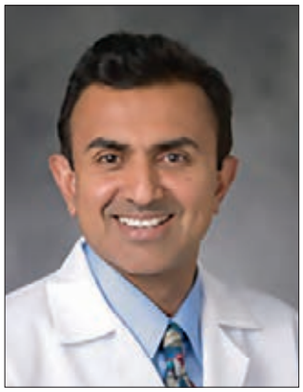
How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Support from Cure Alzheimer's Fund has allowed us to take risks and initiate projects quickly, without waiting years for NIH funding. It has also allowed us to build up preliminary data that has allowed us to get longer-term funding from the NIH.

→ RESEARCH MILESTONES

ALZHEIMER'S GENOME PROJECT

The Alzheimer's Genome Project™ was established as the first large-scale, family-based study of the human genome specific to Alzheimer's disease. The work was listed in TIME's Top 10 Medical Breakthroughs of 2008.
—Rudolph Tanzi, Ph.D. [bit.ly/3LV1KHm]



P. Murali Doraiswamy, MBBS

Professor of Psychiatry and Behavioral Sciences; Director, Neurocognitive Disorders Program; Professor in Medicine, Duke University

My Research
My Cure Alzheimer's Fund research project is examining why women develop Alzheimer's disease at a higher rate than men. I am collaborating with a team from Boston University to study how gender/sex impacts the risk for Alzheimer's disease using the 70 years of health-related data from a large population study called the Framingham Heart Study.

Women have a higher risk of developing Alzheimer's disease compared with men in the United States, but this is not simply because women on average live to older age than men. Understanding how sex/gender impacts the risk for Alzheimer's disease will help us develop more personalized ways to treat or prevent it.

My Inspiration
Helping patients and families.

My Motivation to Research Alzheimer's Disease
It's one of the biggest challenges of our time.

My Personal Connection to Alzheimer's Disease
As an Indian, I am curious as to why India has a low rate of Alzheimer's.

Most Exciting Career Moment to Date
Doing a briefing on Alzheimer's to a gathering of world leaders in Davos.

Biggest Unanswered Question in Alzheimer's Disease
When does Alzheimer's disease start? Where in the brain does it first start?

What I Wish Most People Understood About Science
How to spot fake news.

Outside of Work, I Like...
I am working on an archeological project in my hometown in Chennai, India, to uncover a 1,000-year-old "missing" temple complex. Legend has it that in the 8th century, there was a spectacular golden temple complex with seven pagodas at the Mahabalipuram Harbor, but this was largely dismissed as a myth. During the 2004 tsunami, when the ocean receded, a number of structures were revealed in the ocean bed—suggesting the myth may be real. I am raising funds to use a submersible with sonar to discover this missing temple complex!

Uncovering a submerged 8th century temple complex in his hometown of Chennai, India, is a passion project of Dr. Murali Doraiswamy.

Eckhard Mandelkow, Ph.D.

Senior Group Leader, German Center for Neurodegenerative Diseases (DZNE), Germany

Eva-Maria Mandelkow, M.D., Ph.D.

Senior Group Leader, German Center for Neurodegenerative Diseases (DZNE), Germany

Our Research

We are investigating how nerve cells in the brain lose their function and cause memory deficits in Alzheimer's disease, and we would like to find ways to stop or prevent this. We are a wife and husband research team—Eva Mandelkow is a medical doctor, Eckhard Mandelkow is a physicist—and together this background enables us to look at the problem from different directions. For example, we are studying proteins that are suspected to go awry in the disease, or animal models like mice where we can study how memory deficits appear and how this can be delayed or even prevented by drug treatment. The support from Cure Alzheimer's Fund is used to test certain drugs that improve the functioning of nerve cells.

Our work can be described as basic research, where we look at the functions of nerve cells and how they get lost during Alzheimer's disease. This includes the transport of proteins along the long cell extensions, and the communication between cells by electrical or chemical signals. Based on these findings, we try to find methods to restore the normal functions by drugs. If successful at the level of nerve cells and animal models, these drugs could be further developed for applications in humans; that is, the drugs would have to be designed to reach the brain and their specific targets in the brain. Later clinical trials on humans will have to make sure that the drugs are safe and effective

Our Inspiration

The most inspiring aspect is perhaps the opportunity to discover novel features of how brain cells work, achieved by a team of researchers from diverse backgrounds, qualifications and nationalities, working together on common goals.

Our Motivation to Research Alzheimer's Disease

During our Ph.D. period at the Max Planck Institutes in Heidelberg, we were initially working on distinct problems in molecular biology. Later, as postdocs in the United States (Brandeis University), we were introduced to the cell biology of microtubules, fibrous structures that are responsible for transport processes along neurons and cell division (hence of medical interest for cancer biology). Microtubules are associated with several other proteins, one named "tau protein," which subsequently was discovered to be a main constituent of the "neurofibrillary tangles" of Alzheimer's disease. After returning to Germany, this was the point where we seized the opportunity to focus on the cell biology of tau protein. In pursuing this research, we benefited greatly from the network of scientists or medical doctors working on similar issues and reporting them at major international meetings (such as American Society for Alzheimer's disease, Neuroscience, Cell Biology and others).

Our Personal Connection to Alzheimer's Disease

In our times, given the general increase in longevity (thanks to improvements in living conditions and advances in medicine), there is hardly any family that is not affected by Alzheimer's or other neurodegenerative diseases.

Most Exciting Career Moment to Date

Exciting moments are usually those where unexpected new findings appear that open up new vistas and lead to new paths of research. In our case, such moments occurred with the discovery of assembly pathways of tau protein, the successful design of mouse models where changes in memory could be experimentally switched on or off, or of drugs that reverse and normalize the memory deficits in mice.

Biggest Unanswered Question in Alzheimer's Disease

So far there are no efficient drugs that can prevent or cure Alzheimer's in human patients. In spite of the ongoing worldwide efforts, the drugs currently available have only a modest influence on the course of the disease. This begs the question whether the prevailing ideas about the origin of Alzheimer's disease are precise enough to identify the root cause(s). Alois Alzheimer described several proteins forming clumps in nerve cells as abnormal signs of the disease, and therefore research and drug development efforts have largely been aimed at preventing or dissolving those clumps ("amyloids"). But what if those clumps are just hallmarks, rather than causes of the pathology? Some basic assumptions deserve to be reevaluated.

What We Wish Most People Understood About Science

Scientific discovery, whether curiosity-driven or applied, has yielded breathtaking advances in medicine and technology since it began in an organized fashion in the 17th century, and it still does so today. It is a privilege to be part of this effort. Moreover, it has been a very rewarding experience to be embedded in an international community of students, collaborators and colleagues with open discussion on issues of common interest. On a personal level, it allowed both of us to collaborate on joint scientific goals, in spite of distinct backgrounds, and to combine this with family life, including two children.

Outside of Work, We Like...

Outside of the normal working hours, we enjoy communication with family and friends, taking walks, reading informative books, enjoying opera and playing piano.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

The support has been crucial in several respects: (1) the possibility of obtaining research support with a minimum of bureaucracy and time delay, enabling one to tackle new research projects quickly, (2) the flexibility of use of funding, depending on outcomes of the research, and (3) the accelerated exchange of information on new results or methods between researchers.

Sangram S. Sisodia, Ph.D.

Thomas Reynolds Sr. Family Professor of Neurosciences; Professor, Departments of Neurobiology and Neurology; Director, Center for Molecular Neurobiology, University of Chicago

My Research
I am interested in examining the role of the trillions of bacteria in the gut, termed the gut microbiome, which can influence the principal pathologies of Alzheimer's disease (AD) in the brain, namely, amyloid beta deposition and neuroinflammation.

We have already shown a very important role of the gut microbiome in modulating AD-type pathology in the brains of mice. The goal of these studies is to identify specific bacterial species and metabolites that influence neuropathology in the brain, with the notion that these factors will be utilized for therapeutic intervention in disease.

My Inspiration
Every day is a surprise….I await new discoveries and testing novel hypotheses.

My Motivation to Research Alzheimer's Disease
I took a chance…didn't know what a neuron was before I started.

Most Exciting Career Moment to Date
Meeting my mentors: Don Cleveland, Ph.D., who is a pioneer in the mechanisms of chromosome movement and breakthrough research into Huntington's Disease; and Don Price, M.D., who was founding director, Division of Neuropathology, at the Johns Hopkins School of Medicine.

Biggest Unanswered Question in Alzheimer's Disease
What are the Influences of environmental factors in mediating alterations in brain biology?

What I Wish Most People Understood About Science
It's challenging, and there will be a lot of hiccups, but we are committed to understanding the genetic, molecular and cellular basis of disease. We will get there!

Outside of Work, I Like…
Playing squash, mentoring and supporting kids in an underserved neighborhood (mine).

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Taking risks and being supported for testing novel hypotheses that would never have been funded by the National Institutes of Health (NIH)—microbiome studies wouldn't have happened without CureAlz.

Caleb Finch, Ph.D.

ARCO/William F. Kieschnick Chair in the Neurobiology of Aging; Professor, University of Southern California

My Research
Air pollution increases risk of Alzheimer's disease and accelerates brain aging. We would like to find a diet and drugs that reduce the impact of air pollution and reverse its effects.

My Inspiration
Training the next generation of scientists to attack Alzheimer's disease.

My Motivation to Research Alzheimer's Disease
The belief that Alzheimer's disease is not inevitable.

Most Exciting Career Moment to Date
Discovery in my lab that oligomeric Abeta was toxic (1995, Oda et al. Exp Neurol).

Biggest Unanswered Question in Alzheimer's Disease
Why is Alzheimer's disease linked to aging?

What I Wish Most People Understood About Science
Slow steps between unpredictable discoveries.

Outside of Work, I Like…
Traditional Appalachian fiddling.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
The support from Cure Alzheimer's Fund allowed me to explore new ideas.

"We would like to find a diet and drugs that reduce the impact of air pollution and reverse its affects."

Cameron McAlpine, Ph.D.

Assistant Professor, Cardiovascular Research Institute and the departments of Medicine and Neuroscience at the Icahn School of Medicine at Mount Sinai

"[Cure Alzheimer's Fund's] support has enabled us to ask important questions at the intersection of immunology and neuroscience, and perform experiments that will have a profound impact on the treatment of Alzheimer's disease."

My Research

My lab studies the connections between sleep and Alzheimer's disease. We believe immune cells and the factors they secrete link poor sleep with the development of Alzheimer's disease. We are investigating how disturbed or inadequate sleep causes inflammation and immune cell dysfunction in organs and tissues outside of the brain to perpetuate neurodegeneration in the brain.

The cellular and molecular mechanisms that link sleep to Alzheimer's disease are poorly understood. By investigating novel biological pathways and connections, we may identify new targets that can be harnessed therapeutically. Further, our work will have an important impact on public health policy, advocating for good-quality sleep as a component of Alzheimer's disease management and prevention.

My Inspiration

I am inspired and motivated by my team and their exciting and unexpected findings. My team conducts innovative experiments and I am always astounded by their data and discoveries. My team challenges me and asks profound questions, motivating all of us to pursue hard but impactful ideas.

My Motivation to Research Alzheimer's Disease

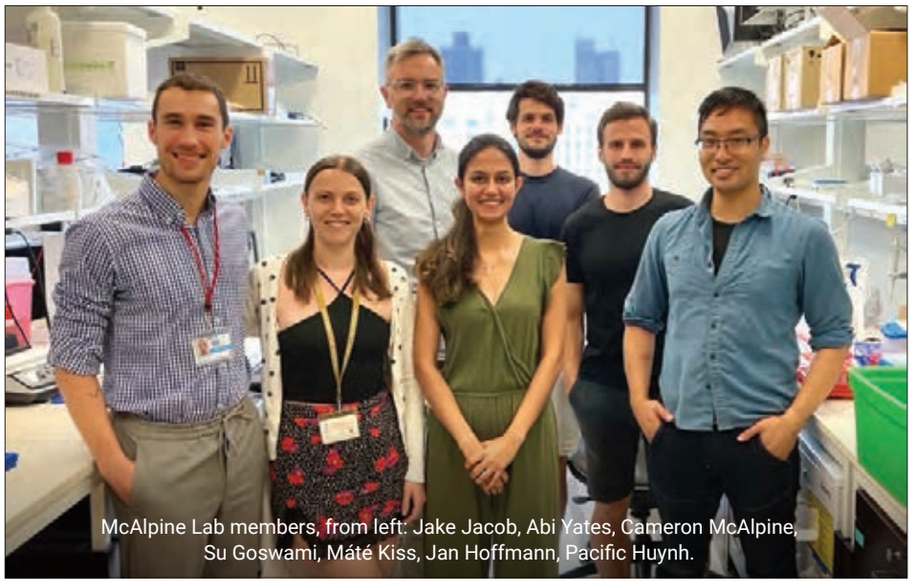
I am intensely curious about how bodily systems communicate with one another. No system, organ, structure or cell is a silo, and they all communicate with one another in remarkable and underappreciated ways. I am motivated to study interactions between sleep, the immune system and neurodegeneration to reveal new biological pathways.

Biggest Unanswered Question in Alzheimer's Disease

I think that the biggest unanswered question in Alzheimer's disease is how peripheral immune cells in organs and tissues outside of the brain impact the pathology of Alzheimer's disease inside the brain, and how lifestyle factors, like sleep, interfere with this communication axis.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

As a new and growing lab, the support of Cure Alzheimer's Fund has been instrumental in allowing us to tackle big and ambitious projects and develop new ideas. Their support has enabled us to ask important questions at the intersection of immunology and neuroscience, and perform experiments that will have a profound impact on the treatment of Alzheimer's disease.



McAlpine Lab members, from left: Jake Jacob, Abi Yates, Cameron McAlpine, Su Goswami, Máté Kiss, Jan Hoffmann, Pacific Huynh.

Liisa Myllykangas, M.D., Ph.D.

Associate Professor of Neuropathology, Consultant Neuropathologist, University of Helsinki and Helsinki University Hospital

My Research

I am a neuropathologist studying tissue-level and genetic changes associated with neurodegenerative diseases. In the project funded by Cure Alzheimer's Fund, we characterize tissue-level changes in tissues collected from Alzheimer's disease patients in order to understand the causes of Alzheimer's disease.

Our work aims to reveal mechanisms of Alzheimer's disease in human patients. This can lead to novel treatment or prevention options in the future. In the project funded by Cure Alzheimer's Fund, we specifically focus on neuroinflammation mechanisms in human patients suffering from Alzheimer's disease. Neuroinflammation has been found to be a key player in Alzheimer's disease, but the exact mechanisms still remain to be elucidated.

My Inspiration

As a neuropathologist, I can often find out the exact cause for the symptoms of the patient. During my career I've seen how basic scientific findings—for example, genetic findings—are now being used as diagnostic tools that really help patients to get more accurate diagnoses and sometimes even more effective treatments.

My Motivation to Research Alzheimer's Disease

Brain diseases are often longstanding, holistic and particularly devastating diseases, affecting not only the patient but also the loved ones. Alzheimer's disease is very common, thus influencing a very large number of people worldwide, and clearly is one of the diseases where most research and effort need to be focused in order to find effective treatments.

Most Exciting Career Moment to Date

In March 2020, I performed the neuropathological examination of my first COVID-19 case; the person had had a severe comatose disease. At that time there were no publications on COVID-19-related brain changes and no one seemed to have an idea what kind of brain alterations these patients have. I immediately noticed that the brain changes of COVID-19 are different from what we see in most other virus diseases. I felt I was working in the scientific front line.

Biggest Unanswered Question in Alzheimer's Disease

In my routine work as a neuropathologist, I see that there is a lot of heterogeneity in tissue changes of Alzheimer's disease patients. It seems that there are different subtypes of Alzheimer's disease, most likely with different etiologies. Our understanding in this area is still limited, but it is possible that these subtypes will require different treatment/prevention options, once they will become available. Thus, I think it will be very important that these subtypes are recognized and their specific etiologies are investigated.

What I Wish Most People Understood About Science

I would like people to understand that achieving scientific advancements requires extensive multidisciplinary studies and takes a long time. Even the revolutionary findings are, in most cases, just the tip of an iceberg, based on long-term and concerted ground work of the scientific community.

Outside of Work, I Like...

I enjoy skiing, swimming and listening to audio books. I love to spend time in my garden, where I've established a small arboretum.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

The support from Cure Alzheimer's Fund has enabled us to establish this interesting collaboration project with the Lehtinen group. We are able to perform extensive immunohistochemical stainings using tissue samples of human Alzheimer's disease patients and controls, and to combine our results with the data of mouse models generated in the Lehtinen lab.

"I would like people to understand that achieving scientific advancements requires extensive multidisciplinary studies and takes a long time. Even the revolutionary findings are, in most cases, just the tip of an iceberg, based on long-term and concerted ground work of the scientific community."

Colette Cywes-Bentley, Ph.D.

Assistant Professor in Medicine, Department Medicine, Division of Infectious Diseases, Brigham and Women's Hospital, Harvard Medical School

My Research

We believe that we have found evidence that microbes shed membrane fragments that end up in the brain, where they can accumulate and subsequently elude the brain's garbage collection mechanisms. Our hypothesis is that these undisposed-of microbial fragments can then lead to a "sterile inflammation" in brain tissue, and that the inflammatory process can get stuck in the "On" mode. The inflammation fails to clear its source and becomes a factor in neuropathy, including Alzheimer's disease (AD), AD-related dementias and the acceleration of pathology in some traumatic brain injuries.

Our current work explores whether we can tag these microbial fragments with an antibody to promote the garbage disposal. Using this antibody, we can facilitate the brain's natural garbage collection processes—by the body's cells called phagocytes. The key is that many of these microbial fragments share a common polysaccharide structure, PNAG, a structure not found in healthy tissue—and that PNAG can be marked by antibodies specific to PNAG. It is exciting that the PNAG antibodies do not bind to healthy brain tissue—but do bind to a significant amount of microbial garbage.

Using these PNAG-specific antibodies, we can help focus the inflammatory response's complement deposition process in a way that activates phagocytes to eat up microbial fragments, which we propose are a significant source of the brain's inflammation, and allowing the body to eliminate them. The brain's general inflammatory response is then given a chance to calm down—significantly reducing levels of chronic inflammation driving neuropathology and cognitive decline.

Mariana Vinacur Franklin
TEAM MEMBER

During 2020 and 2021, we vaccinated a strain of Alzheimer's disease mice, either at 5 weeks of age or 5 months of age, when beta amyloid deposits in their brains were already present. We were able to protect our experimental cohorts from significant levels of cognitive decline suffered by the control groups.

This year, funded by Cure Alzheimer's Fund, we are working with a more severely afflicted strain of Alzheimer's disease mice to confirm and refine our hypothesis. Our goal is to find therapeutic and preventative mechanisms that can play a role preventing, stopping and even ameliorating cognitive declines found in AD in humans.

We have a vaccine and antibodies to PNAG that have already been in early clinical trials in humans and shown to be safe. The key determinant now is demonstrating the presence of PNAG-containing fragments in the affected areas of the brains from AD individuals that are not seen in uninjured controls, and showing that the vaccine and antibody to PNAG have significant impact on cognitive and behavioral decline in mouse models of AD, and eventually humans with AD.

My Inspiration

How little we really know about the connectedness of the vast number of systems that make us human.

My Motivation to Research Alzheimer's Disease

For almost my whole career, I have focused on host response mechanisms involved in infectious disease—with particular interest in common but stubborn public health challenges: tuberculosis, strep, staph. My interest in Alzheimer's disease came from a growing intuition that my skills in infectious disease might be able to play a role in understanding part of the phenomenon of Alzheimer's disease.

Most Exciting Career Moment to Date

The moment I realized that the PNAG-vaccinated Alzheimer's mice were behaving like wild type, nontransgenic mice in the water T maze assessment of cognitive function.

Biggest Unanswered Question in Alzheimer's Disease

When and how does the process of neurodegeneration, that results in the system of symptoms that we call Alzheimer's disease, begin and how does it work?

What I Wish Most People Understood About Science

Science is a process that requires tremendous levels of effort and time, much of it collaborative, to establish even small findings. Diseases often are perceived as monoliths, but can turn out to be a number of pathogenic and pathological systems. Viewed up close, maybe at a single bench, it can seem almost static—in the span of a generation, however, a field can find entirely new ways of seeing and responding to medical challenges.

Outside of Work, I Like...

Exploring new places.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

As a researcher that comes to the Alzheimer's field via a nonstandard route, Cure Alzheimer's Fund has not only provided funding, but also access to numerous Alzheimer's disease researchers with vast knowledge and insight into this disease.

Gerald B. Pier, Ph.D.

Professor of Medicine, Microbiology and Immunology, Harvard Medical School; Microbiologist, Brigham and Women's Hospital

My Research
There are a large number of microbes in and on human bodies and they have a profound influence on many diseases. We are trying to understand how they impact diseases, particularly ones like Alzheimer's disease, and to come up with vaccines or other treatments to ameliorate the effect of these microbial cells on brain health.

We believe the microbial cells, or more likely small pieces, get into the brain over time and are key factors in the inflammation that occurs there. This inflammation destroys the brain cells and leads to neurologic diseases. We are testing vaccines and antibodies that react to a large number of different microbes for their ability to prevent this destruction of brain cells when microbes get there.

My Inspiration
The potential to discover new causes of diseases like Alzheimer's disease, and design and test interventions.

My Motivation to Research Alzheimer's Disease
The lack of progress in finding new treatments and the associations shown between microbial cells in and on the body and the development of Alzheimer's disease led us to investigate the relationship of these factors from the viewpoint of a microbiologist and immunologist, not a neurosciences investigator.

My Personal Connection to Alzheimer's Disease
My mother's mother (grandmother) was severely affected by Alzheimer's disease.

Most Exciting Career Moment to Date
Discovery of a highly conserved factor many different infectious-causing microbes make has brought us to the point of being able to test a vaccine and antibody to this factor for efficacy against not only many different infectious diseases, but also diseases wherein the normal microbes on a human body also contribute to the disease process.

Biggest Unanswered Question in Alzheimer's Disease
Is there a unifying cause or factor that leads to destruction of brain cells and tissues and the signs and symptoms of Alzheimer's disease?

What I Wish Most People Understood About Science
That it is a long process with many starts and stops and missteps but, overall, it is self-correcting and the process has markedly improved the quality of life on Earth.

Outside of Work, I Like...
Spending time with my grandchildren, cooking, skiing, beach vacations.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
It has allowed us to extend our vaccine and antibody intervention in preclinical mouse models of Alzheimer's disease to show we can vaccinate against microbial factors and prevent the Alzheimer's disease mice from undergoing cognitive and behavioral changes.

"[Science] is a long process with many starts and stops and missteps but, overall, it is self-correcting and the process has markedly improved the quality of life on Earth."

DID YOU KNOW?

The first CureAlz research grant was awarded in 2004 to Dora Kovacs, Ph.D., to study the development of novel ACAT inhibitors with the potential to prevent and treat Alzheimer's disease.

Doo Yeon Kim, Ph.D.

Associate Professor of Neurology, Genetics and Aging Research Unit; McCance Center for Brain Health, Harvard Stem Cell Institute; MassGeneral Institute for Neurodegenerative Disease; Massachusetts General Hospital/Harvard Medical School

My Research

We have been studying the disease mechanism of Alzheimer's disease (AD) to find new drug candidates using our three-dimensional human cellular models of Alzheimer's disease. With generous support from Cure Alzheimer's Fund, we are screening and validating novel AD drug candidates from FDA-approved drugs and natural product chemical libraries.

We hope some of our drug candidates can be tested and validated for human AD therapies in the future.

My Inspiration

It is exciting to see how miniatured human brain models in a dish accelerate basic mechanistic studies and drug discovery.

My Motivation to Research Alzheimer's Disease

Understanding Alzheimer's disease mechanism is one of the most challenging questions in neuroscience research, which scientifically motivates me.

My Personal Connection to Alzheimer's Disease

My father-in-law passed away last year with severe AD symptoms. I have been studying Alzheimer's for 20-plus years but found that there was nothing I could do for him. I also understand how devastating it is for close families. I sincerely hope that my studies contribute to finding a cure for this tragic disease.

Most Exciting Career Moment to Date

I was awarded the Smithsonian American Ingenuity Award in 2015 for developing a three-dimensional human neural cell culture model of Alzheimer's disease.

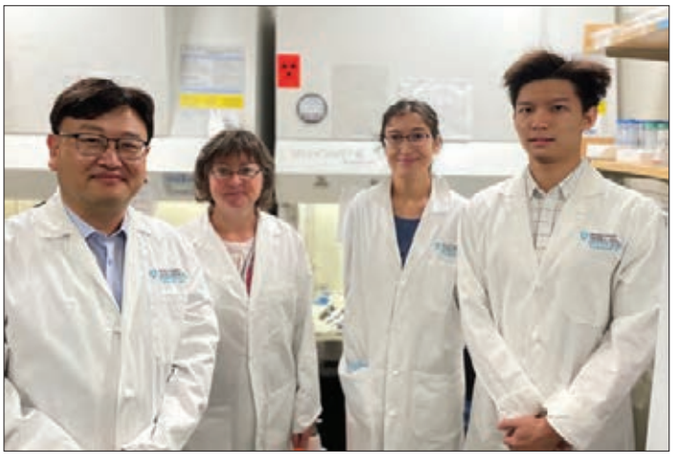
Biggest Unanswered Questions in Alzheimer's Disease

1) Can anti-amyloid therapies be sufficient for reversing the pathogenic cascades in AD patients?

2) Can we restore damaged brain functions in AD patients? (Current AD clinical trials focus on slowing down the disease progression, not reversing brain damages/functions.)

What I Wish Most People Understood About Science

Although it seems to take forever to find a cure for AD, I would like to assure you that there has been tremendous progress, making me convinced that better therapeutic solutions for AD patients will be available soon.



3D Drug Screen Team at Massachusetts General Hospital/Harvard Medical School. From left: Doo Yeon Kim (principal investigator), Luisa Quinti (co-principal investigator), Jasmin Richter (research associate), Dajun Kang (research associate).

Outside of Work, I Like...

I am a big fan of computer games. It is helpful to distance myself from all the stresses.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund's initial support was critical for developing the 3D human neural cell culture model of Alzheimer's disease in 2014. I had been failing to get NIH funding for the same project due to the lack of preliminary publications in this direction. Nevertheless, Cure Alzheimer's Fund believed and supported my project, which led to exciting new innovations.

Later, Cure Alzheimer's Fund's support also plays a crucial role in starting a big drug screening effort, which leads to identifying multiple drug candidates that reverse AD pathology in our dish model. We hope some of our drug candidates can be tested and validated in human clinical trials.

RESEARCH MILESTONES

ALZHEIMER'S IN A DISH

Alzheimer's in a Dish™ is a 3D model of Alzheimer's disease, replicated in a Petri dish. This tool is recognized as invaluable for research by providing shorter time requirements for key studies, including the evaluation of existing drugs for potential treatments. —Rudolph Tanzi, Ph.D., Doo Yeon Kim, Ph.D., and Hansang Cho, Ph.D. [bit.ly/3CjWeuG]

Luisa Quinti, Ph.D.

Instructor in Neurology, Massachusetts General Hospital

My Research
I am a chemist by training and work on drug screening, the initial stage of identification of a drug that can alter the path of a disease. The road from drug screening to a commercialized therapy is long, windy and very costly. As the Alzheimer's disease field advances, we try to make more educated and accurate drug predictions—for example, looking at drugs that have been successful in other related diseases. We hope that our work will shed light toward faster development of a cure.

My Inspiration
It is teamwork and I am lucky enough to be surrounded by amazing colleagues.

My Motivation to Research Alzheimer's Disease
Our mind is what makes us human.

My Personal Connection to Alzheimer's Disease
On my paternal side I have a strong connection to dementia. My maternal grandmother and one of her sisters had it and now one of my uncles does as well.

Most Exciting Career Moment to Date
With the help of a few technicians, we were able to screen a collection of 803 compounds on three different assays.

Biggest Unanswered Question in Alzheimer's Disease
How to prevent it.

What I Wish Most People Understood About Science
Science is driven by passion and requires a lot of commitment in terms of time, patience and effort. Once a question is answered, it is time to tackle the next one.

Outside of Work, I Like...
Traveling, art, going to see any type of performance, spending time with my family.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
The lab was able to work on several innovative projects thanks to Cure Alzheimer's Fund and decide whether they were worthy of pursuing further.

David Holtzman, M.D.

Andrew B. and Gretchen P. Jones Professor; Professor of Developmental Biology; Associate Director of the Knight Alzheimer's Disease Research Center; Scientific Director of the Hope Center for Neurological Disorders, Washington University School of Medicine in St. Louis

Born and raised in St. Louis, Dr. David Holtzman's passion for the sciences drew him to medical school, where he graduated from Northwestern University at the age of 23, followed by postgraduate work at the University of California, San Francisco. "They had a great clinical and research program and I had the opportunity to work with people who were doing cutting-edge research in neurology. The logic of the anatomy of the nervous system was really compelling—it's the one field where there's still not a lot of understanding and not great treatments, yet has some of the most important diseases in humans, including Alzheimer's," Dr. Holtzman says.

After a decade on the West Coast, Dr. Holtzman returned home to continue his research on Alzheimer's disease. "The opportunity was appealing because of Washington University's Alzheimer's disease research center, its Department of Neurology and its superb neuroscience community," he says. At the same time, some of his family members began to develop the disease he was studying. "My great aunt had died of Alzheimer's and lived almost 20 years with it. My father's brother and sister, and finally my father, all became symptomatic—my dad at age 71. He died 10 years later."

For more than 25 years, Dr. Holtzman has been a leader in Alzheimer's research as well as a practicing neurologist. His patients have provided an expanded understanding of the disease. "I've always made sure that if I'm going to study something, it should be directly relevant to what's going on in human beings," he says. "That has led directly to some of our unique findings." Dr. Holtzman co-developed with Dr. Randy Bateman a technique to determine the synthesis and clearance rates of proteins in the human brain. Dr. Holtzman also created a biobank of cerebral spinal fluid and plasma used to carry out a series of fluid biomarker studies. These studies demonstrated that measurements of certain proteins could be utilized to diagnose preclinical Alzheimer's disease as well as to predict who may become cognitively impaired. "Initially, this biobank was for my own research on APOE," he said, "but it burgeoned into a huge biomarker program."

Some of Dr. Holtzman's latest work focuses on how sleep influences Abeta metabolism. "We found that, in the brains of animals and humans, Abeta is regulated by neuronal activity," he says. "The levels of Abeta fluctuated during the day and night. During wakefulness, the levels of protein were higher than when sleeping, and if an animal was sleep-deprived, it caused a much earlier onset of Abeta deposition in the brain. This suggests that if you optimize non-REM (deep) sleep, it might delay the onset of Alzheimer's disease. But once you get the pathology, it further disrupts your sleep."

Filip Swirski, Ph.D.

Arthur and Janet C. Ross Professor of Medicine (Cardiology), Professor of Diagnostic, Molecular and Interventional Radiology, Icahn School of Medicine at Mount Sinai; Director of the Cardiovascular Research Institute

> "Science is difficult and a scientist encounters many failures. But the successes are worth the effort and the disappointments along the way."

My Research

We try to understand how the various systems in the body talk to each other. There is the nervous system, which is composed of the brain and spinal cord. There is an immune system, which defends us against infection. There is a metabolic system. All of these systems work together. Understanding how they work together will allow us to better understand, and cure, diseases.

We are studying how cells in the brain communicate and contribute to or prevent Alzheimer's disease. We perform fundamental studies to better understand how Alzheimer's disease develops at the tissue, cellular and molecular scales. By doing so, we are identifying potential new treatment targets.

My Inspiration

The mystery of biological systems. The process of discovery is most exciting.

My Motivation to Research Alzheimer's Disease

I have already worked on a chronic disease (atherosclerosis, the lipid-driven inflammatory disease that causes heart attacks and strokes). I recognized that atherosclerosis and Alzheimer's disease share some mechanistic links that might be worth investigating. Alzheimer's is an important disease to study, and there is great promise in better understanding the role of the immune system and inflammation in Alzheimer's disease pathology.

Most Exciting Career Moment to Date

The most exciting moments are those little discoveries that take place over years, and that can eventually add up to a larger discovery that's published as a paper. In many ways, the most exciting moments are the little moments.

Biggest Unanswered Question in Alzheimer's Disease

Etiology. We really do not yet know what causes Alzheimer's disease. We know a lot about how the disease manifests. We know that it is a neurodegenerative disease that typically affects people later in life. But we do not know what causes it, and therefore we cannot predict who will and who will not suffer from it.

What I Wish Most People Understood About Science

Science is a beautiful pursuit. As a scientist, you are generating knowledge. There is great responsibility to that. Science is difficult and a scientist encounters many failures. But the successes are worth the effort and the disappointments along the way.

Outside of Work, I Like...

I am a lifelong runner. Four years ago, I took up piano. It's important to keep the body and mind occupied and healthy!

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund has been very important for us. Without the support of the foundation, it is unlikely that we'd be working on Alzheimer's disease.

→ RESEARCH MILESTONES

BRAIN VASCULATURE DYSFUNCTION AND NEURODEGENERATIVE DISORDERS

Lab studies show that amyloid plaques and tau lead to blood vessel abnormalities and a breakdown of the blood-brain barrier and precedes the full pathology of Alzheimer's disease.
—Berislav Zlokovic, M.D., Ph.D. [bit.ly/3C3T3pU]

Jean-Pierre Roussarie, Ph.D.

Assistant Professor, Anatomy and Neurobiology, Boston University School of Medicine

My Research

We are trying to compare neurons that are dying very early on during Alzheimer's with neurons that are much more resistant. We think that if we understand the reasons for the vulnerability of these neurons, this will shine a spotlight on cellular mechanisms that are central in the degeneration process.

Once we find genes that drive the degeneration of vulnerable neurons, we then could target these genes with drugs to counter neuron death. These drugs would need to be administered very early on in the disease, but could potentially save the precious neurons indispensable to forming new memories.

My Inspiration

When we observe the memory-forming neurons of mice, monkeys and humans under the microscope, the idea that we are looking at the neurons that are so central in forming traces of all individual experience is always mesmerizing to me. Working in the lab every day with a fantastic team of trainees to better understand these neurons and try to protect them is truly inspiring.

Most Exciting Career Moment to Date

Creating my independent laboratory at Boston University School of Medicine is the most humbling, intimidating but also exciting scientific endeavor I was ever confronted with.

Biggest Unanswered Question in Alzheimer's Disease

The events occurring downstream of amyloid plaque deposition and glia activation are very largely unknown. In particular, why neurons accumulate neurofibrillary tangles and degenerate, and why this happens only in memory-forming neurons, is still a mystery. The consequence is that there is a whole set of molecular events that would be excellent therapeutic targets that still escapes our understanding.

What I Wish Most People Understood About Science

I wish the general public could have a sense of the temporality of basic research on Alzheimer's disease. The disease is so complex, and the cells that take part in the disease so diverse, that basic research inevitably goes slower than the general public knows. But at the same time, the current approaches to tackle the disease are so creative and the current technologies in molecular neuroscience so empowering that we seem closer than we ever were to understanding the disease, and landing meaningful therapeutic interventions.

Outside of Work, I Like...

I love classical music in general and opera in particular. I also love singing (poorly) by myself or in a choir.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Support from Cure Alzheimer's Fund is absolutely crucial to my work; I am trying to understand how the genetic susceptibility factor APOE influences neuronal vulnerability. Thanks to Cure Alzheimer's Fund, I got to be embedded in a group of amazing scientists led by Dr. David Holtzman working on different facets of APOE research, which nurtured my project in a tremendous way.

Roussarie Lab members. Back row, from left: Myles Joyce, JP Roussarie, Han Kahvecioglu. Front row, from left: Manas Dhanuka, Ana Morello Megias, Emily Yang, Irena Feng.

Meike Vernooij, M.D., Ph.D.

Neuroradiologist, Head & Neck Radiologist; Professor of Population Imaging at the Departments of Radiology & Nuclear Medicine and Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands

My Research
I study how the brain ages and whether we can better understand diseases like dementia by using brain scans in aging populations. My research leads to more insight in disease etiology (causes of disease), which ultimately can help find targets to intervene upon before people actually develop disease.

My Inspiration
My work as a neuroradiologist makes me passionate about using images to pinpoint disease processes or their sequelae, like a detective.

My Motivation to Research Alzheimer's Disease
I have always been intrigued by how the brain works and what happens when it dysfunctions. During my Ph.D. studies, I had the quote "If the brain would be so simple that we could understand it, we would be so simple we couldn't" on my door, to remind me of how complex this organ is and how we should actually cherish the difficulty to understand it, as it also makes us who we are.

My Personal Connection to Alzheimer's Disease
My grandmother suffered from Alzheimer's disease (AD) and in my patient-based work as a clinical neuroradiologist I read scans of patients visiting the memory clinic. Learning their stories, which brought them and their loved ones to seek help, always deeply affects me. I hope we can reduce their burden someday through our research.

Most Exciting Career Moment to Date
My first Ph.D. student successfully defending her thesis, as it symbolized my ability to let others grow through my skills and knowledge, and in that way to enlarge our ability to together tackle this field with its pressing questions.

Biggest Unanswered Question in Alzheimer's Disease
What causes AD?

What I Wish Most People Understood About Science
That research often doesn't give fast answers, but if done correctly it will hopefully give answers that are useful.

Outside of Work, I Like...
I have a 2-year-old daughter who takes up most of my free time nowadays, and I greatly enjoy spending time with her. If I have time outside of my role as a mother, I enjoy reading fiction, and I love the outdoors (hiking, skitouring, alpinism).

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
The Cure Alzheimer's Fund funding we acquired earlier this year will help us join forces in two research fields, my own on population neuroimaging and that on vascular imaging by my colleague, Dr. Daniel Bos. It enables us to study how vascular arteriosclerosis affects neurodegenerative processes such as amyloid brain pathology.

Jeffrey N. Savas, Ph.D.

Assistant Professor, Department of Neurology, Northwestern University, Feinberg School of Medicine

My Research

We study the pioneering changes that occur in the brain during the earliest stage of mild cognitive impairment and Alzheimer's disease. We are particularly interested in determining the mechanisms that initiate the long and gradual process that ultimately culminates as impaired cognition. To kick-start these efforts, we search for proteins that are not properly degraded in Alzheimer's disease model mouse brains, and work to apply and develop strategies to minimize these defects.

Our research philosophy is that if we can prevent amyloidogenic processing of the amyloid precursor protein (APP), then we can prevent the production of amyloid beta peptides and the downstream associated pathology. Our current interest is focused on modulating vesicle dynamics in axon terminals using the FDA-approved small molecule levetiracetam, which is currently the subject of several ongoing clinical trials based on other studies showing that it can reduce circuit hyperactivity. What's new about our finding is that we found that chronic administration of levetiracetam can reduce amyloid beta levels and the amyloid plaque load by restoring nonamyloidogenic processing of APP.

My Inspiration

The thrill of scientific discovery.

My Motivation to Research Alzheimer's Disease

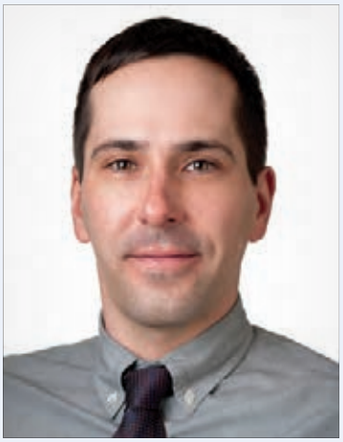
I am drawn to study Alzheimer's disease based on the fact that it is a proteopathy and I am crazy about proteins.

My Personal Connection to Alzheimer's Disease

My grandfather, Walter Thayer, had dementia.

Most Exciting Career Moment to Date

The identification of extremely long-lived intracellular proteins that in some cases are as old as the organism itself.



Biggest Unanswered Question in Alzheimer's Disease

How do amyloid-dependent processes contribute to or trigger downstream accumulation of phosphorylated tau?

What I Wish Most People Understood About Science

Most experiments are inconclusive.

Outside of Work, I Like...

Playing tennis and spending time with my two young daughters (4 and 6 years old).

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

The support from Cure Alzheimer's Fund has been tremendous because it has allowed me to explore high-risk aspects of our research on Alzheimer's disease, and has provided an opportunity to increase my professional network.

Members of the Savas Lab, from left: Timothy Hark, Nalini Rao, Miguel Ramirez, Arun Upadhyay, Jintao Yu, Seby Edassery, Stephanie Ellwood, Jeff Savas, Yi-Zhi Wang, Ewa Bomba-Warczak.

Ronald Schnaar, Ph.D.

John Jacob Abel Professor of Pharmacology and Professor of Neuroscience, Johns Hopkins University School of Medicine

My Research

Alzheimer's disease is caused by the buildup of debris in the brain. The cells in the brain with the job of cleaning up debris are called microglia. We are seeking new ways to spur microglia to be more efficient in their job, clean up debris in their local environment and halt Alzheimer's disease progression.

If we discover molecules that enhance debris clearance by microglia, those molecules can be the basis for drug development.

My Inspiration

Every day is a new mystery with new clues, in the way of data. Finding these clues and putting them in the context of human disease is a daily inspiration.

My Motivation to Research Alzheimer's Disease

We had discovered molecules that regulate immune diseases in human airways. Other scientists reported that the molecules we were studying are genetic predictors of Alzheimer's disease susceptibility, so we turned our attention to Alzheimer's disease.

My Personal Connection to Alzheimer's Disease

My paternal grandmother suffered from dementia in the 1950s. At that time, she was called senile—believed to be a common effect of "old age," and she was said to have "hardening of the arteries." We have come so far in understanding Alzheimer's disease since then. The next steps to the cure will put those old concepts away for good.

Most Exciting Career Moment to Date

Data drives my excitement in my work. Every day has new data, but every once in a while data emerges that are so novel, so clear and so instructive that it takes one's breath away.

Biggest Unanswered Question in Alzheimer's Disease

Putting together all of the steps in Alzheimer's disease progression, from misfolded proteins to cognitive decline, remains a challenge. The more we know about the pathological pathway, the better we can design ways to alter disease outcomes.

What I Wish Most People Understood About Science

"…it will always be a caprice of chance or fortune or of intuition that decides which investigator gets into his hands the substances which turn out to be the very best materials for fighting the diseases…But the chances in favour of finding a real cure, and so of winning the big prize, will naturally rise with the number of those who occupy themselves with the definite problem." —Paul Ehrlich, 1913

Outside of Work, I Like…

Vacationing with family—my spouse, my children and their spouses, and my grandchildren—is a real joy. We are outdoor people and love hiking, water sports and especially being together.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

We are working hard to build a context for understanding the factors that lead to Alzheimer's disease susceptibility and protection from Alzheimer's disease. Without Cure Alzheimer's Fund support, that effort would stop in its tracks.

Roberto Malinow, M.D., Ph.D.

Shiley Endowed Chair in Alzheimer's Disease Research; Distinguished Professor of Neurobiology and Neurosciences, University of California, San Diego

Dr. Roberto Malinow of the University of California, San Diego, has always felt at home in a lab. As a child, Dr. Malinow remembers his father was always very excited about his work. "He would say things like, 'I'm thinking about this great experiment.' Then he would draw graphs and make predictions." That's how Dr. Malinow was introduced to the world of science. Dr. Malinow attended a lecture by Rodolfo Llinas on synapses while at New York University Medical School. After that, he was hooked on the subject.

Dr. Malinow's father was diagnosed with Alzheimer's disease at the age of 84. "I had been trained as a doctor so I knew about the disease, but I hadn't ever experienced it firsthand," says Dr. Malinow. "My mother, who was very gregarious and loving, took care of my dying father on her own at home for four years, and then with full-time help until he died three years later. She was pretty heroic.

"Historically, I've always worked on synapses. I find them beautiful and I love studying them. Some of the earliest signs of Alzheimer's are at synapses, so we've looked at what might be happening there," says Dr. Malinow. For instance, when you learn, it is thought that some synapses get stronger and some weaker. "We think that Alzheimer's hijacks the normal process of synaptic weakening (which has been rigorously elucidated) and makes some of the synapses too weak," he said.

Overall, Dr. Malinow is trying to understand how some of these normal processes go into overdrive and contribute to the disease. "Science can be very hard, and often you just have to plug away and persevere."

Subhash Sinha, Ph.D.

Assistant Professor of Research Neuroscience, Weill Cornell Medicine

My Research

My research focuses on identification and development of small molecules, both synthetic compounds and semisynthetic natural products, to treat Alzheimer's disease (AD). We have developed several compounds, including Gleevec analogs and oleanolic acid derivatives, that reduce amyloid-beta production through inhibiting and modulating b-secretase and g-secretase cleavages of amyloid precursor protein. Additionally, we are developing compounds to inhibit tauopathy through blocking tau secretion and spreading and neuroinflammation through modulating microglial targets of interest. One of the microglial targets is a sialic acid binding protein (Siglec) that functions through inhibiting microglial uptake and degradation of amyloid beta aggregates. Another microglial target is a cyclic dinucleotide synthase that modulates release of pro-inflammatory proteins and causes toxicity to neurons. Both targets are overexpressed in microglia in AD brains.

Identification of true and potent inhibitors will allow us to further explore and validate the druggability of the targets. Once potent lead hit compounds are identified, such compounds can be tested in animal models of Alzheimer's disease. If found effective in ameliorating memory and cognition, such compounds can proceed to further optimization and into clinical trials for Alzheimer's disease treatment.

My Inspiration

I am inspired by all who work for the betterment of society at any levels. As a scientist, I have greatly been inspired by my postdoc supervisor, Dr. Ehud Keinan of Technion, Israel, and his dedication to solve a burning scientific problem. At work, performing experiments and the results of the experiments inspire me the most, both if the results hold true to my expectation or not. I love to work on collaborative projects.

My Motivation to Research Alzheimer's Disease

I started collaborating with (the late) Dr. Paul Greengard on two Alzheimer's disease projects while I was working at The Scripps Research Institute. My interaction with Dr. Greengard and learning there is no treatment of Alzheimer's disease motivated me to work in this area. The following year I moved to The Rockefeller University to work full time on Alzheimer's disease drug discovery projects.

Most Exciting Career Moment to Date

My most exciting moment of my scientific career has been when we developed chemically programmed antibodies using monoclonal aldolase antibody and small molecule inhibitors to treat human diseases. An equally exciting career moment is my joining The Rockefeller University to collaborate and work with Nobel laureate Dr. Paul Greengard. This led to my career focused on drug development to treat AD and other neurodegenerative diseases.

Biggest Unanswered Question in Alzheimer's Disease

As a medicinal chemist, I find lack of specific targets for therapeutic intervention. Most known targets of interest still remain in discovery and target validation phase, and targeting the very obvious targets, such as beta- and gamma-secretase, has not been successful.

What I Wish Most People Understood About Science

I would say working in science is inventing and reinventing things and knowledge that may or may not exist, but we are not aware of. Scientists work in many ways; all science relies on what is known and testing ideas/hypotheses based on known facts that are gathered over years of hard work by scientists, performing experiments and making observations to check whether the ideas/hypotheses hold true.

Outside of Work, I Like...

Walking, reading the news and journals, and watching comedy TV shows and films.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

In the past, I have been an investigator on proposals funded to Dr. Paul Greengard, and later I received independent funding to identify CD33 inhibitors. Cure Alzheimer's Fund support allowed me to build my career in the Alzheimer's disease field and collaborate with top scientists in the field.

DID YOU KNOW?

In 2004—the first year of CureAlz—$100,000 was distributed in total to research, representing a single project.

Helene Benveniste, M.D., Ph.D.

Sunil Koundal, Ph.D.
TEAM MEMBER

Hedok Lee, Ph.D.
TEAM MEMBER

Zachary Gursky, Ph.D.
TEAM MEMBER

Helene Benveniste, M.D., Ph.D.

Professor of Anesthesiology, Yale School of Medicine

My Research

We investigate the ability of the brain to "wash" itself, which has important implications for overall brain function and health. Uncovering the drivers of "neurofluid" circulation in the brain that is critical for waste clearance will help understand how waste such as amyloid beta and tau builds up in Alzheimer's disease. Once we define these drivers, we can develop therapeutic strategies to sustain it throughout the given life span.

My Inspiration

Working with a multidisciplinary group of scientists focused on a common research goal. Being part of a consortium and learning from each other. Learning by also training the next generation of scientists and having the privilege to watch them succeed.

My Motivation to Research Alzheimer's Disease

I trained as a physician scientist in anesthesiology with focus on neuroanesthesiology. I was keenly interested in "brain states" (i.e., consciousness, unconsciousness), which I encountered daily as an anesthesiologist. I was also intrigued by noninvasive imaging techniques for diagnosing brain diseases. I received a Paul Beeson Fellowship to study the aging brain and develop imaging tools for detecting amyloid beta plaques in human post-mortem brain samples using high-resolution MRI, then using this approach to further develop in vivo diagnostics.

My Personal Connection to Alzheimer's Disease

Yes, I have close colleagues and friends who have developed Alzheimer's disease.

Most Exciting Career Moment to Date

To become involved in the field of "neurofluids" and "glymphatics" and beginning to understand the connections to the lymphatic system outside the central nervous system.

Biggest Unanswered Question in Alzheimer's Disease

Defining the pathophysiological role of cerebrovascular disease for development of sporadic Alzheimer's disease.

What I Wish Most People Understood About Science

The time it takes to sustain funding for the research work and the importance of "investing" in developing new technologies (e.g., imaging, computational science/mathematics) that do not necessarily immediately contribute to therapies for Alzheimer's disease.

Outside of Work, I Like...

Mostly spending time with my husband, family and friends. I love reading, biking and long hikes.

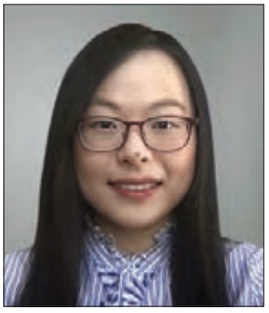
How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Without the support from Cure Alzheimer's Fund I would not have been able to further develop our imaging approaches to study the coupling of the glymphatic-lymphatic systems in Alzheimer's disease. Most importantly, I would not have been able to cross-fertilize my knowledge with expert scientists in alternate fields (e.g., neuroimmunology, blood-brain barrier, quantitative proteomics/biochemistry, genetics, microfluidics). This has fast-forwarded work in my lab as well as my trainees.

DID YOU KNOW?

In 2022, CureAlz reached the milestone of $150,000,000 distributed to research since inception, representing 670 projects.

Allen Tannenbaum, Ph.D.



Xinan Chen, Ph.D.
TEAM MEMBER

Allen Tannenbaum, Ph.D.

Distinguished Professor of Computer Science and Applied Mathematics & Statistics, Stony Brook University

My Research
I apply mathematical methods to various problems in neuroscience and in general medicine, including cancer and certain neurodegenerative diseases, including Alzheimer's. By studying fluid flows and waste clearance mechanisms in the brain, hopefully our joint research with the Yale group led by Prof. Helene Benveniste will impact treatments for the amelioration of symptoms and perhaps prevention of Alzheimer's.

My Inspiration
Trying to move my mathematics to the clinic.

My Motivation to Research Alzheimer's Disease
My work in glymphatics.

My Personal Connection to Alzheimer's Disease
An uncle by marriage suffered from the disease.

Most Exciting Career Moment to Date
Hard to say. Each time I learn something new and apply it, it rejuvenates me.

Biggest Unanswered Question in Alzheimer's Disease
The fundamental underlying causes seem to be still major issues of controversy.

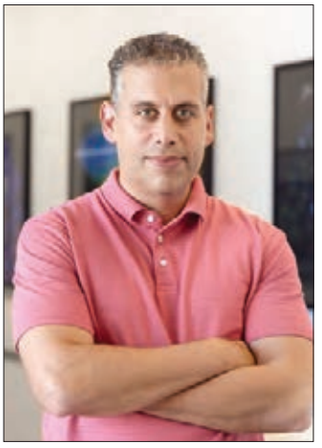
What I Wish Most People Understood About Science
It is a collaborative effort involving multidisciplinary teams of researchers.

Outside of Work, I Like...
Watching bad movies and body surfing in Far Rockaway.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
It has allowed me to support superb students and enriched my collaboration with Prof. Benveniste.

Scott J. Russo, Ph.D.

Professor of Neuroscience, Director of the Center for Affective Neuroscience and the Brain Body Research Center, Icahn School of Medicine at Mount Sinai



My Research
We study how stress contributes to the severity and progression of neurodegenerative diseases such as Alzheimer's disease. Our research aims to identify strategies that will mitigate the negative effects of stress on Alzheimer's disease pathology. In particular, we hope to identify drug targets to limit systemic inflammation and damage to blood vessels in the brain in order to treat, prevent or delay the progression of Alzheimer's disease.

My Inspiration
Working with an amazing group of very talented scientists that care deeply about helping people.

My Motivation to Research Alzheimer's Disease
My own familial history.

My Personal Connection to Alzheimer's Disease
Many of my immediate and extended family members have succumbed to the disease.

Most Exciting Career Moment to Date
Walking into my lab as a brand new assistant professor and wondering what major discoveries lie ahead.

Biggest Unanswered Question in Alzheimer's Disease
What are the respective roles of central (i.e., brain resident immune cells or microglia) vs. peripheral (i.e., monocytes and macrophages) immune cells in Alzheimer's disease pathology?

What I Wish Most People Understood About Science
How incremental science really is. Discoveries that lead to therapeutics may actually take several decades or more of incremental advances through basic science before they can actually benefit patients.

Outside of Work, I Like...
I very much enjoy gardening. It's peaceful—almost meditative.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
It has allowed me to move into brand new and exciting areas of neuroscience.

Liisa Galea, Ph.D.

Treliving Chair in Women's Mental Health, Centre for Addiction and Mental Health; Professor, Department of Psychiatry, Lead, Women's Health Research Cluster; University of Toronto, Canada

My Research

I study how sex hormones influence brain plasticity and memory in males and females, with a focus on dementia. Although sex differences exist in many brain diseases, research targeting sex as a factor in brain health has been scarce. My research is vital in filling this knowledge gap, specifically in understanding how sex and hormones influence neuroplasticity in females, as too often women's health is ignored in research. This preclinical work is essential for developing tailored treatments for brain disease in both women and men. For example, it is my suspicion that many drug or nondrug therapies have different effects in men versus women.

The goal of precision medicine is to have tailored treatment to each person. Focusing on sex is one part of precision medicine that has been largely ignored in the literature. Indeed, research does suggest that certain interventions may be more beneficial in women compared with men, and other therapies more beneficial in men than in women. Why not harness this information to get the best possible treatment for an individual? My research is studying how the plasticity in the brain is quite different in females than in males. While there are not a lot of differences in the end result (a reduction in brain volume), the pathways that males versus females use to get to this reduction are quite different—again suggesting different therapeutic pathways are needed. This is what drives my research.

My Inspiration

Working with the students in my lab, talking to other scientists, and making new discoveries and progress together. Learning from each other. I am NEVER bored. I also really enjoy talking to anyone with an interest in learning more about the brain. I am learning, too—it's great to be on this journey together.

My Motivation to Research Alzheimer's Disease

Because I am interested in why and how females have increased susceptibility to disease than males, I was really intrigued to learn that two-thirds of Alzheimer's disease (AD) patients were women. Why is that? Is it just because they live longer? Do we need to treat the disease differently if it manifests differently in men versus women? Then I realized that not many researchers took a careful look at the biological outcomes between males and females, and this was something that was important for me to dive into.

My Personal Connection to Alzheimer's Disease

Like many of us, my family has been touched by dementia. My mom suffered from dementia as a result of a combination of Parkinson's-like disease and chemotherapy. I was struck by how quickly the dementia set in.

Most Exciting Career Moment to Date

This is too hard to answer. I'll just say it's always joyful and exciting to see new data coming from the lab AND to see the students flourish with the joy of discovery.

Biggest Unanswered Question in Alzheimer's Disease

Biomarkers in middle age at a point where it might be better to intervene in AD are really important. What can we tell people to do at this crucial timepoint to protect their brain health? Is there a way to reverse the earliest stages of AD, and what biomarkers do we need to screen for to do this?

What I Wish Most People Understood About Science

It takes a village…and it can be slow work. The process of research and science is fraught with ups and downs. We are constantly revising our ideas (or we should be!) and we are constantly doing experiments to try to understand the disease better. Sometimes the experiments "work," and other times it leaves us scratching our heads. But sometimes those are the best discoveries, because it means how we thought the brain works (our hypothesis) was totally wrong and we need to revise our thinking to refine our new hypotheses. Experiments don't always work the way we want them to, and it can be slow and tedious—but when we have that aha moment…there is nothing like that in the world. It's like when those pieces of the puzzle start fitting together. But it will frustrate you as well—Vitamin D is good for you, Vitamin D is bad for you—so making sense of all the noise is part of the process and can be frustrating. A word of caution that I think most understand now is that there is misinformation out there and that even scientists get things wrong. That's OK; the whole process of science is failures and wrong turns so we can self-correct and get to that eureka moment, but it does take time and reflection. The process of scientific discovery is slow and tedious, but worth every moment.

Outside of Work, I Like…

I am very proud of my Estonian/Maltese heritage and specialize in baking Estonian Kringle. I am most proud of my two greatest accomplishments, my now adult children, to whom I have passed on my love of science and cookie dough. Right now, I live in North Vancouver, British Columbia, Canada, and enjoy trail hiking with my very bad dog, and then snuggling with the cat and dog after work.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

It allowed me to mobilize quickly to buy new equipment, obtain new models and to employ a team of young scientists. In short, these funds accelerated discovery in the type of research we do, speeding up to find answers to the questions we are asking.

Howard L. Weiner, M.D.

Robert L. Kroc Professor Of Neurology, Harvard Medical School; Chief, Division of Multiple Sclerosis and Neuro-Immunology, Department of Neurology; Co-Director, Ann Romney Center for Neurologic Diseases, Brigham and Women's Hospital

Laura M. Cox, Ph.D.

Assistant Professor, Neurology, Ann Romney Center for Neurologic Diseases, Harvard Medical School, Brigham and Women's Hospital

Drs. Laura M. Cox and Howard L. Weiner

Our Research
We are studying the way in which the gut microbiome (the trillions of bacterial in the gut) affect the brain and disease process in Alzheimer's disease (AD). We hope to find beneficial bacteria that could then be given to prevent or treat AD. It would be a novel, nontoxic form of therapy.

Our Inspiration
The chance to help people with the disease.

Our Motivation to Research Alzheimer's Disease
It is one of the major unanswered health problems in society and it affects so many people and their families.

Our Personal Connection to Alzheimer's Disease
We both had family members affected by Alzheimer's disease—Dr. Weiner's mother and Dr. Cox's grandmother.

Most Exciting Career Moment to Date
Developing treatments for neurologic diseases.

Biggest Unanswered Question in Alzheimer's Disease
How the immune system and the gut interacts with the brain in Alzheimer's disease.

What We Wish Most People Understood About Science
How exciting it is to be a scientist and how hard it is—and how much time it takes time to uncover the secrets of nature.

Outside of Work, I Like...
Dr. Weiner is interested in film and made a Hollywood film starring Martin Landau and Paul Sorvino that premiered at the Tribeca Film Festival called "Abe and Phil's Last Poker Game," in which one character had Alzheimer's disease.

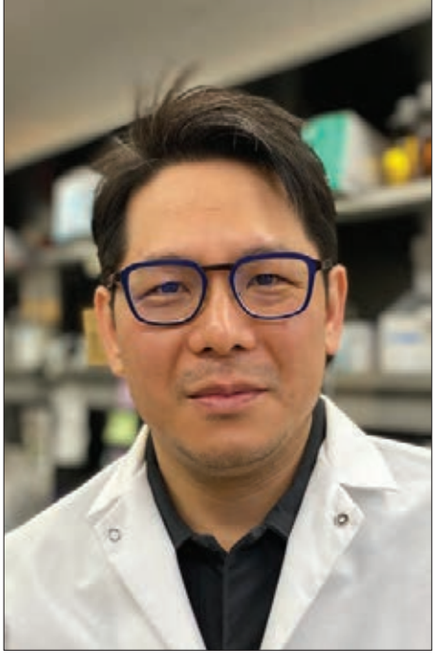
How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
It has provided inspiration for us to keep going in the face of such a difficult problem, and has provided the resources to do our exciting work.

The team investigating how the microbiome modulates innate immunity and Alzheimer's disease. Front, from left: Laura M. Cox, Caroline C. Wasen (postdoctoral). Middle row, from left: Millicent Ekwudo (technical research assistant), Ella Simonsen (undergraduate). Back, from left: Martin Profant (summer student), Christin Chen (technical research assistant).

RESEARCH MILESTONES

MOUSE MODELS

In 2014, CureAlz devised a system for developing mouse models to be provided to all researchers in the field supporting needed studies specific to Alzheimer's disease.
—Wilma Wasco, Ph.D. [bit.ly/3SAP9eG]



Andrew S. Yoo, Ph.D.

Professor, Department of Developmental Biology, Washington University School of Medicine in St. Louis

My Research

We use genetic tricks to turn human skin cells into neurons, a process called direct neuronal conversion (or reprogramming). My lab specializes in using small RNA molecules called microRNAs as reagents that can trigger neuronal conversion. Because direct conversion propagates cellular age stored in starting fibroblasts from human individuals of different ages, directly converted neurons allow us to investigate how aging of neurons contributes to the onset of neurodegeneration in Alzheimer's disease (AD).

We would like to understand genetic networks that underlie aging and define ways to delay or reverse the aging process that may make aged human neurons resilient against neurodegeneration.

My Inspiration

Working with trainees who share the same scientific interests and endless discussions about addressing various research questions.

My Motivation to Research Alzheimer's Disease

I have been interested in understanding why humans become susceptible to developing Alzheimer's disease with aging. We are also inspired by the realization that we can study some of this process by cellular reprogramming.

Most Exciting Career Moment to Date

Remembering exciting moments about discoveries I made when I was a trainee, and seeing the same excitement from the trainees in my lab.

Biggest Unanswered Question in Alzheimer's Disease

Understanding what determines the onset of sporadic, late-onset AD.

What I Wish Most People Understood About Science

Understanding of scientific values of tissue sample donations and modern techniques in stem cell biology and cellular reprogramming that can move the field forward.

Outside of Work, I Like...

To listen to and play music.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?

Cure Alzheimer's Fund gave me intellectual freedom to explore research areas that may seem unconventional, and allowed us to test new experimental approaches.

→ RESEARCH MILESTONES

EXERCISE MAY PROTECT OUR BRAINS

Recent studies confirm that exercise is good for your heart—and your brain. For example, the results of several grants show that the hormone released during exercise, irisin, has beneficial impact to cognitive function, in the lab.
—Christianne Wrann, D.V.M., Ph.D. [bit.ly/3fkzHVx]

Alban Gaultier, Ph.D.

Associate Professor of Neuroscience, Director of the Neuroscience Graduate Program, Center for Brain Immunology and Glia (BIG), University of Virginia

My Research
Myelin, also known as white matter, is an essential brain structure that ensures proper neuronal function. Recently, increasing amounts of data have pointed to myelin disruption as a significant pathological finding in Alzheimer's disease patients, with the concept that myelin disruption is a key event that contributes to cognitive decline in Alzheimer's disease. This research is aimed at exploring the factors that contribute to the lack of white matter integrity observed in patients with Alzheimer's disease.

We hope that our research focused on myelin decay in Alzheimer's disease will offer new solutions to promote neuroprotection and delay the irreversible cognitive decline currently facing Alzheimer's disease patients.

My Inspiration
My group's goal is to make basic discoveries that can help the patients. We are a translational neuroscience lab that focuses on myelin repair and the microbiome.

My Motivation to Research Alzheimer's Disease
The lack of treatment for patients and the incredible impact on caregivers.

My Personal Connection to Alzheimer's Disease
My grandmother had dementia and it was heartbreaking to see the irreversible loss in cognition happening!

Most Exciting Career Moment to Date
Each time we make new discoveries. Our current work on repairing myelin in Alzheimer's disease models is exciting and novel.

Biggest Unanswered Question in Alzheimer's Disease
We need to start thinking differently about Alzheimer's disease; the current research focused on tau and Abeta has not translated to treatment. Exploring the role of the immune system, glia and the microbiome are the next frontiers (to me) for researchers.

What I Wish Most People Understood About Science
Being a scientist is not a job, it's a passion—the discovery of novel knowledge is exhilarating. Being a scientist is being resilient, because we fail more than we succeed. Foundations such as Cure Alzheimer's Fund let us express our scientific creativity!

Outside of Work, I Like...
I love biking and camping in beautiful Virginia.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
The support of Cure Alzheimer's Fund allows us to focus on important research immediately, without wasting time applying for hard-to-get NIH grants.

"Being a scientist is not a job, it's a passion—the discovery of novel knowledge is exhilarating. Being a scientist is being resilient, because we fail more than we succeed. Foundations such as Cure Alzheimer's Fund let us express our scientific creativity!"

Christiane Wrann, D.V.M., Ph.D.

Assistant Professor in Medicine, Affiliate of the Harvard Stem Cell Institute (HSCI) Cardiovascular Research Center (CVRC), McCance Center for Brain Health, Massachusetts General Hospital

My Research
We aim to understand how exercise protects your brain against Alzheimer's disease (AD) on the molecular level. The goal is to develop these exercise mediators into drugs for AD prevention or therapies.

My Inspiration
The possibility to actually change patients' lives/outcomes.

My Motivation to Research Alzheimer's Disease
It is one of the hardest problems.

Most Exciting Career Moment to Date
The discovery that our exercise hormone irisin could indeed be an AD drug target.

Biggest Unanswered Question in Alzheimer's Disease
Which is the best pathway to target for new drugs and is it the same for everyone? How much precision medicine is needed?

What I Wish Most People Understood About Science
That science is a slow, methodological process by nature but does have the potential to transform lives (cue the COVID-19 vaccines).

Outside of Work, I Like...
I enjoy spending time with my family and hiking in beautiful New England.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
Cure Alzheimer's Fund saw the potential of our work early on and continues to support our work while we are striving to get the NIH/federal funding.

→ DID YOU KNOW?

Peer-reviewed, CureAlz-supported papers in high-impact science journals have been cited more than 72,000 times.

Members of the Wrann Lab.

Riqiang Yan, Ph.D.

Professor and Chair, Department of Neuroscience, University of Connecticut Health Center

My Research
The research in my lab is aimed to identify pathological and functional deficits associated with early cognitive dysfunction and dementia in Alzheimer's patients, and to develop drugs that will help patients to decrease pathological developments and to improve their learning and memory, as well as other cognitive functions.

We mainly use mouse models for studying molecular mechanisms underlying the disease progression, and to test potential therapeutic efficacies by our laboratory-developed compounds.

My Inspiration
Discovery of Alzheimer's beta-secretase inspires me to find optimal inhibitory molecules that can be safely used for Alzheimer's disease treatment.

My Motivation to Research Alzheimer's Disease
With the increase of life expectancy, it is unavoidable to see an increase of elderly individuals suffering from Alzheimer's disease. There is an urgency for having more scientists, who have solid training backgrounds and diverse skill sets, to devote their efforts in combating this disease. I am motivated to conduct research in Alzheimer's disease due to my strong interests to find protease targets for Alzheimer's disease treatment.

Most Exciting Career Moment to Date
Engaging students and colleagues to devote their efforts in Alzheimer's research—their important and novel discoveries excite me a lot. Our recent finding of BACE1 deficiency in glia cells opens new strategy for drug discovery.

Biggest Unanswered Question in Alzheimer's Disease
It is still quite intriguing as to why drugs targeting reducing amyloid deposition have not shown clear improvement in Alzheimer's disease patients' cognitive functions.

What I Wish Most People Understood About Science
The knowledge gained in animal studies is essential for ultimate drug discovery, and many therapeutic targets are needed to be first tested in animals.

Outside of Work, I Like...
Hiking and travel.

How Has the Support of Cure Alzheimer's Fund Made a Difference to Your Work?
The support from Cure Alzheimer's Fund allows us to test hypotheses that are likely high risk and potentially high reward.

Dora M. Kovacs, Ph.D.

Associate Investigator, Neurology, Mass General Research Institute; Associate Professor of Neurology, Harvard Medical School; Research Staff, Neurology, Massachusetts General Hospital

Dr. Dora Kovacs always had a passion for science. Born in communist Hungary in the city of Budapest, Dr. Kovacs' mother was an entomologist who introduced her daughter to the world of science. When Dr. Kovacs was 12, her family moved to Bologna, Italy. "Everything was brighter there and the leather shoes were softer," she says. "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 summer internship. "All my other friends in Italy were spending their time at the beach, but I felt lucky to be growing bacteria."

Dr. Kovacs earned a Ph.D. from the University of Padova. 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., "I interviewed with Rudy in 1993 when I accepted a position at Massachusetts General Hospital (MGH) in the Genetics and Aging Research Unit." Little did either know that years later they would get married.

Dr. Kovacs has co-authored more than 40 original articles and is a co-inventor on three patents. She 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."

Dr. Kovacs notes that "because NIH only covers part of my research expenses, funding from Cure Alzheimer's Fund is essential to my work."

Drs. Kovacs and Tanzi were married in 2002 and have a daughter, Lyla. When not playing with their daughter, they are focused on their other greatest shared passion—finding a cure for Alzheimer's disease.

IN MEMORIAM

Over the years, we have lost CureAlz researchers who had dedicated their lives to Alzheimer's disease research.

Here is a tribute to some of these great pioneers whose work moved the science closer to finding a cure. Their contributions, and their friendship, will never be forgotten.

BEN BARRES, M.D., PH.D.

Stanford University
(1954–2017)

In an article published in 2018, The Atlantic described Dr. Ben Barres's work:
"While most of his fellow neuroscientists studied neurons, the branching cells that carry electrical signals through the brain, Barres focused his attention on another group of cells called glia. Even though they equal neurons in number, glia were long dismissed as the brain's support crew—there simply to provide nutrients or structural scaffolding. But Barres showed that glia are stars in their own right. They help neurons to mature, producing the connections that are the basis for learning and memory, and then pruning those connections so that the most useful ones remain."

Dr. Barres forever changed our understanding of the brain. "The intellectual horsepower, innovative turn of mind and humanity Ben brought to some of the world's seemingly intractable medical mysteries had us all in awe. The world has lost an exceptional human being," said Tim Armour, President and CEO of Cure Alzheimer's Fund.

PAUL GREENGARD, PH.D.

The Rockefeller University, Nobel Laureate
(1925–2019)

Dr. Paul Greengard was a pioneer in understanding how brain cells communicate, and his work was rewarded with the Nobel Prize in Physiology or Medicine.

Cure Alzheimer's Fund was privileged to begin working with Dr. Greengard in 2006. So many of the researchers funded by CureAlz looked to Dr. Greengard for his expertise, but also for his willingness to be a mentor, as he truly was committed to the success of others. "Paul was clearly one of the greatest neuroscientists that ever lived; he was a true giant among all scientists," said Dr. Rudy Tanzi. "His legacy of brilliance, originality and unwavering curiosity about the brain, together with his incomparable degree of kindness, generosity and respect for everyone he knew, will be fondly remembered for a long time. While we have lost one of the greatest scientists who ever lived, there is no doubt that his lifelong body of work will inspire innumerable new discoveries for many decades to come."

ROBERT MOIR, PH.D.

Massachusetts General Hospital
(1961–2019)

Dr. Rob Moir was a brilliant scientist whose pioneering research led to a fundamental shift in the understanding of Alzheimer's disease. He challenged the conventional wisdom that the buildup of amyloid in the brain was intrinsically pathological and aided the development of Alzheimer's. While amyloid is understood to have a destructive role in the progression of Alzheimer's disease, Dr. Moir proposed that amyloid defended against toxicity by trapping harmful microbes. After a decade of rejection, Cure Alzheimer's Fund provided a grant to Dr. Moir, and his research results were published in Science Translational Medicine in 2016. His work was recognized as one of the top five discoveries in neurology for 2016. "Rob always thought outside of the box—he didn't even know there was a box!," said Dr. Rudy Tanzi. "He was a great, personal friend who never let anything stand in his way. He enjoyed life and always had a smile on his face."

STEVEN WAGNER, PH.D.

University of California, San Diego
(1958–2022)

After obtaining postgraduate degrees in microbiology and molecular genetics, Dr. Steven Wagner started his career studying Alzheimer's disease at the Salk Institute for Biological Studies. As a member of the team that identified amyloid precursor protein (APP), which has a pivotal role in the pathology of Alzheimer's disease, he established his importance in the field of research early in his career. An extremely warm individual who made those around him feel special, Dr. Wagner was genuine in his personal goal: to find a cure for Alzheimer's disease. "When it came to actually translating scientific research into new therapies that might help patients or even end Alzheimer's disease, once and for all, Steve was second to none," said his friend and colleague, Dr. Rudy Tanzi. Dr. Tanzi continued, "In 2000, Steve and I co-founded a company to develop a drug that is now one of the field's greatest hopes for stopping Alzheimer's disease. When we finally beat Alzheimer's disease, Steve will have played a major role."

Friends and Colleagues: Cure Alzheimer's Fund researchers, from left, Drs. Sam Sisodia, Rudy Tanzi, Steve Wagner, David Holtzman, Guojun Bu, Bob Vassar and Yueming Li celebrated Dr. Wagner's 60th birthday in Chicago in 2018. (Photo courtesy of Dr. Rudy Tanzi)

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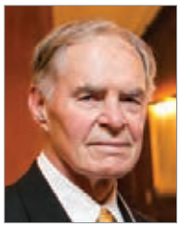

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You can donate directly from our website—please visit www.CureAlz.org/Donate.

MAIL

Please make your check payable to Cure Alzheimer's Fund and mail to our office at: Cure Alzheimer's Fund, 34 Washington St., Suite 310, Wellesley Hills, MA 02481.

TELEPHONE

If you would like to make a donation by telephone, please call us at 781-237-3800. Our business hours are 9 a.m. to 5 p.m. ET. When calling after hours, please leave a message and we will return your call the next business day.

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Donors with funds held by Fidelity Charitable, Schwab Charitable or Great Kansas Community Foundation may use the DAF Direct form on our website to process donations. For all other Donor Advised Fund holders, please mail checks to our office at: Cure Alzheimer's Fund, 34 Washington St., Suite 310, Wellesley Hills, MA 02481.

MONTHLY GIVING

We also offer the option of monthly giving through our online donation form, allowing you to select a specific gift amount for automatic, recurring contributions. Monthly giving is a powerful way to show your support for research to find a cure for Alzheimer's disease.

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We offer a number of planned giving options, some of which may offer tax incentives. These include:

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To explore these and other ways to give, please visit **www.CureAlz.org/Donate** or contact Laurel Lyle at **LLyle@CureAlz.org,** or call **781-237-3800.**

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