



FISHER CENTER FOR
ALZHEIMER'S
RESEARCH FOUNDATION



ANNUAL REPORT

2019

About

Fisher Center for Alzheimer's Research Foundation

In 1994, philanthropists Zachary Fisher and David Rockefeller partnered to establish the Zachary and Elizabeth M. Fisher Center for Research on Alzheimer's Disease at The Rockefeller University (The Fisher Center Lab) after Fisher's wife Elizabeth was diagnosed with Alzheimer's disease. In 1995, Mr. Fisher founded the Zachary and Elizabeth M. Fisher Center for Alzheimer's Research Foundation, whose mission is to raise funds to support the Lab. Each year, the Fisher Center Foundation provides millions of dollars for novel Alzheimer's research.

The Lab, whose original director was the late Nobel Laureate Dr. Paul Greengard, is one of the largest and best-equipped scientific facilities for Alzheimer's research in the country. It is currently directed by Dr. Marc Flajolet and his team of more than 40 internationally-renowned scientists who are working diligently to find the causes and cure for Alzheimer's disease.

Together, we can end Alzheimer's

CAUSES, CARE, CURE



"I know that an answer will not be found in time to help my beloved Elizabeth, but I want to do what I can to find a cure so that others will not have to suffer through the ravages of this disease as my wife and I have had to."

- Zachary Fisher

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Message from the Executive Director



Dear Friends,

As I reflect on the past two years, I'm proud to have served the late Nobel Laureate, Dr. Paul Greengard (2019); Board Trustee, Murray Rubin (2019); and President and CEO, Kent Karosen (2018). Their lives will forever be memorialized in their collective fight to end Alzheimer's disease. I am equally thankful for the 20,089 individuals, foundations, corporations and organizations who help make our work possible through their generous support.

Studies project that the number of Americans diagnosed with Alzheimer's disease will rise to 14 million by 2050, making it a critical public health concern affecting every gender, ethnicity, and socio-economic bracket. Government funding from the National Institutes of Health (NIH) for Alzheimer's research continues to lag significantly behind what is spent annually to research new treatments and discover a cure for other similarly wide-reaching diseases. Alzheimer's research remains urgent, as the disease continues to devastate families financially. As a caregiver and person who has loved ones with Alzheimer's, I am deeply passionate about the Fisher Center for Alzheimer's Research Foundation's mission of understanding the causes of Alzheimer's disease, improving the care of people living with it, and finding a cure.

I'm incredibly proud of the research and findings of our scientists, which would not be possible without the support of friends like you. Thank you.

Lucretia V. Holden, SHRM-CP

Mission & Vision

Fisher Center for Alzheimer's Research Foundation

The principal activity of the Fisher Center Foundation is to provide funding to the Fisher Center lab and faculty research at Rockefeller University. The lab is dedicated to solving the puzzle of Alzheimer's disease, and is considered by many to be a prototype for Alzheimer's research.

The Fisher Center Foundation curates the findings of scientists' research and provides national comprehensive public education and disease awareness through our Information Program. Our website, ALZinfo.org has a unique Resource Locator that allows visitors to input their zip code to pinpoint doctors, nurses, disease centers, elder attorneys, Medicare information, home health agencies and more. Our scientists answer questions through the "Ask the Experts" feature on our website; our free e-newsletter, *Alzheimer's Research News You Can Use*, is the most reviewed Alzheimer's and dementia newsletter on the internet; and caregivers can join our support group through our online Caregiver's Corner. Our 1-800-ALZINFO phone system assists people who do not have access to the internet.

Our award-winning triannual print publication, *Preserving Your Memory*, circulates 52,000 copies per issue and has reached 10.6 million people since its inception. The editorial content is reviewed by our scientific team for accuracy and validity as it addresses concerns of readers affected by the disease—whether caregiver or patient—and provides information about Alzheimer's treatment, care options, and how to take the necessary steps to adequately prepare if they, or someone they love, receive(s) an Alzheimer's diagnosis.

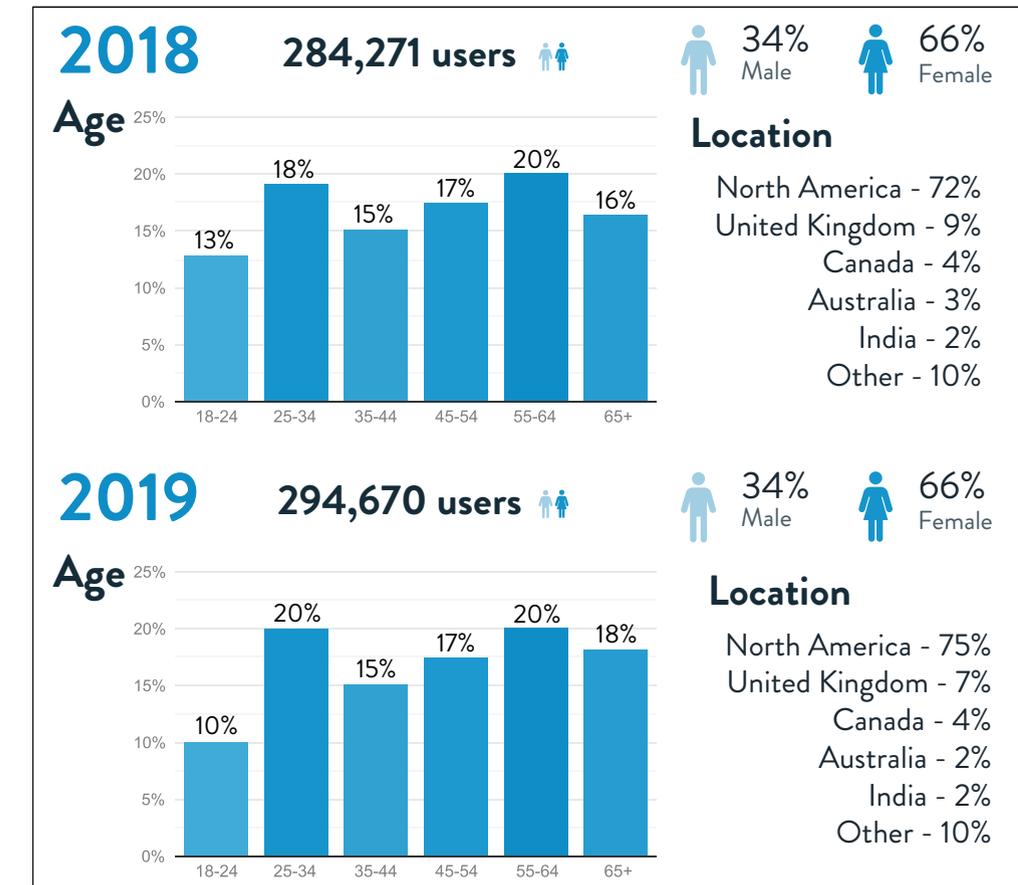
Our mission is to understand the causes of Alzheimer's disease, improve the care of people living with it, and find a cure.

Our vision is working towards a future when Alzheimer's is nothing but a memory.

Impact

This year we added more resources and content to our Information Program such as updated clinical stages, facts, statistics and expanded news articles. We've enhanced our website with more information, including how to tell the difference between Alzheimer's and Dementia, and a new graphic depicting the differences between a healthy brain and one with Alzheimer's. These adjustments helped push our organization to the forefront in the Alzheimer's community.

Website Traffic



Initiatives

- Increased the frequency of our newsletter distribution
- Created specific e-appeals around various holidays
- Strategized campaigns to draw in more donations, like our "Research the Causes" campaign for Giving Tuesday



facebook

In 2019 we had 7,295 fans with 147,625 impressions from our posts, a 16% increase from 2018.

Our Program Work

CAUSES

There are a number of contributing factors to Alzheimer's that the Fisher scientists are actively studying. Historically, the cause of Alzheimer's has been linked almost exclusively to the production of a toxic component that sticks together to form larger formations called amyloid plaques. The field has realized that many other biological processes could also cause Alzheimer's: inflammation in the brain, the loss of synapses, and cell signaling may also be contributing factors to the development of the disease.



CARE

Caregivers and family members face many challenges, both in adjusting to new roles and coping with the profound changes in a loved one. If you're facing this role, knowing what to expect can help you cope better. In turn, you'll be able to do the most good for your loved one. Our Information Program continues to spearhead efforts to increase awareness of, and education about, Alzheimer's disease to help you through this challenging time.

CURE

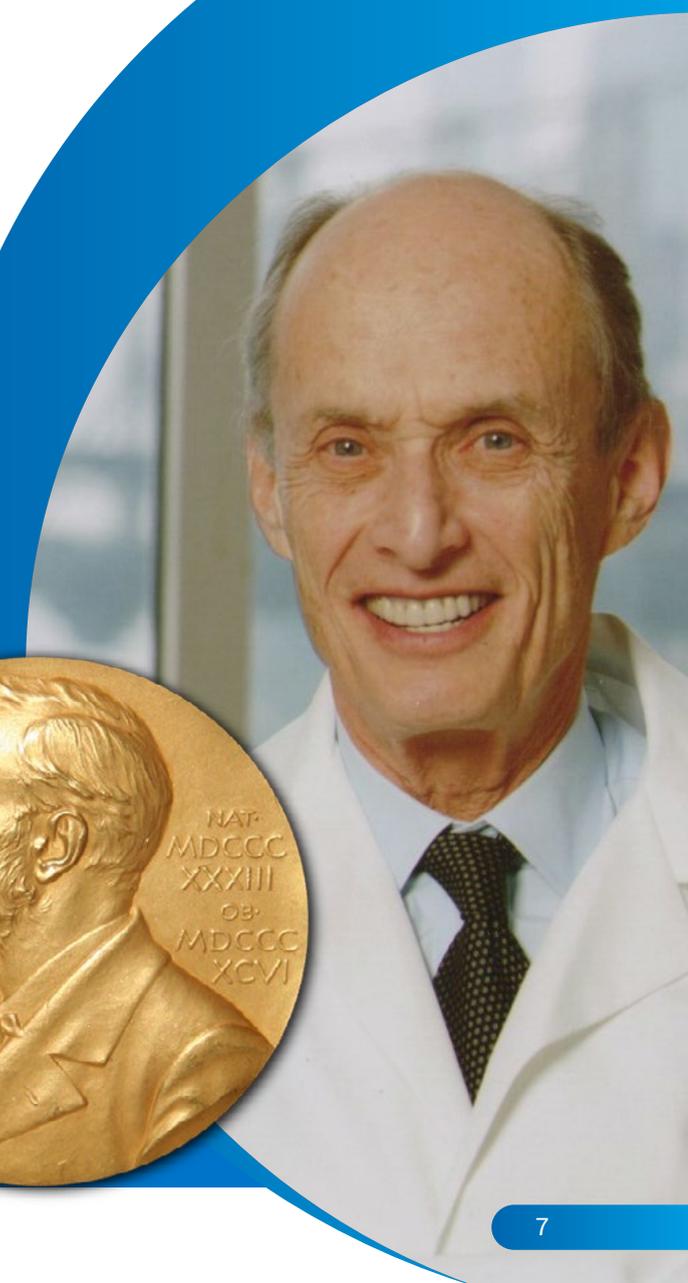
In the past, the strategy for a possible cure has been largely focused on reducing amyloid plaques, however, a number of novel therapeutic strategies are emerging. Currently, the Fisher Center scientists are prioritizing research on target proteins and neural pathways, based on their possibility of being used as a drug target for the cure. In addition, they're also actively performing drug screening and testing to find effective Alzheimer's drugs.

Paul Greengard Professorship

In 2016, the Fisher Center for Alzheimer's Research Foundation endowed the Paul Greengard Professorship to acknowledge Dr. Greengard's devotion to the best of science. The Fisher Center Foundation committed an endowment of \$5M to sustain the novel Alzheimer's disease research that was led by Nobel Laureate Dr. Paul Greengard in the Fisher Center on Alzheimer's Disease Research laboratory at The Rockefeller University.

"I am deeply honored by the creation of this professorship. I owe the Fisher Center Foundation a debt of gratitude for their wonderful generosity and long-standing support of our work on Alzheimer's disease."

-Dr. Paul Greengard
February 24, 2017



The Fisher Center Lab at The Rockefeller University

Over the years, a number of hallmarks strongly associated with Alzheimer's disease (AD) have been discovered. The two most prominent ones being the amyloid precursor protein (APP) and Tau. Other important aspects of the work involve the identification of the molecular mechanisms underlying vulnerability and resistance of neurons. Neurons are crucial for all cognitive functions.

One of the latest lines of research is centered on the use and development of a unique type of cell derived from Alzheimer's patients. These cells can be grown in culture to study the importance of various genes and signaling pathways, with the ultimate goal of building a much better tool for drug discovery.

New lab space has been upgraded and equipped with state-of-the-art equipment. The main activity of this new lab extension is to create an entirely novel drug discovery platform, one that is based on technology called DNA-Encoded Library or DEL. This presents many advantages compared to regular approaches.

Nine manuscripts were prepared, submitted or published this year and are at varying levels of advancement. A brief summary of the most recent findings (including the status of each manuscript) is presented below.

An APP cleavage product called C99 affects neurons of Alzheimer's patients

In a new study, the Fisher scientists provide evidence that C99 (a product of APP) could be responsible for the toxicity that leads to Alzheimer's, and are working on tools to better detect C99. If successful, this approach could bring a very important diagnostic tool to the clinic and should considerably help clinical trials and clinical developments, as well as drug efficacy evaluation. This study has been accepted for publication in the journal *Alzheimer's and Dementia* and was available online in September 2019.

Screening chemical derivatives of Gleevec

Fisher scientists have previously demonstrated that the cancer drug Gleevec, that was known to target certain proteins, has the capacity to lower beta-amyloid, the toxic component thought to lead to Alzheimer's. The original version of Gleevec was not extremely potent and was inefficient at accumulating in the brain. In order to optimize these key aspects, different pharmacological programs were put into place. Several publications have described this work in detail. This work was linked to other families of molecules, one called the "DV Program"

and another one focusing on the testing of natural compounds found in traditional Chinese medicine.

A manuscript related to this work was published in the *Journal of Medicinal Chemistry* (March 2019), and another manuscript about Chinese natural compounds has been prepared and submitted for publication.

Characterization of GSAP function

A few years ago, our scientists identified a protein, Gamma-Secretase Activating Protein (GSAP), that could bind Gleevec, making it more effective. Fisher scientists investigated the role of GSAP in three different ways:

1. The mechanism by which GSAP regulates activity has not been discovered. While removal of GSAP in cultured cells directly reduces activity for Abeta production, it does not affect other important areas. This year, this work has been published in the journal *Proceedings of the National Academy of Sciences (P.N.A.S.)*.
2. Another part of the work is dedicated to understanding the mechanism by which GSAP regulates APP.
3. Biochemical, cellular, pathogenic and human genetic data consistently demonstrate that GSAP plays essential roles in the development of Alzheimer's. Fisher scientists identified all of the proteins interacting with GSAP using global approaches, and report that GSAP regulates multiple Alzheimer's disease pathways. Two manuscripts were produced by the end of 2019, one for each of these last two points.

Understanding the vulnerability of specific neurons

The role of nerve cells (neurons) is important when talking about Alzheimer's disease, because of the way neurons communicate in the brain. The pathways that are important for learning and memory are made up of specific cells, some of which die off early in patients with Alzheimer's disease. Understanding why some cells die off early and others do not is critical to finding a cure. To address this problem, Fisher scientists are using a unique set of tools and technologies that they have developed over the past decade.



This very ambitious and unique body of work has been published partially in 2018 in *BioRxiv*. A more definitive manuscript has been prepared and submitted for publication to the journal *Neuron*. A number of experiments requested by the reviewers are being performed while the manuscript is being updated and should be resubmitted to *Neuron* in the first half of the year 2020.

Regulatory role of accessory cells in the context of Alzheimer's disease

Accessory cells (non-neuronal cells) in the brain play a crucial role in protecting the neurons, feeding them (astrocytes) and also cleaning and removing debris (microglia). The Fisher scientists are actively working on these two cell types, especially in the context of inflammation. Microglia cells (also known as scavengers) seek out damaged areas. Once activated, the microglia cells will engulf and digest anything that is dysfunctional, misshaped or dead, such as dead cells and neuronal debris, and also amyloid plaques.

The Fisher scientists studied the possibility of manipulating microglial Presenilin 1 (the main active component of an enzyme related to APP), targeting cells that lead to Alzheimer's disease.

Two manuscripts were prepared and submitted for publication; we are currently working on requested experiments and revising the manuscripts based on the reviewers' comments. One study is under revision for the journal *Molecular Psychiatry* and the other for *PLoS One*.

The construction of a novel drug discovery platform

Significant progress has been made in several directions. This effort is closely supervised by Dr. Marc Flajolet, a neuro-molecular biologist, and is centered on the revolutionary technology called DNA-Encoded Library (DEL).

This technology is revolutionary contrary to the regular approach (HTS) that typically test on average 500,000 molecules per screen over a period of several months using important resources (both human and financial) and real estate. The DEL approach can easily test 100 million compounds all at once in one tube and in just weeks. This effort should greatly accelerate the drug discovery rate and significantly increase the number of therapeutic targets that can be tested at the Fisher Center as well as in collaboration with other labs and institutions.

The Fisher Alzheimer's Education and Resources Program at NYU Grossman School of Medicine

The Fisher Alzheimer's Education and Resources Program at the NYU Grossman School of Medicine (formerly known as NYU School of Medicine) examined the health outcomes of the Comprehensive, Individualized, Patient Centered Alzheimer's Management Program. Specifically, scientists examined the effects of this program on anti-depressant usage and cost. A poster was prepared which Dr. Kenowsky will present at the Alzheimer's Association International Conference in July 2020. These results are under embargo until presented at the conference.

In addition, the relationship between behavioral disturbances and the progression of persons with subjective cognitive decline (SCD) was studied. Of the 73 people with SCD, the most commonly occurring behavioral symptoms were anxieties in 49.3%, sleep disturbances in 20.5%, tearfulness in 12.3% and verbal outbursts in 9.6%. The subjects were followed for approximately two years. The study found that the occurrence of behavioral disturbances is associated with subsequent mild cognitive impairment (MCI) or dementia -- acting as a harbinger of decline in persons with SCD. Dr. Reisberg presented these findings at the Alzheimer's Association International Conference in Los Angeles this year.



Brain and Spine Institute (ICM) Imagine Institute - Paris, France

Recent studies at the Brain and Spine Institute, Imagine Institute have focused on a drug (Masitinib) used for Mastocytosis, a disease associated with mast cell accumulation. Some Mastocytosis patients experience cognitive dysfunctions that mimic symptoms of Alzheimer's disease. A study has demonstrated that Masitinib improved symptoms of Mastocytosis — including those associated with neurological and psychiatric symptoms. In addition, a clinical study demonstrated that Masitinib slows down cognitive decline in Alzheimer's patients.

Project:

This project focuses on the role of mast cells and enzymes they produce in the development of Alzheimer's disease. A better understanding of the mechanisms of action underlying Masitinib's effect might allow us to define a strategy to improve Alzheimer disease. We investigated:

1. Whether the structure of Amyloid proteins is altered and if the toxic proteins are decreased after Masitinib treatment.
2. Whether Masitinib may improve synapse loss possibly by reducing Tau phosphorylation.
3. Whether a recent theory, suggesting that Alzheimer's might be due to "seeding spreading lesions" like prions diseases, is involved. Mast cells may help to propagate these lesions, and if true one can hypothesize that Masitinib may be beneficial by decreasing lesions dissemination.

Preliminary results:

A daily dose of Masitinib (75mg/kg) versus placebo was orally administered during two months in male mice modeling Alzheimer's disease as well as their control wild-type littermates. Cognition was assessed using a paradigm measuring learning and memory using a Morris water maze. Brain pathology was characterized by histological and biochemical measurements. Complementary analyses were performed using mice with a genetically induced depletion in mast cells.

While mice displayed cognitive deficits in the water maze, chronic treatment with Masitinib restored normal learning performances. Masitinib treatment had neither significant effect on A β plaque loads nor on markers of neuroinflammation. However, Masitinib treatment reduced the number of cerebral mast cells and lead to recovery of synaptic integrity in the mice. Genetic depletion of mast cells in mice similarly rescued synaptic impairments, suggesting that the pro-cognitive effects of Masitinib were associated with mast cell reduction.

These results underline a preclinical efficacy of Masitinib in cognitively-impaired transgenic mice modeling Alzheimer's disease. The mechanism of action of Masitinib does not rely on anti-amyloid or anti-inflammatory effects but appears to be associated with a synapto-protective action in relation with mast cells inhibition.

Message from Chair/Treasurer



Dear Colleagues and Friends,

The first quarter of FY 2019 was unsettling, having lost several of our Trustees just months apart, one of whom was my dear friend Paul Greengard. However, we did not lose our way thanks to our organization's founders — Zachary Fisher and David Rockefeller — who solidified the groundwork for our Foundation 25 years ago. Their legacy is ingrained in the heart and soul of this Foundation.

As you read this report, you saw a plethora of things to celebrate — from our researchers' published discoveries to our award-winning health information and resources, and from our Charity Navigator four-star rating to our financial statements on the next page. Your support enables us to have more impact on the Alzheimer's community than we ever could alone.

Unprecedented years like 2019 remind me that we are all in this work for the long haul. The stakes are high, and the issue is critical, as someone is diagnosed with Alzheimer's every 65 seconds.

Our world-renowned scientists, resourceful and talented staff, committees and Trustee members are determined to overcome these challenges. Our essential and collegiate partnership with the Rockefeller University lab faculty, together with your help, can make finding a cure for Alzheimer's disease a reality.

To all our advocates, grantees, and friends, thank you for your perseverance and support.

Barry R. Sloane

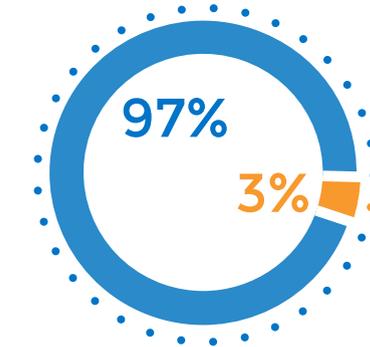
Audited Financial Position

Statement of Financial Position
December 31, 2019
(with comparative amounts at December 31, 2018)

	2019	2018
ASSETS		
Cash and cash equivalents	\$ 7,045,712	\$ 5,219,707
Pledges receivable from federated campaigns	304,851	375,087
Contributions receivable	212,583	377,920
Investments	23,941,098	20,226,002
Other assets	14,851	7,860
Furniture and equipment, net of accumulated depreciation of \$9,941 and \$9,095 in 2019 and 2018	2,865	3,711
	<u>\$ 31,521,960</u>	<u>\$ 26,210,287</u>
LIABILITIES AND NET ASSETS		
Liabilities		
Accounts payable and accrued liabilities	\$ 79,748	\$ 171,203
Grants payable, net of discount	2,810,985	3,373,361
Total Liabilities	<u>2,890,733</u>	<u>3,544,564</u>
Net Assets		
Without donor restrictions	28,326,376	22,284,312
With donor restrictions	304,851	381,411
Total Net Assets	<u>28,631,227</u>	<u>22,665,723</u>
Total Liabilities and Net Assets	<u>\$ 31,521,960</u>	<u>\$ 26,210,287</u>

2019 Financial Report

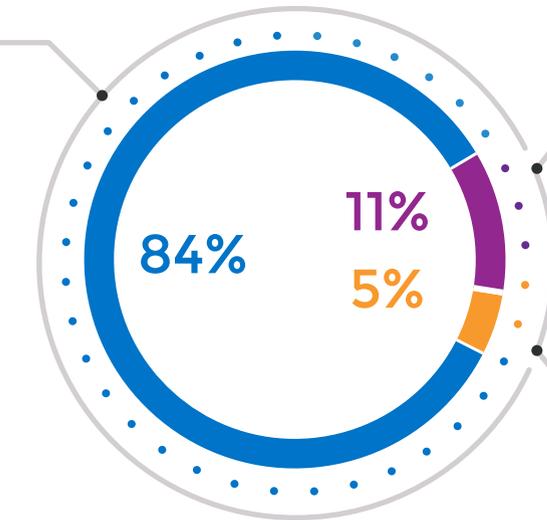
Contributions Breakdown (FYE 12/2019)



- **Contributions, Gifts & Grants**
\$7,063,451
(96.62%)
- **Federated Campaigns**
\$247,000
(3.37%)

Expenses Breakdown (FYE 12/2019)

- **Programs**
\$4,123,503
(83.90%)



- **Administrative**
\$551,259
(11.21%)

- **Fundraising**
\$239,899
(4.88%)

Programs

The Foundation's primary goal is to fund The Fisher Center, underwriting novel research to find a cure and understand the causes of Alzheimer's disease. Programs include:

- Our website, ALZinfo.org, which hosts a wealth of information about Alzheimer's disease.
- *Preserving Your Memory*, a tri-annual magazine filled with caregiving tips and the latest news on Alzheimer's research and treatments.
- *Alzheimer's Research News You Can Use*, an e-newsletter that provides information about how to better live with, and care for, someone with Alzheimer's disease.

Fundraising

Fundraising allows us to promote our mission to end Alzheimer's by raising awareness and providing funding for novel Alzheimer's research.

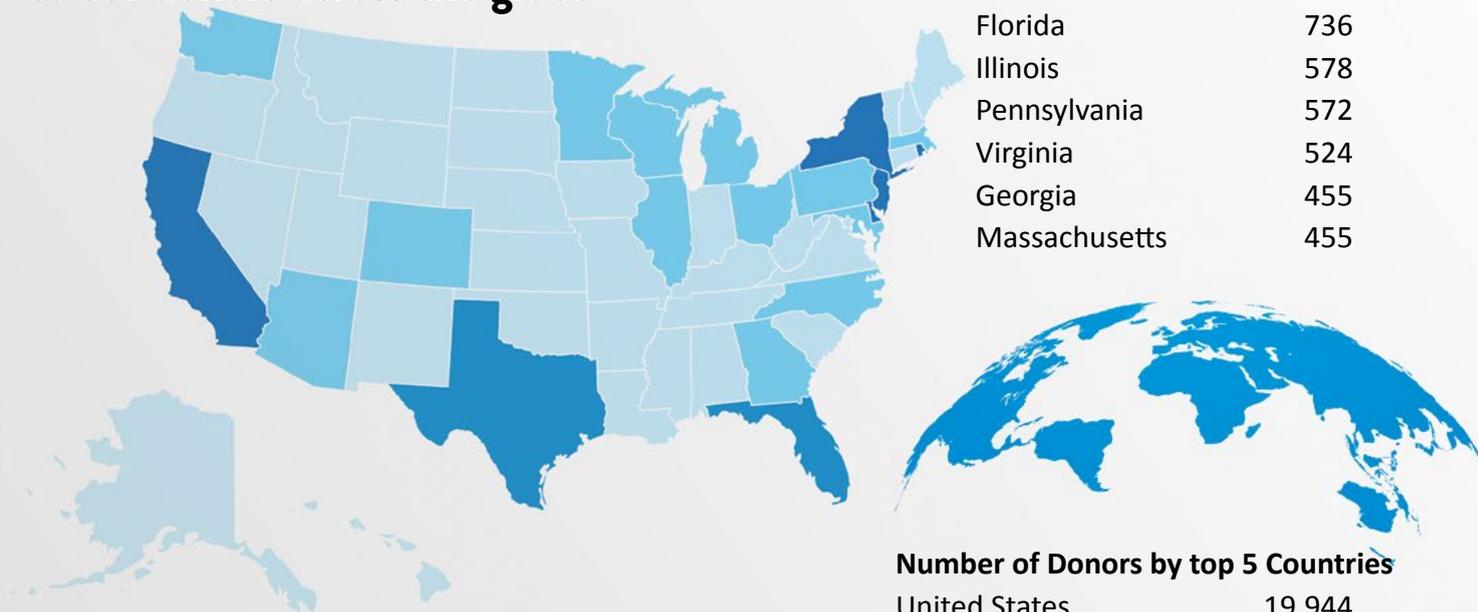
Administrative

Our administrative expenses support:

- A small, talented staff,
- Legal and accounting services,
- Office equipment and supplies. (Office space and furniture is gifted to the Foundation by a donor.)

Thank you

to our donors across the globe



Number of Donors by top 10 states

California	1,542
New Jersey	1,356
New York	1,337
Texas	826
Florida	736
Illinois	578
Pennsylvania	572
Virginia	524
Georgia	455
Massachusetts	455

Number of Donors by top 5 Countries

United States	19,944
Canada	84
Netherlands	26
Germany	14
United Kingdom	6

What's to come...

In 2020, our scientists at The Fisher Center Lab will work on identifying the key protein required for amyloid- β ($A\beta$) formation, plaques thought to trigger Alzheimer's development and degradation.

We also have plans to expand our Information Program, including a redesign of our award-winning website, ALZinfo.org. Our tri-annual magazine (*Preserving Your Memory*), our free bi-weekly e-newsletter, and our expert-reviewed clinical brochures and pamphlets will also receive refreshing new looks.

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Christina Hall
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Rebecca Libed
Database Specialist & Analyst

Jerry Louis
Web Developer & Graphic Designer

Tribute to...

Kent L. Karosen (1965-2018)
President & CEO

Murray M. Rubin CPA (1942-2019)
Secretary

Dr. Paul Greengard (1925-2019)
Director of The Fisher Center Lab

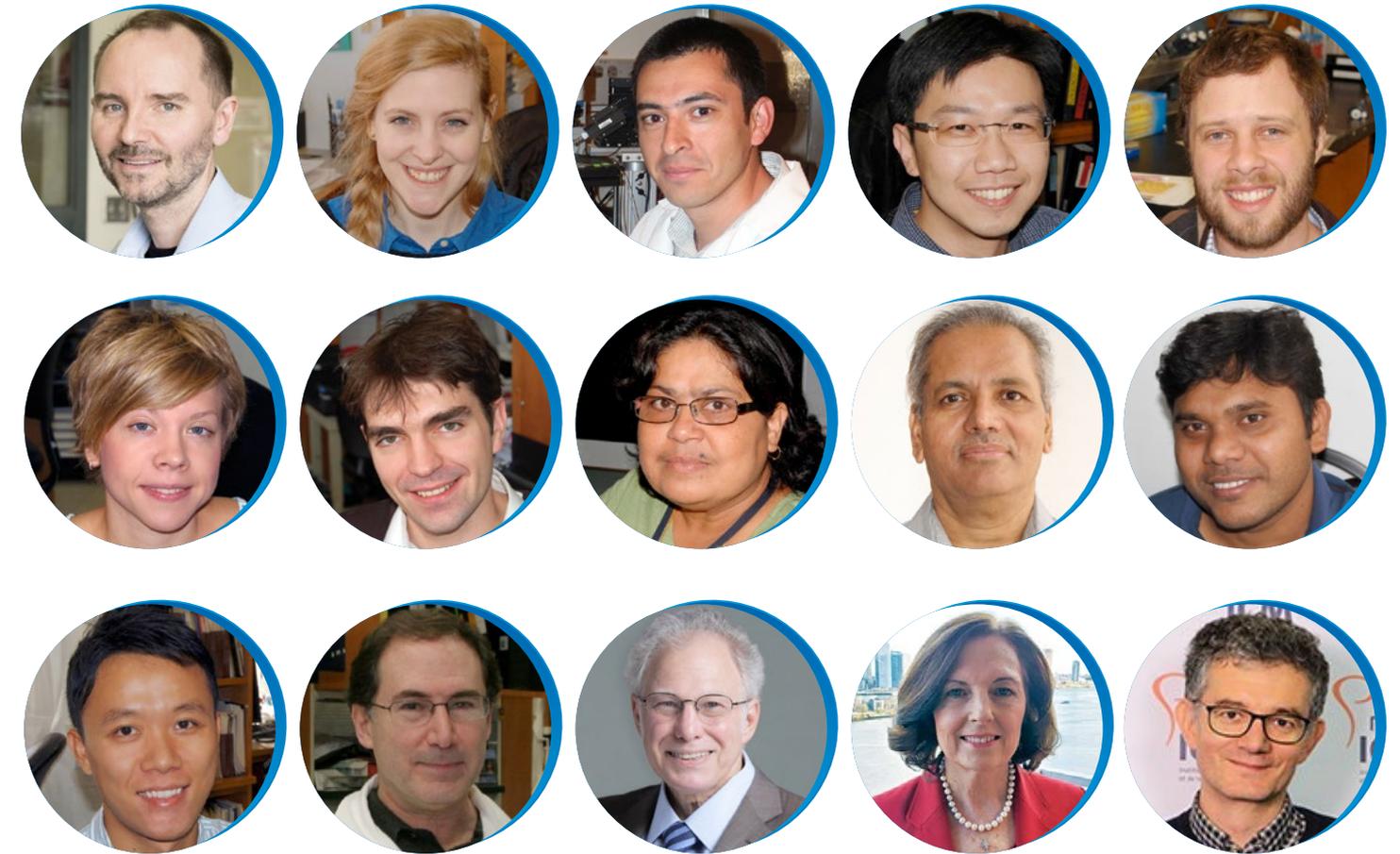
Neuroscience Advisory Committee (2019)

The Fisher Center’s Scientific Advisory Board is comprised of world-renowned doctors and scientists who provide counsel and act as resources for the Foundation.



Scientific Advisory Board from left to right:
 Dr. Marc Flajolet, Dr. Michael W. Young, Dr. Torsten N. Wiesel, Dr. Cornelia Bargmann,
 Dr. Nathaniel Heintz, Dr. Hermann Steller, Dr. Sidney Strickland

Research Team



Research Team from left to right:
 Dr. Marc Flajolet, Dr. Alona Barnea, Dr. Victor Bustos, Dr. Jerry Chang, Dr. Jose Ledo
 Dr. Maria Pulina, Dr. Jean-Pierre Roussarie, Dr. Anjana Sinha, Dr. Subhash Sinha, Dr. Yashoda Sunkari
 Dr. Peng Xu, Dr. William J. Netzer, Dr. Barry Reisberg, Dr. Sunnie Kenowsky, Dr. Benoit Delatour

Researchers not photographed:
 Dr. Marc Dhenain, Dr. Patrice Dubreuil, Dr. Olivier Hermine

Remaining a Leader in Our Field

WITH TOP AWARDS AND RATINGS FOR OUR ACCOUNTABILITY, TRANSPARENCY, AND HIGH QUALITY DIGITAL HEALTH RESOURCES

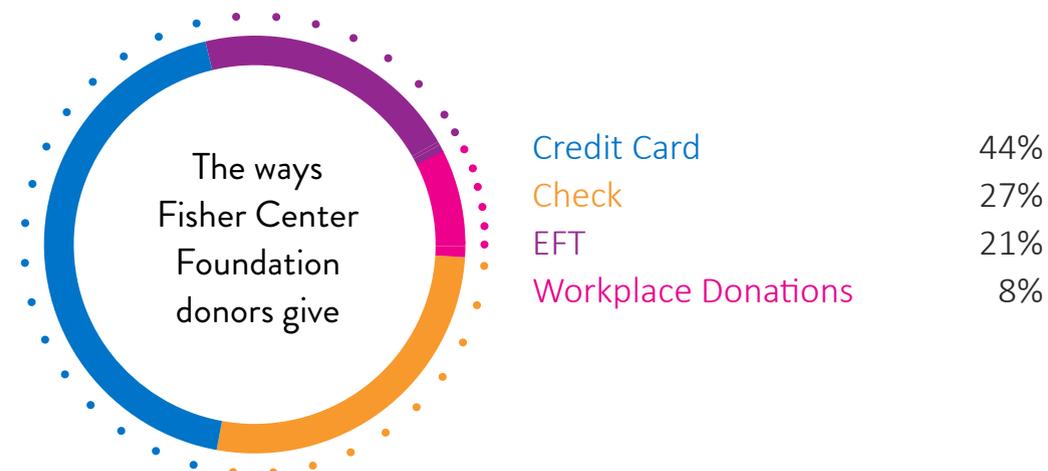


The Fisher Center for Alzheimer’s Research Foundation Board of Trustees, Advisory Committee, and Staff humbly thank our donors who enable us to invest in scientific research and information programs for Alzheimer’s patients and caregivers. We remain committed to fiscal prudence to ensure sustainability and meaningful resources for the Alzheimer’s community.

Our Donors are Bringing Us Closer to a Cure

Here’s how:

ONLINE Donate online by going to alzinfo.org/donate	STOCK TRANSFERS Receiving Bank: Wells Fargo Acct Name: Fisher Center for Alzheimer’s Research Foundation DTC #: 0141 Acct #: 3733-3729	WORKPLACE DONATIONS Inquire with your employer about workplace giving.
BY MAIL FDR Station, PO Box 220 New York, NY 10150	BY PHONE/EMAIL 1-800-259-4636 1-212-915-1328 info@alzinfo.org	MEMORY WALL alzinfo.org/memory-wall
MATCHING GIFTS Tax ID # 13-3859563	BEQUESTS / PLANNED GIVING For more information please call: 212-915-1322	FUNDRAISING alzinfo.org/fundraising





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ALZHEIMER'S
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