Brain Research Foundation




70 Years | A Legacy of Passion

Brain Research Foundation funds research that impacts our understanding of all diseases and disorders of the brain.

AGE-RELATED MACULAR DEGENERATION (AMD) | AGGRESSIVE DISORDER | ALCOHOLISM | ALZHEIMER'S DISEASE | AMYOTROPHIC LATERAL SCLEROSIS (ALS) | ANOREXIA NERVOSA ANXIETY DISORDERS | APHASIA | ARTERIOVENOUS MALFORMATION | ASPERGER SYNDROME ATTENTION DEFICIT DISORDER | AUTISM SPECTRUM DISORDER | BATTEN DISEASE | BELL'S PALSY BIPOLAR DISORDER | BLINDNESS | BRAIN ANEURYSM | BRAIN CANCER | BRAIN DEVELOPMENT BRAIN TUMORS | BULIMIA | CEREBRAL PALSY | CHARCOT-MARIE-TOOTH DISEASE | CONCUSSION CONDUCT DISORDER | CREUTZFELDT-JAKOB DISEASE | DANDY-WALKER SYNDROME | DEMENTIA DEPRESSION | DEVELOPMENTAL DISORDERS | DOWN SYNDROME | DRAVET SYNDROME DYSTONIA | EATING DISORDERS | ENCEPHALOPATHY | EPILEPSY | ESSENTIAL TREMOR FATAL FAMILIAL INSOMNIA | FRAGILE X SYNDROME | FRONTOTEMPORAL LOBAR DEGENERATION GUILLAIN-BARRÉ SYNDROME | HEMIFACIAL SPASM | HUNTINGTON'S DISEASE LEARNING DISABILITY | LEWY BODY DEMENTIA | LOCKED-IN SYNDROME MANIC-DEPRESSIVE ILLNESS | MENINGITIS | MENTAL RETARDATION | MIGRAINE HEADACHES MOTOR NEURON DISEASE | MULTIPLE SCLEROSIS | MUSCULAR DYSTROPHY | MYASTHENIA GRAVIS NARCOLEPSY | NICOTINE ADDICTION | NEUROPATHY | OBSESSIVE-COMPULSIVE DISORDER OPIOID ADDICTION AND DEPENDENCY | PANIC DISORDER | PARKINSON'S DISEASE PICK'S DISEASE | POST TRAUMATIC STRESS DISORDER (PTSD) | PRION DISEASE RESTLESS LEGS SYNDROME | RETT SYNDROME | SCHIZOPHRENIA | SLEEP APNEA SMITH-MAGENIS SYNDROME | SPINAL CORD INJURY | SPINAL MUSCULAR ATROPHY | STROKE SUBSTANCE ABUSE DISORDERS | TAY-SACHS DISEASE | TOURETTE SYNDROME TRANSIENT ISCHEMIC ATTACK | TRAUMATIC BRAIN INJURY (TBI) | TRIGEMINAL NEURALGIA TUBEROUS SCLEROSIS | WILLIAMS SYNDROME

- Advancing our understanding of the brain
- Launching new careers
- Building cutting-edge technology
- Using new approaches to solve persistent problems

Making progress in science takes vision and persistence.

New ideas and technology take time to develop. Young investigators need support to chart new paths in the field. Established investigators need to be able to pivot in revolutionary new directions.

For 70 years, the Brain Research Foundation has focused on a singular goal—advancing brain science. Its efforts focus on supporting the most visionary scientists doing high-risk-high-reward research and have reaped enormous dividends for the field.

BRF Seed Grants have helped generations of young investigators get new lines of inquiry off the ground, build cutting-edge tools, and generate the data needed to secure additional funding. BRF Scientific Innovations Awards have also helped established investigators pursue ambitious new projects that have catapulted neuroscience forward. BRF's perseverance and long-term vision have helped build the cadre of visionary scientists driving the field toward breakthroughs.

Dear Friends,

As the nation's oldest organization dedicated to brain research, BRF has a rich history rooted in scientific discovery, donor support, and widespread impact.

In 1953, BRF was incorporated as a not-for-profit organization by three neurologists, including Dr. Frederic A. Gibbs, who would spend his life researching epilepsy. He broke new ground using electro-encephalography to measure brain activity for the diagnosis and treatment of epilepsy and was widely known as "the father of EEG." Yet instead of focusing on epilepsy, Dr. Gibbs wanted to take a broader approach and try to understand the brain.

Scientists established BRF on innovation, investigation and passion, but it took a group of donors who understood this visionary concept, even before such research was considered possible, to get this idea off the ground. The Foundation's longevity is due to donors who have helped continued BRF's mission for 70 years because of their passion for our mission and hope for the future.

Today, BRF nurtures the projects of researchers across the nation with millions of dollars of funding, resulting in the type of innovative research that promises better treatments for neurological disorders and, ultimately, potential cures. We will continue our mission as long as we have passionate donors that believe in what we do.

In our 2022-2023 Brain Research Foundation Impact Report, we have chosen four research projects to focus on more in-depth. We hope you will find it inspiring to read about how your contributions have advanced neuroscience in areas that include aging, light exposure and brain health, thirst regulation and addiction.

We have made great strides, but more still needs to be done. One miraculous day, a scientist may find the cure for Alzheimer's, depression or another devastating disease; that discovery is built upon many experiments and years of support through organizations like the Brain Research Foundation. The Foundation and its supporters will be able to say that we played a role in making this breakthrough happen.

We look forward to that future which is closer with your help and encouragement. Thank you for helping us continue our legacy of passion.

Sincerely,

Terre A. Constantine, Ph.D.
Executive Director and CEO

As the former President and Chief Executive Officer of Blue Cross Blue Shield Association, I profoundly understand the mission of Brain Research Foundation (BRF) and I am proud to Chair this great organization as we celebrate seven decades of research.

When we were founded in 1953 neuroscience was a relatively new field but there were already technologies and findings that were driving the questions we knew would someday lead to answers. Decades later I know that those questions resulted in answers that have affected our lives today. For instance, I know that my grandson who has recently been diagnosed with an autism spectrum disorder has benefitted from the research and the data from questions that were asked years and years ago. And I am confident that he (and all of us) will continue to benefit from the questions asked today that BRF funding will answer.

None of our past 70 years of work would have been possible without our friends and donors. I share my gratitude for all they have done so that we may continue our path to fully understand the brain and find new treatments and cures. Additionally, I would like to thank the following:

- To my fellow Board of Trustees, thank you for your support and commitment as we continue to reach out to our friends, families, and colleagues to tell them about the BRF and how important it is to spread the word and garner support. Your loyalty and generosity to BRF are one of the main reasons I took on the role as Chairman.
- To the Scientific Review Committee, thank you for continuing to do such critical work on our behalf. Your dedication, expertise and passion for our work is deeply appreciated. You are one of the main reasons that BRF is held in such high regard nationwide.
- To the office of BRF, Dr. Terre A. Constantine, Executive Director and CEO and Sandra Jaggi, Director of Philanthropy. Your steadfastness and devotion in keeping the Foundation running at such a high level, especially during the pandemic, is greatly appreciated by myself and the rest of the Board.

I especially would like to take this opportunity to congratulate Dr. Terre A. Constantine as she celebrates her own anniversary at BRF having joined the Foundation 20 years ago. Thank you for all the enthusiasm, sacrifice, and perseverance you have shown over these many years. BRF is in a tremendously good place because of your leadership and I look forward to working with you for many years to come.

In this report you will learn more about some recent projects that are fascinating, along with a very personal and inspiring story from our past Chairman of the Board and the current Chairman of our Honorary Board, John D. Mabie. And again, I thank you all greatly for your support.

Yours sincerely,

Scott P. Serota
Chairman, Board of Trustees

A Purposeful Approach to Progress

Brain Research Foundation asks universities nationwide to nominate their best and brightest scientists for BRF grants each year. These innovators lay out a vision for how their work will advance neuroscience or a disease affecting the brain with a detailed research proposal.

Currently we are supporting 31 innovative projects that will have an impact on our understanding of many diseases and disorders of the brain.

BRF's Scientific Review Committee (SRC), comprised of a diverse group of highly accomplished scientists, reviews the proposals. They select the projects with the most potential to advance the field of neuroscience now and into the future.

The SRC looks for projects have the potential advance critical areas of inquiry and identify tenacious scientists deploying new approaches to solving stubborn problems. They look for basic science studies that will provide valuable insights applicable to the study of many forms of brain disease.

The SRC's experience and vision have helped BRF to give a leg up to generations of scientists, supporting them as they build sustainable careers. The grants have enabled new insights into the brain and novel approaches to treating brain diseases.

Scientific Review Committee (SRC)

Tracy L. Bale, Ph.D.
University of Maryland School of Medicine

Scott T. Brady, Ph.D.
SRC Chair
University of Illinois Chicago

Monica Carson, Ph.D.
University of California, Riverside

Yamuna Krishnan, Ph.D.
The University of Chicago

Daniel A. Peterson, Ph.D.
Rosalind Franklin University

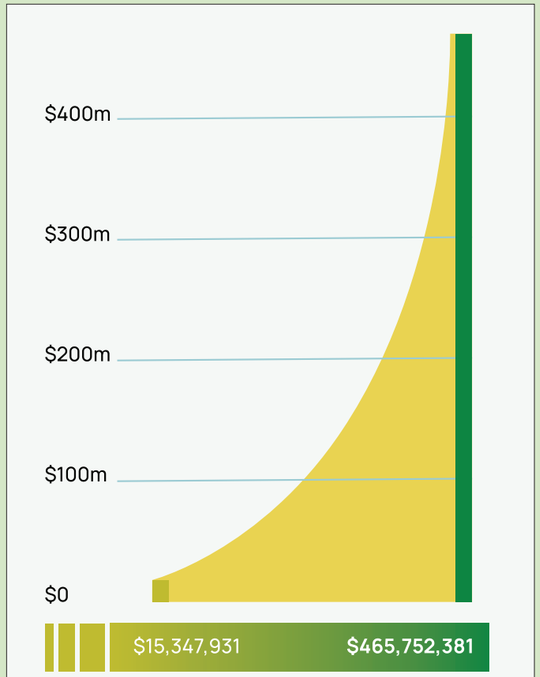
Kerry J. Ressler, M.D., Ph.D.
Harvard Medical School

Nenad Sestan, M.D., Ph.D.
Yale University

Gordon M.G. Shepherd, M.D., Ph.D.
Northwestern University

Brain Research Foundation Seed Grants provide early career scientists with the support they need to build their laboratories and launch new lines of inquiry. Seed Grants provide $80,000 over two years. Young investigators use the grants to answer questions and generate the preliminary data necessary to pursue long-term funding from traditional grant funders like the National Institutes of Health.

Brain Research Foundation Scientific Innovations Award supports established neuroscience investigators pursuing innovative ideas or pivoting in new research directions. The award provides $150,000 over two years that experienced investigators can use to pursue projects that are considered too speculative for traditional funders but have a high potential for yielding field transformative insights.



Brain Research Foundation has awarded **$15,347,931** in Seed Grants from which grantees have obtained an additional **$465,752,381** in funding.

Every dollar BRF awards attracts $30 in additional research funding.

2022 Seed Grant Recipients

ISHMAIL ABDUS-SABOOR, PH.D.

Columbia University
Department of Biological Sciences

Investigating a Skin-brain Neuronal Pathway for Rewarding Social Touch

APPLICATIONS: AUTISM, TOUCH, REWARD, SOCIAL-BEHAVIOR, DOPAMINE, OXYTOCIN

BYOUNG IL BAE, PH.D.

University of Connecticut
Department of Neuroscience

Unique Vulnerability of Developing Human Cerebral Cortex to Loss of Centrosomal Protein

APPLICATIONS: AUTISM, SCHIZOPHRENIA

CARL & MARILYNN THOMA FOUNDATION SEED GRANT

YVETTE FISHER, PH.D.

University of California, Berkeley
Department of Molecular & Cell Biology

Dynamic Modulation of Synaptic Plasticity During Spatial Exploration

APPLICATIONS: NEUROPSYCHIATRIC DISORDERS, COGNITIVE PROCESSING

THE VIRGINIA (GINNY) & ROGER CARLSON SEED GRANT

ERIN M. GIBSON, PH.D.

Stanford University
Department of Psychiatry & Behavioral Sciences

Circadian Regulation of Oligodendroglial Senescence and Metabolomics in Aging

APPLICATIONS: ALZHEIMER'S DISEASE, BRAIN DEVELOPMENT, CIRCADIAN, NEURODEGENERATION

SARAH C. GOETZ, PH.D.

Duke University
Department of Pharmacology & Cancer Biology

Uncovering a Novel Role for Primary Cilia in Eph/Ephrin Signaling in Neurons

APPLICATIONS: DEVELOPMENTAL DISORDERS, NEURODEGENERATIVE DISORDERS

WOMEN'S COUNCIL SEED GRANT

ALEXEY OSTROUMOV, PH.D.

Georgetown University
Department of Pharmacology and Physiology

Elucidating the Role of Paradoxical GABA Signaling in Parkinson's Disease

APPLICATIONS: PARKINSON'S DISEASE, MOTOR DYSFUNCTION

SUNGJIN PARK, PH.D.

University of Utah
Department of Neurobiology

Unveiling the Hidden Architectures of the Brain ECM

APPLICATIONS: LIVE-CELL IMAGING, JUVENILE-ADULT TRANSITION, EXTRACELLULAR MATRIX, NEURONAL PLASTICITY

CHRISTIAN PETERS, PH.D.

University of Illinois at Chicago
Department of Anatomy and Cell Biology

Mu-opioid Receptor Regulation by Golgi Satellites in Opioid Use Disorder

APPLICATIONS: ADDICTION, OPIOID USE DISORDER

MICHAEL LEE CIARDULLO SEED GRANT

AKHILA RAJAN, PH.D.

Fred Hutchinson Cancer Research Center
Basic Sciences Division

Fat to Brain Communication: Inter-organ Transport of Mitochondrial Molecules

APPLICATIONS: DEMENTIA, OBESITY, NEURODEGENERATION, BLOOD BRAIN BARRIER

DEMENTIA SOCIETY OF AMERICA SEED GRANT

JOHANNES SCHÖENEBERG, PH.D.

University of California, San Diego
Departments of Pharmacology and Chemistry and Biochemistry

The Role of 4D Mitochondrial Morphology in Impaired Neurogenesis

APPLICATIONS: ALZHEIMER'S DISEASE, LEARNING AND MEMORY, SEIZURES, MENTAL DISABILITIES

MAX A. TISCHFIELD, PH.D.

Rutgers University
Department of Cell Biology and Neuroscience

Investigating Habitual Behavior and Cholinergic Modulation of Dopamine Release in Tourette Disorder

APPLICATIONS: TOURETTE SYNDROME, TICS, HABITS, DOPAMINE

NILAY YAPICI, PH.D.

Cornell University
Department of Neurobiology & Behavior

Neural Dynamics of Taste and Hunger Integration in the Mammalian Brainstem

APPLICATIONS: OBESITY, FOOD INTAKE, METABOLISM, TASTE PERCEPTION

2022 Scientific Innovations Award Recipients

ANGELIQUE BORDEY, PH.D.

Yale University

The Role of Ribosomes in Synaptic Circuit Formation and Socio-Communicative Deficits

APPLICATIONS: AUTISM, TUBEROUS SCLEROSIS COMPLEX, RIBOSOME, SYNAPTIC CONNECTIVITY

ADAM E. COHEN, PH.D.

Harvard University

To spike or not to spike? Mapping dendritic computations in vivo.

APPLICATIONS:: MEMORY, ALZHEIMER'S DISEASE, AUTISM, DENDRITIC COMPUTATION

GINA TURRIGIANO, PH.D.

Brandeis University

Homeostatic Maintenance of Neocortical Excitation-inhibition Balance by Ciliary Neuropeptidergic Signaling

APPLICATIONS: NEUROPSYCHIATRIC DISORDERS, AUTISM, MENTAL HEALTH, LEARNING

2023 Seed Grant Recipients

REBEKAH C. EVANS, PH.D.

Georgetown University
Department of Neuroscience

In Vivo and Ex Vivo Dissection of Midbrain Neuron Activity During Exercise

APPLICATIONS: EXERCISE, BRAIN HEALTH, ALZHEIMER'S DISEASE, PARKINSON'S DISEASE, NEURODEGENERATIVE DISORDERS

DEMENTIA SOCIETY OF AMERICA SEED GRANT

WILLIAM J. GIARDINO, PH.D.

Stanford University
Department of Psychiatry and Behavioral Sciences

Deciphering the Neuropeptide Circuitry of Emotional Arousal in Narcolepsy

APPLICATIONS: NARCOLEPSY, SLEEP DISORDERS, MENTAL HEALTH CONDITIONS

HOWARD GRITTON, PH.D.

University of Illinois
Department of Comparative Biosciences

Attention Mechanisms Contributing to Auditory Spatial Processing

APPLICATIONS: SOUND PROCESSING; AUTISM SPECTRUM DISORDER (ASD); ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADD/ADHD)

NORA KORY, PH.D.

Harvard University
Department of Molecular Metabolism

Elucidating the Fates and Functions of Lactate in the Brain

APPLICATIONS: EPILEPSY, NEURODEGENERATIVE AND PSYCHIATRIC DISORDERS, BRAIN METABOLIS

HOJOON LEE, PH.D.

Northwestern University
Department of Neurobiology

Deciphering the Neural Circuitry of Nausea

APPLICATIONS: NAUSEA, MOTION SICKNESS, BRAIN STEM

HUAIJIN KEN LEON LOH, PH.D.

Yale University
Department of Comparative Medicine

Synapses in the Periphery: Uncovering Molecular Connections Between Nerves and Organs

APPLICATIONS: AUTONOMIC NERVOUS SYSTEM, SYNAPSES, PERIPHERAL NEUROPATHIES, DIABETES

EIRENE MARKENSCOFF-PAPADIMITRIOU, PH.D.

Cornell University
Department of Molecular Biology and Genetics

Neuronal Vulnerability to Heterochromatin Dysregulation in Development

APPLICATIONS: AUTISM SPECTRUM DISORDER, NEURODEVELOPMENT DISORDERS, CELLULAR DIVERSITY

CARL & MARILYNN THOMA FOUNDATION SEED GRANT

BRIDGET OSTREM, M.D., PH.D.

University of California San Francisco
Department of Neurology

Investigating the Therapeutic Potential of Human Milk Oligosaccharides

APPLICATIONS: CEREBRAL PALSY, WHITE MATTER INJURY, PRETERM BIRTH

WOMEN'S COUNCIL SEED GRANT

BENJAMIN SCHOLL, PH.D.

University of Pennsylvania
Department of Neuroscience

Elucidating Synapse Dysfunction Using In Vivo Single-Cell CRISPR/Cas9 Manipulations

APPLICATIONS: AUTISM SPECTRUM DISORDER, FRAGILE X SYNDROME,SYNAPSE DYSFUNCTION

NATALE R. SCIOLINO, PH.D.

University of Connecticut
Department of Physiology and Neurobiology

Impact of Locus Coeruleus Dynamics on Gustatory Cortex Function

APPLICATIONS: TASTE PROCESSING, CONDITIONED TASTE AVERSION, TASTE NEOPHOBIA

MICHAEL LEE CIARDULLO SEED GRANT

AAKANKSHA SINGHVI, PH.D.

Fred Hutchinson Cancer Center
Basic Sciences Division

Roles of Glia in Neural Aging

APPLICATIONS: AGING, NEURODEGENERATION, NERVOUS SYSTEM FUNCTION

ANDRE M. M. SOUSA, PH.D.

University of Wisconsin-Madison
Department of Neuroscience

Cerebellin 2 Dysregulation Mediates Synaptic Deficiency in Down Syndrome

APPLICATIONS: DOWN SYNDROME, NEURODEVELOPMENT, SYNAPTIC FUNCTION

DMITRY VELMESHEV, PH.D.

Duke University
Department of Neurobiology

Understanding the Role of Epigenetic Regulation During Human Neural Lineage Commitment

APPLICATIONS: AUTISM, BRAIN DEVELOPMENT, NEURODEVELOPMENTAL AND PSYCHIATRIC DISORDERS

2023 Scientific Innovations Award Recipients

YUKI OKA, PH.D.

California Institute of Technology

Molecular Mechanisms of Osmolality Sensing in the Mammalian Brain

APPLICATIONS: OSMOSENSOR, HOMEOSTASIS, BRAIN THIRST CIRCUIT

JASON SHEPHERD, PH.D.

University of Utah

Virus-like Intercellular Signaling Underlying Autoimmune Neurological Disorders

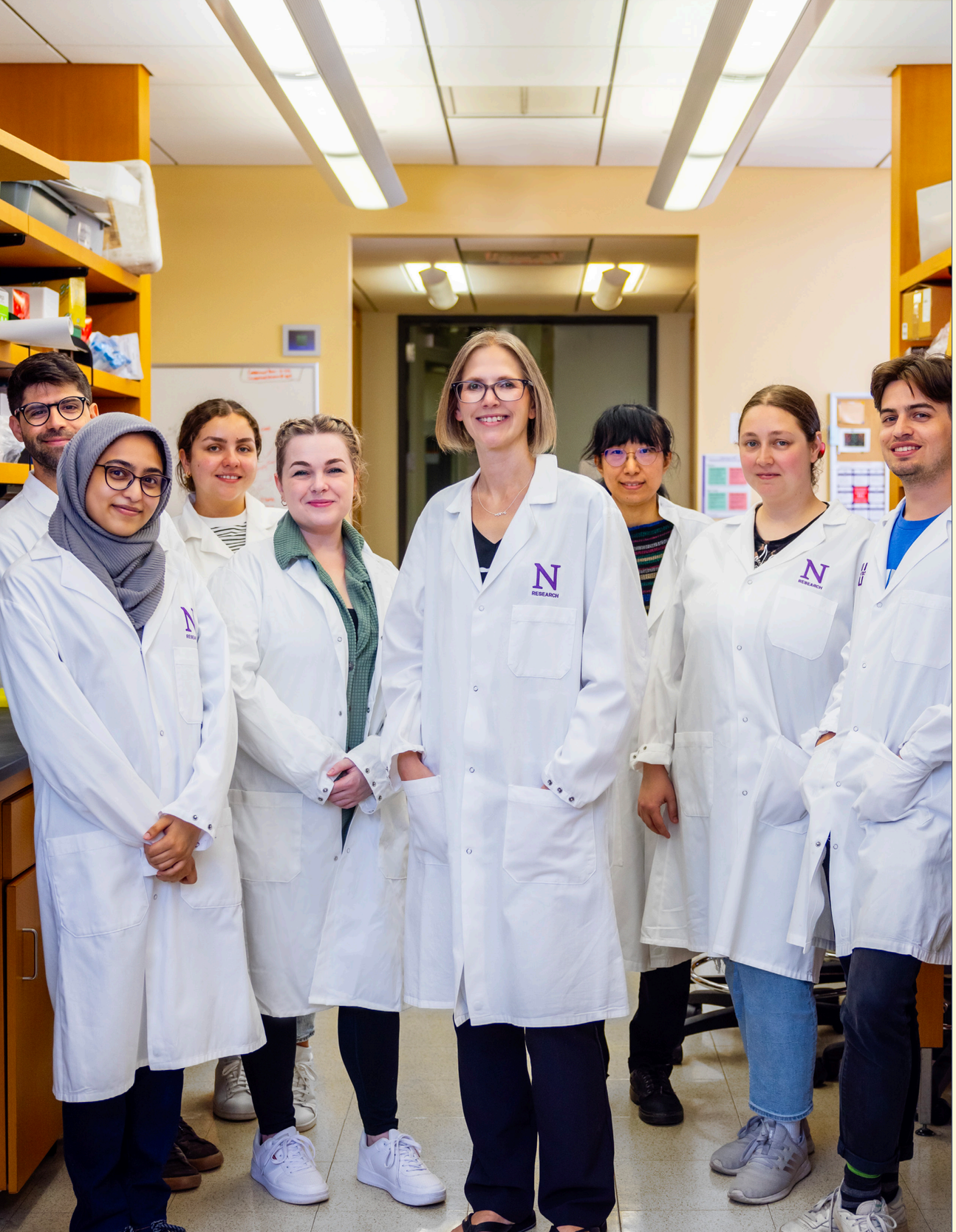
APPLICATIONS: INTERCELLULAR SIGNALING, AUTOIMMUNE DISORDERS, CANCER, VIRUSES

CHAOLIN ZHANG, PH.D.

Columbia University

Human-specific Alternative Splicing, Brain Development, and Ciliopathies

APPLICATIONS: BRAIN DEVELOPMENT, EVOLUTION, HUMAN-SPECIFIC ALTERNATIVE SPLICING



Perseverance

- **An unexpected result leads a scientist in a new direction**
- **An intractable problem demands new approaches**
- **A new technology unlocks previously unattainable insights**

It takes determination for scientists to propel science forward. They must boldly follow their data in new directions, shake off setbacks, and challenge the status quo. They must venture to try new approaches to difficult-to-solve problems.

That's why Brain Research Foundation steadfastly backs the most visionary scientists asking the most provocative questions. Because BRF knows it takes courage and commitment to drive science forward.

BRF's work over the past seven decades shows how funding scientists working to uncover how the brain works at the most basic level can lead to major progress. By staying the course, BRF lays the groundwork for tomorrow's advances.

Focused on a Cure

BRF Seed Grant Helps Dr. Sung Han Bring a New Focus to the Hunt for a Cure to Opioid Addiction and Safer Pain Medication

An epidemic of opioid addiction and overdoses has gripped the United States for more than two decades. But by zeroing in on the exact mechanism of how opioids slow or stop breathing, causing overdose deaths, Sung Han, Ph.D., an Associate Professor at the Salk Institute for Biological Sciences in La Jolla, California, hopes to help scientists develop new solutions to this persistent public health crisis.

Dr. Han's research focuses on the role of brain cells in the parabrachial nucleus, part of the brain stem which helps relay messages from the brain to the body. His laboratory initially focused on studying the role of brain cells in the parabrachial nucleus in anxiety, but a 2020 BRF Seed Grant allowed him to expand his laboratory's focus to understanding the role of these cells in opioid-induced respiratory depression.

"The brainstem plays a critical role in breathing, pain perception, and emotions," Dr. Han explained. Understanding the brain circuits that contribute to both pain relief and opioid-induced respiratory depressing could lead to new approaches to reducing this life-threatening side effect.

Confidence Boost

As a young investigator, Dr. Han said the BRF Seed Grant—his lab's first private funding—provided an enormous confidence boost. And the BRF grant allowed him to pivot to apply his expertise studying brain circuits in the brain stem to understanding how this part of the brain contributes to overdose deaths in addition to his ongoing work studying anxiety. It can often be difficult for scientists to secure funding from traditional funding sources to apply their skills to new problems. But BRF knows that bringing fresh approaches to persistent problems can lead to breakthroughs, and the Foundation is eager to support scientists willing to chart new research paths.

Dr. Han's research showed that brain cells interact with opioid drugs via receptors called μ-opioid receptors, which are highly concentrated in part of the brain stem called the parabrachial nucleus.

"The μ-opioid receptor controls pain relief, opioid addiction, and opioid's effects on breathing," Dr. Han explained. "But scientists didn't know where in the brain the μ-opioid receptors were concentrated."

A study Dr. Han published in 2021 in the *Proceedings of the National Academy of Sciences* with support from the BRF Seed Grant, showed that μ-opioid receptors in the parabrachial nucleus play a central role in opioids effects on breathing. Normally, mouse breathing patterns are coordinated with the activity of parabrachial nucleus brain cells. But giving the mice morphine disrupts their breathing pattern by slowing the activity of the parabrachial nucleus brain cells. Reactivating these brain cells restores normal breathing patterns in the mice.

A second study by Dr. Han showed that brain cells in the parabrachial nucleus with μ-opioid receptors change the breathing rate in mice in response to pain and anxiety. His research since then has shown that brain circuits in the parabrachial involved in regulating pain suppression, breathing depression (slow, shallow breating rate), and emotions like anxiety are distinct.

"There are actually three different clusters of cells operating in the parabrachial nucleus that are involved in different aspects of opioid addiction," he said. "Because they are not overlapping, we should be able to develop pain medications that don't cause addiction or breathing depression."

Since his BRF grant, Dr. Han has been awarded an NIH RO1 grant that will continue to support his research on the role of the parabrachial nucleus in opioid addiction. He also simultaneously has NIH RO1 grant that is continuing to support his research on anxiety.

Ultimately, Dr. Han's goal is to use what he's learning about the circuits, cells, and receptors involved in opioid-induced respiratory depression to develop safer pain medications. He is also hopeful that what he's learning might contribute to progress on a cure for opioid addiction.

Meaningful Connections

Dr. Lindsay De Biase Uses Her BRF Seed Grant to Decode the Mysteries of the Brain's Microglia Cells

During her Ph.D. training, Lindsay De Biase became captivated by a little-understood type of brain cells called microglia and their important role in the brain—from brain development through its aging. "Our BRF Seed Grant helped my laboratory establish a foundation for an entire line of research."

A 2021 BRF Seed Grant has helped De Biase, an Assistant Professor in the Department of Physiology in the David Geffen School of Medicine at the University of California, Los Angeles (UCLA), turn that early fascination into discoveries about the vital role microglia play in healthy brain development and neurodegenerative disease. The BRF Seed Grant was one of the first grants De Biase received, and it gave her laboratory the support needed to fund a graduate student, begin developing techniques to study microglia and gather the preliminary data necessary to apply for longer-term funding.

Unexpected Direction

Microglia are immune cells that scientists initially thought were "garbage disposals" that helped remove damaged cells or eliminate brain cell connections called synapses that are no longer needed. But De Biase's research has begun to reveal that they do so much more than trash removal.

Microglia in the midbrain appear to be early responders to aging in the brain. Specifically, when enzyme-producing structures called lysosomes in the microglia become overloaded, it destroys synapses and brain cells, making an aging brain more susceptible to neurodegeneration.

With her Seed Grant, De Biase wanted to learn how microglia and their lysosomes impact synapses during early life. First, she had to develop the techniques necessary to study the complexities of lysosomes. Using these tools in her study led to an unexpected discovery. An accumulation of lysosomes in the microglial during early brain development appeared essential for healthy synapse development rather than detrimental, as it is later in life.

"Unrestricted funding from a BRF Seed Grant allows you that freedom to rigorously look at a particular question and then pivot if it takes you in a different direction than what you were expecting," De Biase said. "That's critical."

Partnering to Pivot

The unexpected discovery has taken De Biase's work in a new direction.

"We're building a lot of experiments to investigate the possibility that microglia are actually supporting synapse generation during the development of the central nervous system," she said.

And now, De Biase has teamed up with another BRF grantee, 2020 BRF Seed Grant recipient Laura DeNardo, Ph.D., Assistant Professor in the Department of Physiology in the David Geffen School of Medicine at UCLA. Together, they plan to study if the microglia also support the formation of synapses that play a central role in decision-making, emotions, social behaviors, and dysfunction in this area is linked with addiction, autism, anxiety, and depression.

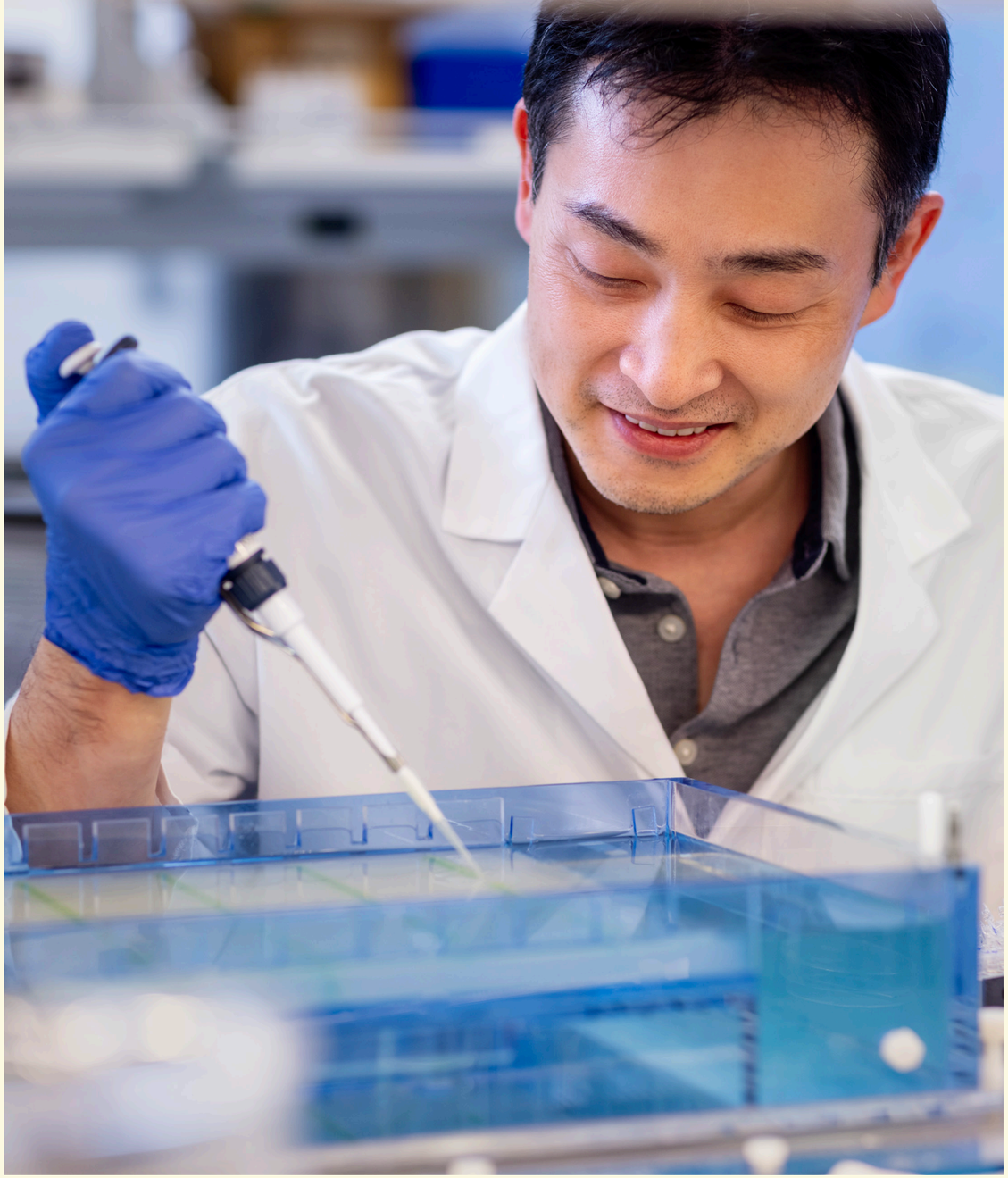
This partnership demonstrates how BRF's approach to funding the most innovative and bold young investigators can help catapult the field of neuroscience forward. Working together will allow the pair to leverage

De Biase's molecular and genetic techniques skills with DeNardo's animal studies and brain circuit mapping expertise.

"There may be critical developmental windows when microglia promote synapse generation," De Biase said. "Anything that perturbs the supportive role of microglia during development may contribute to neurodevelopmental disorders."

De Biase is also continuing to study the role of lysosomes in microglia during aging. The data and techniques she developed with her Seed Grant funding helped her secure additional funding from the National Institute on Aging and the Parkinson's Foundation.

"Throughout the lifespan, we think there may be important links between what happens in microglia lysosomes affecting brain health and function, and how the brain ages."



Yuki Oka, Ph.D., Professor of Biology at the California Institute of Technology in Pasadena, first mapped the circuits of brain cells that trigger thirst in 2015. Now, he's using a 2023 BRF Scientific Innovations Award (SIA) to identify the molecular sensors within these brain cells that detect when the body needs water.

Thirst for Knowledge

Dr. Yuki Oka Leverages Scientific Innovations Grant to Decode Thirst-Regulation Dehydration in Older Adults

"We know which cells are involved, but we need to screen through thousands of genes to identify which molecular channels within these cells detect water levels," Oka explained. "Traditional funders would consider this kind of project too risky. But BRF's SIA grant focuses on funding this kind or high risk-high reward research." Oka's work is critical to understanding why many older adults become chronically dehydrated, which can contribute to deteriorating health.

"If we can identify the receptors or channels that act as water sensors in the brain, it may help us identify water sensors in other parts of the body that use the same channels or receptors."

Water Detectors

Adequate hydration helps lubricate and protect the joints and organs of the body. It is also essential to transport nutrients to the cells or waste out of the body. But while scientists have identified many of the cells, molecules, and mechanisms involved with other internal sensors, such as those that monitor body temperature or how much pressure is on the skin, water sensing is still largely a mystery.

"Water sensing is a basic function of every cell," Oka explained. A 2022 study by Oka and his colleagues showed that cells in the gut and kidney also detect hydration levels and relay information to the brain that either stimulates or inhibits thirst.

Understanding the mechanisms that control hydration sensing and thirst in the brain could be pivotal to understanding the systems regulating water balance throughout the body.

The pay-off from the project could be huge, allowing scientists to understand how the body maintains a healthy balance of water and electrolytes and what goes wrong with aging or disease to disrupt that balance.

In a 2020 study published in *Nature*, Oka used cutting-edge single-cell gene sequencing technologies to identify which specific cell types in the brain are sensitive to water and which are not. "Now, we can compare gene expression patterns in water-sensitive brain cells and water insensitive brain cells," he said.

If Oka finds a small subset of genes that are only expressed in the water-sensing cells he can use more traditional experiments where a gene is turned on or off in the water sensing brain region in an animal to see how it effects thirst and water balance. Identifying each water-sensing gene and what it does will help Oka and his laboratory begin to understand how mutations in these genes may contribute to diseases or age-related changes in water regulation.

"Aging is known to affect water balance," he explained.

"Older individuals tend to be more dehydrated than younger individuals. But the brain doesn't seem to detect the dehydration in older adults and trigger thirst like it does in younger people."

Without cues from the brain triggering drinking, older people may be chronically dehydrated which may contribute to kidney disease or other health conditions that are more common in this population.

"Once we identify water-sensing molecules and cells, we can trace how those cells and molecules change with aging," he said. "Then, we may be able to find a drug can rescue water sensing and help restore older people to a well-hydrated state."

Once Oka's laboratory has data on which genes are involved in water sensing in the brain it should open the door to additional funding from more traditional funding sources.

"BRF plays a critical part in funding the first step," Oka said. "We expect to discover exciting things."

Shining Light on the Eye

Dr. Tiffany Schmidt Uses BRF Seed Grant to Build Tools to Study Light's Effects on the Brain

Light exposure has enormous effects on health. It controls daily wake-sleep cycles, influences mental health, and shifts hormone levels. Studies link nighttime light exposure caused by shift work to higher rates of depression, cancer, and obesity.

"We have no idea how light signals are getting from the eye to the brain and what brain circuits are involved," said Tiffany Schmidt, Ph.D., Associate Professor in the Department of Neurobiology at Northwestern University.

"If we knew that, we could try to mitigate or treat the health effects of nighttime light exposure," said Schmidt.

A Leg Up

A 2019 BRF Seed Grant gave Schmidt the funding she needed to pursue a novel idea. She wanted to focus her newly launched laboratory on mapping the brain circuits that might mediate light exposure's health effects.

In mice, about 40 different cell types transmit information about light exposure from the eye to the brain. "We wanted to try to isolate all the different cells in the eye that drive the effects of light on health," she said. "But to do that, we needed a set of tools."

Traditional funding organizations tend to shy away from funding pioneering projects. Many funders also set limitations on how the funds can be used and may not support projects that focus on building new research tools or testing new techniques. But BRF recognizes that making breakthroughs in neuroscience takes persistence and that building new tools and trying innovative approaches is essential.

The funding provided by the Seed Grant gave Schmidt the springboard she needed to get her toolkit off the ground. "It was game-changing," Schmidt said. "It allowed us to take some risks to develop tools no one had."

The BRF Seed Grant enabled Schmidt to develop and validate a mouse model that will allow researchers to turn on and off individual cells that connect the retina of the eye with the brain using drugs, viruses, or light exposure.

By doing this, they can systematically test how signals from specific retina cells communicate with the brain in response to light and what impact those signals have on the brain. They are working to make their 'toolkit' work on other cell types in the eye and be transferable to other mice models used by scientists.

"Our tools will give researchers the power to manipulate any cell type in the eye," she said.

The tools and data generated using the BRF grant helped Schmidt secure a $225,000 two-year R21 grant from the National Institutes of Health to continue building this technology. It's a huge undertaking with enormous potential to impact health. Learning how a healthy eye communicates with the brain may help scientists determine what goes wrong in diseases of the eye.

"If we can understand how things work in a healthy animal, we can learn how to right the ship when things are not functioning properly," Schmidt said.

It may also help scientists understand how light transmitted through the eye affects brain health. Already, Schmidt and her team have discovered that light signals travel to unexpected places in the brain that may impact cognitive function or health conditions like addiction.

"Light therapy is accessible to everyone and easy to do," she said. "If we could find ways to use it to decrease relapses in addiction or to improve cognitive function, it could be a great treatment option."

Schmidt is also making the mice and her toolkit available to other researchers as they validate each tool, which could help her field rapidly expand the impact of her work.

"Our BRF Seed Grant gave us opportunities that wouldn't have been possible with other grants," Schmidt said. "It put our lab and our entire field in a good position to answer critical questions in neuroscience."

A Legacy of Commitment

"I always say to my younger colleagues that you get so much more out of these relationships (like BRF) than you give to them. These relationships have enriched my life."

—John D. Mabie, Chairman and Founder of Mid-Continent Capital, LLC
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Imagine reading a letter that was so powerful it inspired a volunteer commitment for 63 years. Now imagine that the letter was not even written to you! This is how John Mabie began his involvement with Brain Research Foundation (BRF) back in 1960. At the time he was working for his father, William Mabie, and William received a letter from BRF co-founder, Clint Frank. William stated it was the "best fundraising letter he'd ever read" and handed it to John. Clint and his co-founder, Bill E. Fay, Jr., had daughters that were both afflicted with epilepsy and had sent a truly compelling letter asking for donations to continue their support of neuroscience research.

John had already decided that he wanted to "give back" through charity work, and the letter written by two fathers who were desperate to help not only their daughters with epilepsy, but also all those suffering from diseases and disorders of the brain, was so compelling to John that he asked his father if he would contact Bill on his behalf. John then met with Bill to express his willingness to help but told him he was just starting out in his career and therefore had little financial capability at that time. Bill sensed the young man's passion and invited him to join the board. The rest, as they say, is history.

Back in the 1960s, BRF adopted the phrase, "no family left untouched." It was a simple and universal phrase, yet John was one of the rare ones whose family had no such issues. All of this changed in 1984 when his involvement took a more personal turn, as his father died of Parkinson's at the age of 82.

"John was one of the first people I met when I joined BRF 20 years ago. It was powerful to learn of his steadfast passion for the Foundation. Even more powerful was that he innately understood that to be a part of BRF meant to be a part of the journey for the long haul—science requires patience. Without a doubt, BRF would not be as successful today if it wasn't for John's passion, perseverance, and generosity. It's been a great honor to work alongside him these many years, I count it as one of the most meaningful relationships I've had since joining."
Dr. Terre A. Constantine
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All of us at BRF are deeply grateful to John for his commitment over these many decades and thank him for all he did and continues to do for our mission.

Gratitude

BRF's generous donors have funded seven decades of progress in brain science. Your dedication and steadfast support for BRF's innovative approach have enabled countless neuroscience breakthroughs. We are grateful for your passion and commitment.

Thank you.

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Letter from the Treasurer

Brain Research Foundation continues to fund groundbreaking research thanks to the increasingly generous contributions of our donors and our superior investment performance. During the last two years, more than 100% of our annual donor contributions have been used to fund research and educational programs in neuroscience. We are proud of having achieved these results, on average, over the last eleven years.

BRF continues to fund the most innovative neuroscience research in the most beneficial ways to advance the understanding of the brain. Currently, we are supporting 31 research projects at 21 institutions throughout the United States. As we review all of our research programs, we funded almost 3.5 million dollars of projects in the last 2 years. That amount exceeded our contributions by almost $171,000, thus exceeding our objective of investing at least 100% of our annual support in worthy neuroscience programs. We are proud of our ability to be good stewards of our donor dollars during the last two years of the COVID-19 pandemic.

We have included a summary of our income and major expenses and a condensed balance sheet for fiscal years 2022 and 2023. We encourage you to review our audited financial statements on our website or contact the BRF office.

The Board of Trustees and staff continue to work hard to sustain your support to fulfill our mission. As we celebrate our 70th year, we look forward to building our donor base and funding more researchers who are focused on improving life through innovative neuroscience research.

Sincerely,

David H. Fishburn
Treasurer

Statement of Activities and Changes in Net Assets

Highlights of Income Statement for the Years Ended June 30, 2023 and 2022

		2023		2022
Beginning Net Assets	$	18,251,469	$	24,088,659
Contributions		1,476,021		1,545,615
Contributions -In Kind		-		110,000
Interest and Dividends		517,689		486,881
Net Realized and Unrealized Gains (Losses) on Investments		1,516,878		(5,164,443)
Total	**$**	**21,762,057**	**$**	**21,066,712**
Expenses				
Program Services	$	2,111,179	$	2,384,417
Supporting Services		461,570		430,826
Total	$	**2,572,749**	$	**2,815,243**
Total Net Assets	**$**	**19,189,308**	**$**	**18,251,469**

Statement of Financial Position

As of June 30, 2022 and 2023

Assets	2023	2022
Cash	$ 112,769	$ 146,145
Investments	19,912,541	18,863,317
Prepaid Expenses and Other Current Assets	-	286
Security Deposits	5,200	5,200
Operating Right-of-Use Asset	245,969	-
Total Assets	**$ 20,276,479**	**$ 19,014,948**

Liabilities and Net Assets	2023	2022
Liabilities		
Accounts Payable and Accrued Expenses	$ 66,804	$ 58,479
Operating Lease Liability	275,367	-
Grants Payable	745,000	705,000
Total Liabilities	$ 1,087,171	$ 763,479
Net Assets		
Net Assets Without Donor Restrictions	$ 17,385,840	$ 16,504,879
Net Assets With Donor Restrictions	1,803,468	1,746,590
Total Net Assets	$ 19,189,308	$ 18,251,469
Total Liabilities and Net Assets	**$ $20,276,479**	**$ 19,014,948**

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Left to right, from top:

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Norman R. Bobins
David H. Fishburn
David D. Olson
Terre A. Constantine, Ph.D.

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Brain Research Foundation

Innovate. Explore. Discover.

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