Summer 2022

Discover

News from Brain Research Foundation

Dear Friends,

As the oldest neuroscience charity in the country, our mission of accelerating discoveries of the brain by funding pioneering neuroscience research has been the same for almost seven decades. That is why, at the end of each fiscal year, it is important to review, assess and verify that Brain Research Foundation (BRF) is still succeeding in fulfilling its mission and using our donors' contributions to support the most impactful research.

How do we accomplish this? We are **angel investors** in science startups, providing researchers with "seed money." In our case, the startups are innovative, early-stage research projects that are designed by bright, creative scientists at university research labs across the country. We are helping them get their boldest ideas off the ground, betting on advancing the understanding of the brain.

Of course, this is the "big picture" of what we do. Donors want to know our success stories. Defining success at BRF can't be measured in earnings. We aren't a for profit. We are in the business of giving money away to worthy research projects to gain discoveries, not profits.

Most businesses look at their **return on investment** (ROI) as a performance measure to evaluate the efficiency or profitability of an investment. BRF measures its ROI by determining how the researchers leverage our seed money into additional funding from larger institutions like National Institutes of Health. On average, for every $1 they receive from us, our grantees have gone on to secure $27 in future funding. This 1:27 ROI enables the scientists to do more experiments and continue to move their research forward.

Many successes cannot be measured in numbers but are successes just the same. A BRF grant may help accelerate a lab and advance the career of a researcher. A researcher that obtains larger grants of support can grow their lab, hire more staff, attract talented graduate students and brilliant postdoctoral fellows. This growth and success can assist in a promotion to a tenured position or help a postdoc become established as an independent researcher.

All these elements keep science moving forward. While the path is long and sometimes unexpected, I am pleased to let you know that BRF funded projects are advancing to clinical breakthroughs. One is in clinical trials to create a neuroprosthetic for people with paralysis. And this newsletter highlights an exciting new discovery that could reduce opioid relapse and contribute to the end of the opioid crisis.

Each project funded by our donors brings us closer to our collective vision of improving lives through new treatments and cures for all neurological disorders—which is our ultimate **success story**.

I hope you continue with us on this amazing journey.

Sincerely,

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

An Exciting New Discovery Could Reduce Opioid Relapse

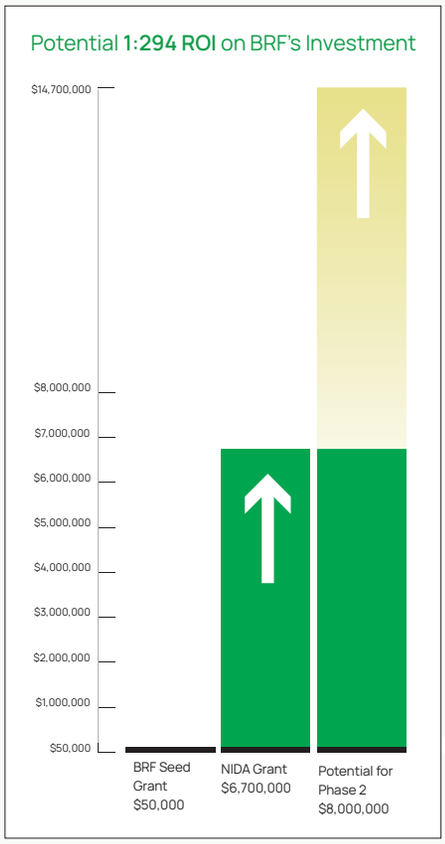
Opioids are recognized as among the most dangerous drugs in the US. An estimated 10.1 million people aged 12 or older misused opioids in the past year. [1] This resulted in 49,860 deaths from opioid drug overdose – over 136 people daily.[2] Nearly a staggering 90% of those who seek treatment for opioid use disorders experience a relapse, and there is an urgent need to develop a relapse prevention theraputic. **These startling statistics were the driving force behind BRF's call to action.**

With generous support from the Blue Cross Blue Shield Association, BRF committed to funding research projects that were working to develop and repurpose drugs that could prevent the opioid cravings that lead to relapse.

Barbara Waszczak, Ph.D., professor in the Department of Pharmaceutical Sciences at Northeastern University in Boston, had been studying a protein called glial cell-derived neurotrophic factor (GDNF) as a potential treatment for Parkinson's disease for about a decade.

The challenge has been finding a way to get GDNF into the brain. Her team published studies in the early 2000s showing that intranasal delivery of GDNF in rats with an experimental Parkinson-like condition protected the dopamine producing cells. Dr. Waszczak later refined her GDNF delivery approach by partnering with a company called Copernicus, Inc. that makes nanoparticles of the DNA that encodes GDNF.

In addition to Parkinson's disease, Dr. Waszczak discovered evidence that GDNF might be useful for treating a range of other diseases, including addiction. She was awarded a $50,000 grant from BRF to test whether nasal delivery of Copernicus' nanoparticles of the DNA that encodes GDNF could reduce relapse-like behavior in a rodent model of opioid use disorder.



Her hypothesis proved to be correct. The funding received from BRF made it possible for Dr. Waszczak and associates to gather enough evidence to secure a $6.7 million grant from the National Institute of Drug Abuse (NIDA) to complete a Phase 1, two-year trial, on the intranasal treatment which should be completed by the end of 2023. If successful, there is potential to receive an additional $8 million for Phase 2 funding to further move this therapy to human clinical trials. **BRF's small investment of $50,000 could lead to $14.7 million in additional funding to move this toward a novel treatment – that's a 1:294 return on our investment.**

BRF is proud to have played such an important role in getting this extraordinary project off the ground, advancing research into opioid relapse reduction. Dr. Waszczak says, "Without seed funding from the BRF, we could not have taken the first steps in testing this intriguing idea. Support from that grant provided key preliminary data that later helped us get the $6.7 million NIDA grant to move it closer to clinical trials."

This ground-breaking research not only has the capacity to change the lives of those with opioid dependencies but make a positive impact on the lives of their families too.

[1] 2019 National Survey on Drug User and Health, 2020. [2] NCHS Data Brief No. 394, December 2020.

Our 2022 Grantees

Selected by our Scientific Review Committee and Board of Trustees, BRF's Seed Grant Winners and Scientific Innovations Award Winners advance neuroscience and the understanding of neurological diseases.

2022 Seed Grant Winners

Ishmail Abdus-Saboor, Ph.D.
Columbia University
Department of Biological Sciences

Project Title: Investigating a Skin-brain Neuronal Pathway for Rewarding Social Touch

Keywords: Autism, touch, reward, social-behavior, dopamine, oxytocin

Byoung Il Bae, Ph.D.
University of Connecticut
Department of Neuroscience

Project Title: Unique Vulnerability of Developing Human Cerebral Cortex to Loss of Centrosomal Protein

Keywords: Autism, schizophrenia

CARL & MARILYNN THOMA FOUNDATION SEED GRANT

Yvette Fisher, Ph.D.
University of California, Berkeley
Department of Molecular & Cell Biology

Project Title: Dynamic Modulation of Synaptic Plasticity During Spatial Exploration

Keywords: Neuropsychiatric disorders, cognitive processing

THE VIRGINIA (GINNY) & ROGER CARLSON SEED GRANT

Erin M. Gibson, Ph.D.
Stanford University
Department of Psychiatry & Behavioral Sciences

Project Title: Circadian Regulation of Oligodendroglial Senescence and Metabolomics in Aging

Keywords: Alzheimer's disease, brain development, circadian, neurodegeneration

Sarah C. Goetz, Ph.D.
Duke University
Department of Pharmacology & Cancer Biology

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

Keywords: Developmental disorders, neurodegenerative disorders

WOMEN'S COUNCIL SEED GRANT

Alexey Ostroumov, Ph.D.
Georgetown University
Department of Pharmacology and Physiology

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

Keywords: Parkinson's disease, motor dysfunction

Sungjin Park, Ph.D.
University of Utah
Department of Neurobiology

Project Title: Unveiling the Hidden Architectures of the Brain ECM

Keywords: 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

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

Keywords: Addiction, opioid use disorder

MICHAEL LEE CIARDULLO SEED GRANT

Akhila Rajan, Ph.D.
Fred Hutchinson Cancer Research Center
Basic Sciences Division

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

Keywords: 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

Project Title: The Role of 4D Mitochondrial Morphology in Impaired Neurogenesis

Keywords: Alzheimer's disease, learning and memory, seizures, mental disabilities

Max A. Tischfield, Ph.D.
Rutgers University
Department of Cell Biology and Neuroscience

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

Keywords: Tourette syndrome, tics, habits, dopamine

Nilay Yapici, Ph.D.
Cornell University
Department of Neurobiology & Behavior

Project Title: Neural Dynamics of Taste and Hunger Integration in the Mammalian Brainstem

Keywords: Obesity, food intake, metabolism, taste perception

2022 Scientific Innovations Award Winners

Angelique Bordey, Ph.D.
Yale University

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

Keywords: Autism, tuberous sclerosis complex, ribosome, synaptic connectivity

Our proposal aims at identifying a molecular mechanism responsible for autism-like socio-communicative defects in the developmental disorder, tuberous sclerosis complex (TSC). TSC is a genetic disorder with a 30-60% incidence of autism and is characterized by a spectrum of sensory and socio-communicative abnormalities. Despite accounting for 4-14% of all autism cases, there is currently no treatment for TSC-associated autism. We propose to test the transformative hypothesis that an overactive production of ribosomes, the molecular machines inside cells necessary for the making of proteins, contributes to abnormalities of brain circuit and autism-like socio-communicative defects in TSC. **We hope to identify novel therapeutic targets (e.g., specific altered genes responsible for overproduction of ribosome RNA) to rescue socio-communicative deficits observed in individuals with autism in TSC.**

Adam E. Cohen, Ph.D.
Harvard University

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

Keywords: Memory, Alzheimer's disease, autism, dendritic computation

The brain is made of neurons, and neurons convert synaptic inputs to spiking outputs. How does a neuron decide when to spike? Neuronal dendrites often have highly nonlinear responses, which lead to complex relationships between synaptic inputs and the membrane voltage at the neuronal cell body, which ultimately determines whether a neuron spikes. We know little about how these nonlinearities manifest in live animals, or even what conceptual framework to use to describe information processing in neuronal dendrites. This BRF project aims to combine advanced voltage imaging tools with optogenetic stimulation to map the membrane voltage and calcium dynamics throughout the dendritic trees of cortical pyramidal neurons in the brains of awake mice. By combining precisely timed sensory and optogenetic stimuli, we will determine how excitation, inhibition, neuromodulation, and action potentials interact in the dendritic tree. **This information will help us understand dendritic computation, will inform models of activity-dependent plasticity, and may serve as a baseline for studies of dendritic dysregulation in nervous system diseases that affect memory, such as Alzheimer's disease and autism spectrum disorders.**

Gina Turrigiano, Ph.D.
Brandeis University

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

Keywords: Neuropsychiatric disorders, autism, mental health, learning

Brain circuit wiring is adjusted during adolescence to generate fully functional circuits, and this process depends on an interaction between genetics and experience. During this period of experience-dependent development, excitatory and inhibitory synapses must be carefully balanced so that circuits do not become either too excitable or not excitable enough, but the mechanisms that allow excitation and inhibition within brain circuits to be dynamically adjusted are poorly understood. Here we will examine the role of a small subcellular organelle, the primary neuronal cilium, in this process. Cilia concentrate a number of neurotransmitter and neuropeptide receptors, and couple these receptors to signaling pathways that we recently found are able to adjust excitatory synapse formation. In this proposal we aim to test the hypothesize that release of the neuropeptide somatostatin from inhibitory neurons acts as a network-wide signal of circuit excitability, that then activates somatostatin receptors within cilia to adjust excitatory synapse number. This would act as a novel form of network-wide homeostatic compensation that would adjust excitatory synaptic drive to keep network activity stable. **These experiments will have relevance for a wide range of neurological disorders characterized by imbalances in network activity (e.g. autism-spectrum disorders, epilepsies), as well as human ciliopathies that lead to intellectual disability.**

Guiding Our Path to Progress

Brain Research Foundation's Scientific Review Committee (SRC) is made up of well-regarded researchers in the field of neuroscience. This committee lends its scientific expertise when reviewing the various research proposals submitted to the Foundation, evaluating proposals and making suggestions for funding.

Working together, SRC members leverage their diverse backgrounds and years of experience to identify the most promising nominees and projects with the greatest potential to propel brain research forward.

Their objective is to not only look for projects that lead to immediate breakthroughs in neuroscience, but also projects that are likely to yield collateral benefits, for many years to come. We are tremendously grateful for their expertise and dedication to the mission of BRF.

BRF's Scientific Review Committee

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

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

Tammy Kielian, Ph.D., University of Nebraska

Yamuna Krishnan, Ph.D., The University of Chicago

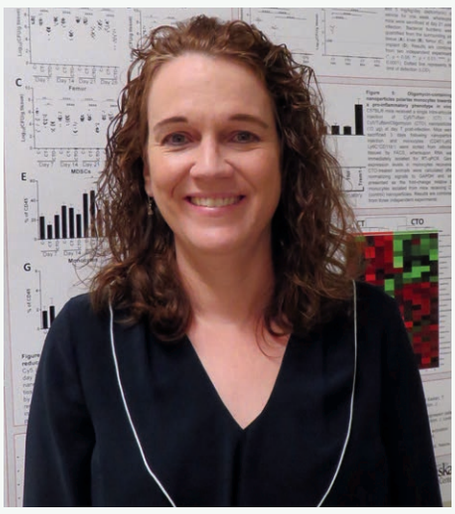
Daniel A. Peterson, Ph.D., Rosalind Franklin University

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

BRF announces new Scientific Review Committee Member



Tammy Kielian, Ph.D.
University of Nebraska Medical Center,
Choudari Kommineni, D.V.M., Ph.D. Professor of Pathology

Tammy Kielian received her Ph.D. from the University of Kansas Medical Center in 1998 and performed a postdoctoral fellowship in neuroimmunology at Dartmouth Medical School.

In 2001, she established her independent laboratory at the University of Arkansas for Medical Sciences and was recruited to the University of Nebraska Medical Center in 2008 where she is a professor and holds the Choudari Kommineni, D.V.M., Ph.D. Endowed Professor of Pathology.

Dr. Kielian's research interests span the fields of neuroimmunology, infectious diseases, and neuroscience with a unifying theme of innate immunity. Her laboratory has a long-standing interest in studying the pathogenesis and immune responses elicited by Staphylococcus aureus (S. aureus) in the CNS, with a particular emphasis on microglial and astrocyte activation. Her group utilizes a mouse model of S. aureus craniotomy infection that was developed in her laboratory to understand the mechanisms that prevent bacterial clearance in an immune competent host. Her group is also performing translational studies with samples from patients with craniotomy infection to identify leukocyte molecular signatures that are responsible for infection persistence.

Dr. Kielian has served as a regular and ad-hoc member on numerous NIH study section panels and her research program has been continuously funded by the NIH since its inception in 2001.

BRF Says Goodbye

Matt Rahn (1974-2022)

In 2012 BRF staff was introduced to Matthew Scott Rahn. Matt was interested in the work of BRF because he was a brain cancer and stroke survivor. His mother was diagnosed with Alzheimer's a few years before his own diagnosis, and he despised what the disease stole from her. Matt was passionate about the research BRF funded because it gave him and his family hope that groundbreaking ideas in science were getting the funding they needed to move the needle that much closer to treatments and cures.

He was a graduate of Northwestern University and received his MBA from the University of Chicago. He had a successful career as a consultant before his diagnosis. When you hear about someone being "cut down in their prime" that was truly Matt's story. Yet he was unstoppable in his recovery. He was hilarious and optimistic, easy to be around and inspirational to all those who knew him. His true passion was being a devoted family man to his wife, Mia, and their two daughters, Emma and Lena.

We send all our support to his family members, including his sisters and his father. Matt will be missed dearly.

Brain Research Foundation
Innovate. Explore. Discover.

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Did you know that 100% of your donation went to brain research?

How was that possible?

It was possible because in FY2022 100% of every dollar donated for research was invested in our research grants. Operating expenses were covered by separate funds. **When you donated to BRF your entire donation went towards neuroscience research at the top institutions across the country.**

Without your support, many visionary research projects into brain conditions, diseases and injuries wouldn't happen. Additionally, BRF seed grants often are the cornerstone to scientists securing further funding that continues to bring their innovative ideas to reality.

Brain Research Foundation is a 501 (c) (3) nonprofit. Our tax ID # is 36-2477928.