

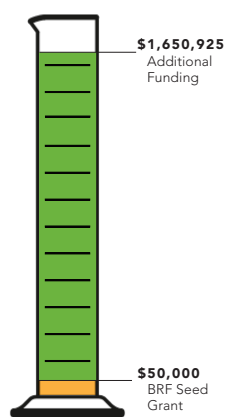
Discover!

news from Brain Research Foundation

“The BRF Seed Grant was an essential catalyst for my research.”

—Dr. Helen Bateup

A 1:33 Return on Investment



Dr. Bateup's BRF Seed Grant led to \$1,650,925 in additional funding

The Seed Grant from Brain Research Foundation was the first grant I received as a new junior faculty member at UC Berkeley. This grant was essential in enabling my lab to develop new, clinically relevant research. With Seed Grant funds, we were able to establish an optimized protocol for genetically engineering human stem cell-derived neurons to generate research models for brain disorders (Blair, J.D. et al, 2016). We have used this approach to establish a novel three-dimensional human brain organoid model of the neurodevelopmental disorder Tuberous Sclerosis Complex (TSC) which is characterized by the growth of numerous

noncancerous (benign) tumors in many parts of the body, including the brain.

We have found that loss of function mutations in the TSC1 or TSC2 genes, which are responsible for TSC, cause alterations in early cortical development that may underlie the epilepsy and intellectual disability observed in TSC patients. We have further shown that treatment with the drug rapamycin, which reverses the biochemical effects of TSC1 or TSC2 mutations, can improve neuronal development in our model. We are currently preparing a manuscript for publication on this work. In addition to helping us establish this new research model, the preliminary data generated with

Seed Grant funds allowed us to successfully compete for further research support and we were recently awarded a Hellman Family research grant and an R01 from National Institute of Neurological Disorders and Stroke (NINDS).



Dr. Helen Bateup
University of California, Berkeley

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I am extremely proud to play a key role in this organization, supporting the research that will have a profound influence on the quality of human life. It is a mission in which I truly believe. Brain Research Foundation invests in worthy, innovative neuroscience research, with the ultimate goal to enable research to evolve from discovery, to application, to testing, and finally, to treatment of patients.

Each year BRF takes calculated risks, supporting a project in its early stages.

Each year BRF grant recipients publish in scientific journals. Each year BRF grant recipients gather the much-needed preliminary data that will enable them to obtain additional outside grants to continue their work. Each year the grant projects answer questions about the brain.

In this issue you will see six projects that BRF decided to fund. Some illustrate the science we will be advancing as well as the successes that have already been achieved or are on the horizon. The cover story illustrates how 2014 Seed Grant recipient Dr. Helen Bateup utilized our support to create an amazing return on our scientific investment. **Because of a \$50,000 BRF Seed Grant Dr. Bateup obtained an additional \$1.65 million in research funding—a 1:33 return on BRF’s investment.**

We want our donors to know that we will continue to provide consistent funding and support to these talented researchers to play an integral role in helping advance cutting-edge science and technologies. The funding we provide is truly making a critical difference.

We thank you for helping us continue our important mission.

Sincerely,



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

“The Seed Grant was an essential catalyst for my research that gave me both practical support and the confidence to pursue a relatively high risk-high reward project early in my career. Our success in garnering long-term NIH support and translating our pilot data into a full scale project is a direct result of support by Brain Research Foundation.”

—Helen Bateup, Ph.D.



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Research Update

“BRF Grantees focused on brain cancer are moving research forward—from discovery, to application, to clinical trials and finally to treatment.”

—Dr. Terre A. Constantine

We all hope to live a full, happy and healthy life. That is what we want for ourselves, our children and all of our loved ones. However, many times something unexpected happens that alters that course. Often it is a debilitating neurological disease.

I have seen it happen with two of my grandparents who struggled with dementia, and that was hard to witness. But I felt some comfort knowing that many research projects BRF supports are focusing on memory, dementia and Alzheimer’s disease. And it renewed my passion for what the Foundation does. But as I watched my mother succumb to brain cancer, I also realized how much more we needed to do.

My story is not unique. Most, if not all of you, have a similar story of a loved one that has suffered or is suffering with a neurological issue. But what is unique is my close-up perspective on the advancement of neuroscience research. I know our organization is making a positive difference in the world through the innovative research we support and that knowledge makes my job very rewarding. Even though the answers did not come in time to help my mother, I know that they are coming.

As I read the progress reports of the many research projects BRF funds, all are extremely pioneering, but two recent projects which focus on brain cancer are of particular interest.

Dr. Beata Chertok, University of Michigan, is working on a novel delivery system to treat brain cancer. She has made great progress with her 2015 Seed Grant project, using nanotechnology to create a non-invasive therapy for not only brain tumors but also neurodegenerative diseases like

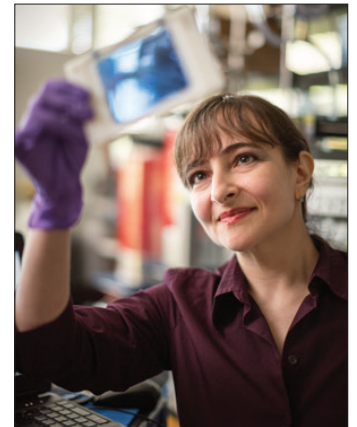
Parkinson’s disease and ALS, as well as traumatic brain injuries.

A second project that was also funded through BRF’s Seed Grant Program in 2015 specifically focuses on the very type of brain tumor my mother had – glioblastoma – which has no cure and a life expectancy of one to two years with treatment.

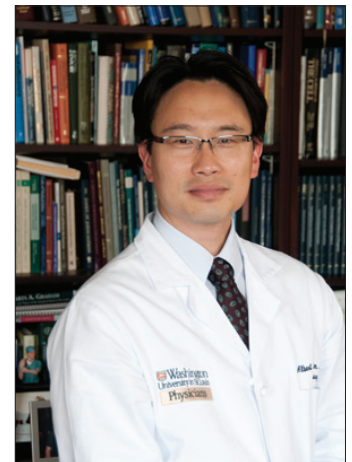
Like all the research we fund, these projects are hastening our understanding of the brain.

Dr. Albert Kim, Washington University in St. Louis, is focusing on cancer cells with stem cell-like properties that have been found in glioblastomas. These cancer stem cells are thought to be responsible for treatment failures and disease reoccurrence. The long-term goal of this project is to develop novel treatment strategies against glioblastomas by utilizing therapeutic reprogramming to convert the malignant cell state of cancer stem cells into a non-tumorigenic state.

These projects, like all of the research we fund, will hasten brain research from discovery, to application, to clinical trials, and finally to treatment of patients. I am lucky to have found such a worthwhile path in life, making a difference by helping fulfill the mission of this unique organization. I am comforted that the work we do today will help many in the future.



Beata Chertok, Ph.D., University of Michigan



Albert H. Kim, M.D., Ph.D.
Washington University in St. Louis

Board News

We are pleased to announce that Scott P. Serota has joined our Board of Trustees.



Scott P. Serota, President and CEO, Blue Cross Blue Shield Association

At last year's Discovery Dinner Scott P. Serota accepted the Frederic A. Gibbs Discovery Award for Community Service on behalf of the Blue Cross Blue Shield Association (BCBSA). As Mr. Serota learned more about the vision and mission of Brain Research Foundation, he decided to become more involved. In January, the Board of Trustees voted unanimously to appoint Mr. Serota to the Board of BRF.

Mr. Serota is President and Chief Executive Officer of BCBSA, a national federation of 36 independent, community-based and locally operated Blue Cross and Blue Shield companies. The Blue Cross and Blue Shield System is the nation's largest health insurer, covering nearly 106 million members—one-in-three of all Americans.

Mr. Serota was named BCBSA President and CEO in 2000, after serving four years as a senior executive, including two years as Chief Operating Officer. Before that, he was Executive Vice President for system development, responsible for new business, strategy and the BCBS Technology Evaluation Center, the nation's leading source for evaluating the safety and efficacy of emerging medical treatments.

Prior to joining BCBSA, Mr. Serota was President and CEO of Chicago-based Rush Prudential Health Plans, where he led the integration of Rush-Presbyterian-St. Luke's Medical Center Health Plans and The Prudential. Earlier in his career, Mr. Serota also created and led Physicians Preferred Health Inc., a Missouri-based PHO.

Mr. Serota is a founding member of the National Business Group on Health's Institute on Healthcare Costs and Solutions, a board member of BCS Financial Corporation, advisory board member of Marathon Pharmaceuticals, and board chairman of Plans' Liability Insurance Company. He also serves on the Leadership Council of the

Healthcare Financial Management Association, the American College of Healthcare Executives, the Dean's Leadership Council for the College of Science at Purdue University and the Washington University School of Medicine National Council.

Mr. Serota was appointed by President George W. Bush to the Policy Committee of the White House Conference on Aging—advising the Administration and Congress on policies, programs and services affecting the nation's older citizens—and served as chairman of the Subcommittee on Health.

He also was a charter member of the American Health Information Community, a federally chartered commission formed to work with former Health and Human Services Secretary Michael Leavitt to advance health information technology, including electronic health records.

Among civic leadership roles, Mr. Serota serves on the CEO Advisory Board for Building a Healthier Chicago. He is a frequent featured speaker at leading business and industry forums, and has spoken at the U.S. Chamber of Commerce, the Detroit Economic Club, the Executives Club of Chicago, the Jonathan Club in Los Angeles and the World Healthcare Congress in Washington, D.C.

Mr. Serota earned a bachelor's degree from Purdue University and a master's in health administration and planning from the Washington University School of Medicine. He holds an honorary doctorate of science from Purdue University and has been named a distinguished alumnus of both Purdue and Washington University.

A unique event leads to the formation of BRF's Young Leadership Board.

When they were still in grade school, the Shapiro kids – Lauren, Joe and Jonathan – had their world turned upside down when their mother was stricken with a rare brain aneurism that left her mentally and physically disabled. Their mom suffered two brain hemorrhages which are called cavernous angiomas. Less than one in a million are struck with this injury. These hemorrhages struck both sides of her brain and left the 42-year old mother of three permanently impaired. She could no longer drive and had to use a wheelchair, but more difficult were the significant emotional and personality changes.

As they learned to manage the new reality, the siblings built stronger bonds among themselves and learned to manage their new lives with a renewed sense of strength and compassion. And as they moved into professional lives and families

of their own, they realized a common vision of helping others similarly affected.

On September 8, 2016 they hosted "Let's Put Our Head's Together for Brain Research Foundation" at the Godfrey Hotel. Over 200 colleagues, friends and supporters attended and together they raised almost \$25,000 to fund neuroscience research.

Many members of the audience were so impressed with the innovative research that BRF funds that the seeds of a new idea were planted. Six months later we are proud to announce the formation of the **Brain Research Foundation Young Leadership Board**. Their first meeting took place in February and a schedule of events with locations and topics geared toward a younger audience is being developed. Already they determined that they would make



From left to right: Jon Shapiro, Dr. Terre A. Constantine, Lauren Shapiro-Mandel, Joe Shapiro. Pictured at "Let's Put Our Heads Together." © Bob Carl Photo

"Let's Put Our Head's Together for Brain Research Foundation" an annual event and have scheduled it for Thursday, September 7th at the Godfrey.

Stay tuned for more information, more updates and more great stories from this dynamic board of young professionals.

Brain Research Foundation Young Leadership Board

Lauren Mandel, *Co-Chair*
Joe Shapiro, *Co-Chair*
Jon Shapiro, *Vice Chair*
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Emily Golin
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Once again, BRF has been designated a Four Star Charity.

Four Stars from Charity Navigator means Brain Research Foundation is consistently managed with best practices in place, exceeding nonprofit industry standards.

Lab Notes

2017 Scientific Innovations Award Program Grants \$450,000 to Advance Neuroscience Research.

Federal funding for exploratory research can be extremely difficult to obtain. Brain Research Foundation helps to fill the funding gap so breakthrough projects like these can get off the ground.

Our ultimate goal is to facilitate the discovery of new scientific knowledge that will result in improved treatments and cures for neurological diseases.



Schahram Akbarian, M.D., Ph.D., Icahn School of Medicine at Mount Sinai

Brain Research Foundation awarded our 6th annual Scientific Innovations Awards (SIA), a grant program that provides funding for innovative science in basic and clinical neuroscience. This year we are pleased to award a total of \$450,000. Three distinguished scientists were selected to receive the two-year grants for \$150,000 each.

The SIAs were established to provide funding and support for creative, exploratory, and cutting edge neuroscience in recognized research laboratories under the direction of established investigators. Brain Research Foundation's Scientific Review Committee, consisting of neuroscientists from various institutions throughout greater Chicago and the nation, reviewed the SIA proposals and made recommendations for funding to the Brain Research Foundation.

Following is the research that our SIAs are funding.

Schahram Akbarian, M.D., Ph.D., Icahn School of Medicine at Mount Sinai

Retrospective Neurogenomics in the Mouse

Applications: cognition, psychiatric disease, artificial epigenetic tag, retrospective genomics

Brain function and behavior is heavily shaped by past experiences and exposures. Furthermore, very often neurological or psychiatric disease becomes manifest only many months or years after the initial stressor was encountered. Adaptive or maladaptive changes of the epi- (Greek for 'over', 'above') genome, broadly defined as structure and spatial organization of the chromosomal material inside the cell nucleus, are thought to play a key role for long term changes in behavioral plasticity and cognition, but are very difficult to assess. Therefore, the field would greatly benefit from a molecular

toolbox that allows for retrospective assessment of genome organization and function dating back many months prior. With BRF support, **Dr. Schahram Akbarian** will test and develop a toolbox for 'Retrospective Functional Genomics' (RFG) in the mouse.

Edward Callaway Ph.D., The Salk Institute

Epigenetic Mechanisms Linking Cerebral Cortical Cell Types to Gene Expression and Connectivity

Applications: autism, epigenetics, schizophrenia, neuronal connectivity

Many neural circuit disorders such as autism and schizophrenia are thought to arise from interactions between predisposing genetic factors, experience and the environment. There is extensive evidence that experience influences development of brain circuits, but the mechanisms by which these influences interact with genetics (epigenetics) are poorly understood. Through BRF-funded research, **Dr. Edward Callaway's** lab is investigating correlations between the connections of brain cells and their "epigenetic profiles." Understanding such correlations will lay a foundation for future mechanistic studies that explore how genetics, cell fate and neuronal connectivity all interact with



Edward Callaway Ph.D., The Salk Institute

environmental influences and experience to give rise to normal brain connectivity and function.

BRF's Scientific Review Committee

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University of Iowa

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Marina Picciotto
Yale University

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

BRF's Scientific Review Committee (SRC) was established to identify the most innovative neuroscience research projects. This committee is comprised of researchers from institutions nationwide. Their scientific expertise is invaluable when reviewing BRF research grant proposals.

Dr. Steve Goldman joins our Scientific Review Committee



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

We are pleased to welcome Dr. Steve Goldman to the SRC. Dr. Goldman's expertise will continue to strengthen the committee as it looks for the most innovative neuroscience projects to support.

Dr. Goldman is Professor of Neuroscience and Neurology at both the University of Copenhagen Faculty of Health, and the University of Rochester Medical Center (URMC). At Copenhagen, he co-directs its Center for Basic and

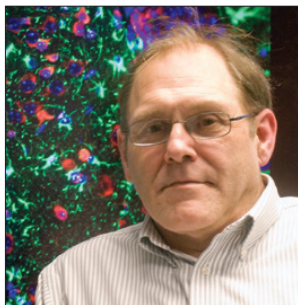
Translational Neuroscience. At Rochester, he is the URMCDistinguished Professor of Neuroscience and co-directs its Center for Translational Neuromedicine. Dr. Goldman is interested in cell genesis and neural regeneration in the adult brain, with a focus on the use of neural stem and progenitor cells in treating demyelinating and neurodegenerative diseases. His lab focuses on the use of stem and progenitor cells for the treatment of neurodegenerative disorders such as Huntington's disease, as well as for the treatment of glial diseases such as the pediatric leukodystrophies and multiple sclerosis. He also has a strong interest in the conversion of resident cells into brain cancers, and is board certified in neuro-oncology. Goldman has published over 200 papers in his field. Dr. Goldman remains active clinically, with subspecialty interests in stroke, myelin disease and neuro-oncology, and he is the program director for Rochester's neuro-oncology fellowship. He serves on standing committees of the NIH, and is a voting member of the FDA Cellular, Tissue and Gene Therapy Advisory Committee.

James Eberwine, Ph.D., University of Pennsylvania

Single Mitochondrion Analysis and Engineering for Human Neurological Disease

Applications: mitochondrial mutations, Alzheimer's disease, Parkinson's disease

Mitochondria provide energy to cells. Mutations of the mitochondrial genome, contribute to pathologies such as cancer, aging and neurodegeneration. While mammalian genome engineering has been performed for decades, mitochondria engineering has been hindered by lack of knowledge of individual mitochondrial differences. Additionally, it hasn't been possible to easily modify genes in the mitochondria to assess the biological consequences of such changes. Even if modification were possible, there are hundreds of mitochondria in a cell, making it difficult to modify all mitochondria in the same way. **Dr. James Eberwine** is using his BRF SIA to identify novel approaches to overcome these issues, providing a technical and theoretical framework to create therapeutic mitochondria to treat neurological illnesses. In particular he will detect, quantify and functionally evaluate single mitochondrion DNA mutations in neurons. It is hoped that new insights into the roles mitochondria play in modulating neuronal cell functioning and dysfunction during disease become apparent.



James Eberwine, Ph.D., University of Pennsylvania



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Save These Dates!

4.7.17 | Neuroscience Day

Friday, April 7
Poster Presentations 9-11 a.m.
Lectures 11 a.m. - 4 p.m.
All events are free and open to the public
Northwestern University Lurie Research Center

9.7.17 | Let's Put Our Head's Together for Brain Research Foundation

Thursday, September 7
6:30 - 8:30 p.m.
Tickets include open bar and a raffle ticket.
The Godfrey Hotel

10.12.17 | 2017 Discovery Dinner

Thursday, October 12
6-9 p.m.
Reservations start at \$500 and tables
start at \$5,000
The Ritz-Carlton Chicago

For more information on events and to
purchase tickets call Sandra Jaggi at
312.759.5157.