2019 CURE Program Accomplishments:

CURE Background:

Citizens United for Research in Epilepsy (CURE), is the leading nongovernmental agency fully committed to funding research in epilepsy. CURE's mission is to find a cure for epilepsy, by promoting and funding patient-focused research.

The organization was founded by Susan Axelrod and a small group of parents of children with epilepsy who were frustrated with their inability to protect their children from seizures and the side effects of medications. Unwilling to sit back, they joined forces to spearhead the search for a cure.

Since its inception in 1998, CURE has raised more than $70 million to fund epilepsy research and other initiatives that will lead the way to cures for the epilepsies. CURE awards grants for novel research projects to prevent epilepsy related to post-traumatic epilepsy, advancing the search for a cure, eliminating treatment side effects, and reversing deficits caused by frequent seizures. CURE funds grants for young and established investigators and to date has awarded more than 230 cutting-edge projects in 15 countries around the world.

CURE has led a dramatic shift in the epilepsy research community from simply treating seizures to enhancing understanding of underlying mechanisms and causes, so that cures and preventative strategies can be found. CURE's research program is cutting-edge, dynamic and responsive to new scientific opportunities and directions through both investigator-initiated grants and unprecedented scientific programs and initiatives.

2019 Financial Metrics:

Total Revenue	$7,518,776
Total Expenses	$6,272,194
Awareness	$1,004,242
Research	$4,339,296
Program Expenses	$5,343,538
Fundraising	$497,829
Administration	$430,827
12/31 Net Assets	$6,880,437

CURE Officers:

Beth Dean - Chief Executive Officer

Laura Lubbers – Chief Science Officer

John Anderluh – Chief Financial Officer

CURE Board of Directors:

Stacey Piggott – Chair

Kathy McKenna – Treasurer

Kelly Cervantes – Secretary

Other Board Members – Ann Benschoter, Marilynn Kelly Gardner, Celia Pohani Huber, Mike Axelrod, David Reifman, Lisa Cotton, Blake Cunneen

Program Research Focus Areas:

Epilepsy Genetics Initiative:

Made possible by a generous contribution from the John and Barbara Vogelstein Foundation, Epilepsy Genetics Initiative (EGI), a Signature Program of CURE, is advancing our understanding of the genetic causes of epilepsy. The vision is to improve the ways we prevent, diagnose, and treat this devastating disease. EGI is an initiative created to bridge the gap between people with epilepsy, clinicians, and researchers, and to advance precision medicine in epilepsy. EGI's centralized database holds the genetic (exome) data of people with epilepsy, and the data will be analyzed and reanalyzed until the cause of the patient's epilepsy is found. Findings will then be reported to the patient's treating physician and the data will be made available to advance cutting-edge research projects.

See "Our Research/Signature Programs" on our website for further details

Post-Traumatic Epilepsy:

With the help of a $10 million grant from the U.S. Department of Defense, CURE has implemented a research program focusing on post-traumatic epilepsy as a result of traumatic brain injury (TBI). This multi-disciplinary program devotes significant resources towards research benefiting veterans affected by traumatic brain injury (TBI) and resulting post-traumatic epilepsy (PTE). The goal of CURE's PTE Initiative is to establish a multi-center, multi-investigator research team to improve ways to study PTE in a laboratory setting, develop biomarkers, and understand risk factors that will help us predict who will develop PTE following TBI. In this way, we will lay the groundwork for the creation of novel therapies to prevent the development of PTE.

CURE's PTE Initiative assembles thought leaders in the field to address questions with a peer-reviewed approach. An External Advisory Council also provides scientific and logistical oversight over the selected investigative team. As science drives the initiative, it adapts to make outcomes as impactful as possible, with the key aim of positively affecting the lives of those affected by TBI and PTE.

See "Our Research/Signature Programs" on our website for further details

Sudden Unexpected Death in Epilepsy:

Sudden Unexpected Death in Epilepsy (SUDEP), which occurs when a seemingly healthy person with epilepsy dies for no known obvious reason, is perhaps the most devastating possible consequence of epilepsy. SUDEP can happen to anyone with epilepsy, although certain individuals are at a greater risk. While certain steps can be taken to reduce this risk, there is a critical need for continued SUDEP research to understand the underlying mechanisms in order to prevent SUDEP.

In response to bereaved families looking for answers, CURE, in 2004, launched the first ever private US research program dedicated to advancing understanding of SUDEP and its prevention. Since this time, CURE has supported over 40 investigators who have dramatically changed our understanding of this phenomenon. Simultaneously, CURE, in partnership with families, other non-profits and governmental agencies, have created a strong movement driving research, awareness, advocacy and increased funding to tackle this problem. CURE remains committed to unraveling the mysteries of SUDEP. We will continue to work closely with families and the research community to identify pressing needs while pushing for innovative solutions that ultimately lead to SUDEP prevention.

See "Our Research/Signature Programs" on our website for further details

Infantile Spasms Initiative:

Infantile spasms is a rare and particularly severe epilepsy syndrome that typically begins within the first year of life. Infantile spasms is characterized by subtle seizures which can have large neurological effects and an atypical EEG pattern; these symptoms can lead to large developmental delays and cognitive and physical deterioration.

The exact mechanisms underlying infantile spasms are not completely understood.

Sadly, many primary care doctors and parents alike are not familiar with the signs and symptoms of infantile spasms. So, many children with infantile spasms do not receive treatment during the critical window within the weeks and months after the emergence of symptoms. Many other children do not respond to available treatments for infantile spasms or these treatments have substantial adverse side effects, giving these children a dire prognosis.

CURE has made infantile spasms research an important part of our mission to address gaps in the field. Since 2011, CURE has funded cutting-edge infantile spasms research, and in 2013 awarded grants to a team of investigators through a groundbreaking, multidisciplinary 'team science' initiative to advance front-of-the-line research to find a cure for infantile spasms.

See "Our Research/Signature Programs" on our website for further details

2019 Research Grant Awards

2019 CURE Epilepsy Awards: Two-year, $250,000 awards focusing on scientific advances that have the potential to truly transform the lives of those affected by epilepsy, with prevention and disease modification as critical goals. Priority areas include: 1) Basic mechanisms of epilepsy, 2) Acquired epilepsies, 3) Pediatric epilepsies, 4) SUDEP, and 5) Treatment-resistant epilepsies.

Genetic-Based Cardiac Arrythmia as a Risk Factor for SUDEP

Christopher Reid, PhD

Florey Institute, Australia

There is evidence suggesting that a combination of epilepsy and changes in genes associated with heart conditions could increase the risk of Sudden Unexpected Death in Epilepsy (SUDEP). This has been difficult to test in humans. Associate Professor Chris Reid and his team will develop new rodent models which replicate having both epilepsy and a genetic heart abnormality, and compare these for incidence of SUDEP against existing models. This novel work could identify key risk factors for this frightening condition and provide the starting point for treatment.

Investigating the Role of Aberrant Methylation in the Etiology of Developmental and Epileptic Encephalopathy

Heather Mefford, MD, PhD

University of Washington

Developmental and epileptic encephalopathies (DEE) are severe, early-onset epilepsy disorders associated with developmental delays and seizures that are often difficult to treat. Clinically, a genetic cause can be identified in 40-50% of cases, providing a precise diagnosis, improving prognosis and recurrence risk counseling, connecting families to gene-based support groups, and facilitating investigation of precision therapies. However, more than 50% of patients with DEE remain without a genetic diagnosis despite state-of-the-art genetic testing.

In this study, Dr. Mefford and her team, will search for a different type of causative change – abnormal methylation which is a type of chemical modification of DNA in a large set of individuals with DEE without a known cause. Abnormal methylation has been identified as a cause in other human disorders but has not been explored much in epilepsy. As they identify novel methylation changes associated with DEE, they will perform additional studies to understand why certain methylation changes lead to epilepsy, and will develop clinical tests that can be used to diagnose affected individuals.

Therapeutically Targeting Brain Invading Monocytes to Prevent the Deleterious Consequences of Status Epilepticus

Nicholas Varvel, PhD

Emory University

Status epilepticus (SE) is a frequent neurological emergency. These unabated seizures reduce quality of life, promote the development of epilepsy, and can cause death.

Dr. Varvel and his team identified a blood-borne immune cell, called a monocyte, which invades the

brain after seizures, and contributes to damage and inflammation. They discovered that monocytes are pathogenic after SE, elevating brain inflammation, increasing neuronal damage, and contributing to morbidity. For their project, Dr. Varvel and his team are interested in using a small drug to block monocyte entry in mouse brains after SE. They propose to determine the feasibility of this approach in humans to relieve the effects of seizures and prevent the development of epilepsy and associated behavioral impairments.

2019 Taking Flight Awards: One-year, $100,000 awards that promote the careers of young epilepsy investigators, allowing development of a research focus independent of their mentor(s). We encourage studies that will provide new directions for epilepsy therapy, prevention, and ultimately a cure, and that will allow applicants to collect the data necessary to support a further funding by the National Institutes of Health (NIH) or other agencies.

Identification of Pathophysiology and Genetic Mechanisms of SUDEP Using an Innovative Genetic Reference Population of Collaborative Cross Mice

Bin Gu, PhD

University of North Carolina at Chapel Hill

SUDEP is the sudden, unexpected death of someone with epilepsy who otherwise appeared healthy. The substantial lifetime risk of SUDEP and the lack of a clear cause have increased attention to this unpredictable cause of death. Understanding the cause of SUDEP is paramount to developing preventive strategies.

Animal models offer a means to study SUDEP in a controlled environment, in addition to providing a level of experimental testing and validation that is not possible or ethical in human subjects. By utilizing a unique resource of genetically diverse mice Dr. Gu aims to identify genes that control SUDEP susceptibility. By using genetic and electrophysiological techniques, Dr. Gu is also interested in understanding the physiological changes that can act as SUDEP triggers. These goals will further our understanding of the causes of SUDEP and will ultimately help lead to its prevention.

A reverse genetic screen using CRISPRi and calcium fluorescence to identify novel seizure resistance genes in zebrafish

Chris McGraw, MD, PHD

Children's Hospital of Boston

Epilepsy that remains poorly controlled despite multiple trials of antiepileptic drugs (AEDs) is widely considered the greatest therapeutic challenge in the field of epilepsy today, and there is a crucial need to identify new drugs that work better and have fewer side-effects. Dr. McGraw is developing a system

in larval zebrafish that integrates the latest advances in genetic engineering (Crispr/Cas9) and non-invasive monitoring of neural activity (genetically encoded calcium sensors) to enable a rapid whole-genome screen for genes that enhance seizure resistance. Dr. McGraw predicts that if we systematically identify genes that enhance seizure resistance in an animal model, many of these genes and their protein products could serve as targets for the next generation of anti-epileptic drugs in human patients.

Post Traumatic Initiative Awards: Funded out of a $10 million grant from the U.S. Department of Defense, these are research programs that focus on post-traumatic epilepsy (PTE) as a result of traumatic brain injury (TBI)

Genetic and Protein Biomarkers of Post-Traumatic Epilepsy to Improve Prediction of PTE: A Prospective Study in an Enriched Patient Population

Pavel Klein, MD

Mid-Atlantic Epilepsy and Sleep Center, LLC

Post-traumatic epilepsy does not develop until weeks or years after a traumatic brain injury, offering a window of opportunity for preventative treatment. However, it is currently not possible to predict who will develop epilepsy following a traumatic brain injury, nor do any preventative measures exist. In fact, there are currently no clinical studies being conducted that seek to prevent the development of post-traumatic epilepsy, despite the availability of a number of approved drugs with antiepileptogenic properties. A major reason for the lack of clinical trials in this area is the relatively low rate and unpredictability of post-traumatic epilepsy among individuals with a traumatic brain injury, making such studies large and costly.

Dr. Pavel Klein and his team seek to address this problem by examining a group of “high-risk” patients with a greater chance of developing post-traumatic epilepsy. Using this group of individuals, Dr. Klein and his team will search for biomarkers for the development of post-traumatic epilepsy by determining if there are indicators that can be measured in the EEG signature, MRI or blood that might predict increased risk of a person developing post-traumatic epilepsy. By identifying ways to identify individuals most at risk of developing post-traumatic epilepsy, the team will pave the way for the development of therapies to prevent its development in the first place.

Targeting Epileptogenic Effects of Subarachnoid Blood in TBI

Dr. Jeffrey Loeb

University of Illinois, Chicago

A major challenge to the study of post-traumatic epilepsy (PTE) is that there are vast differences in the types of traumatic brain injury (TBI) that can lead to epilepsy, including blows to the head, blasts, and penetrating brain injuries. To better understand and prevent epilepsy following TBI, it is essential to

understand common changes in the brain that might lead to PTE.

Dr. Jeffrey Loeb and his team have chosen to focus on studying subarachnoid hemorrhage, or bleeding in the space between the brain and the tissue surrounding the brain, a phenomenon that commonly occurs following a brain injury. In fact, in both animals and humans, subarachnoid hemorrhage occurs in almost all severe TBIs and is known to produce seizures. By examining patients with subarachnoid hemorrhage and an animal model of subarachnoid hemorrhage, the Loeb team will use methods such as MRI and EEG to characterize the development of PTE with the aim of understanding and predicting who is at risk for developing this condition and identifying potential treatment strategies.

2019 CURE Sponsored Research Conferences:

Park City Epilepsy Meeting

Sunday, October 6, 2019

This unique meeting hosted by the University of Utah brings trainees, junior investigators, and established researchers together with leaders in the field of epilepsy research! Presenters will discuss cutting-edge approaches to transforming epilepsy therapy, exploring state of the art neuroscience as it is being applied to therapy development.

The organizing committee has assembled an outstanding group of speakers – including many former and current CURE Grantees – and provided an agenda that will provide a unique venue for interaction, discussion, and building collaborations in the spectacular Wasatch Mountain setting of Utah.

Day of Science: Epilepsy Conversations in Orange County

Saturday, September 21, 2019

Day of Science: Epilepsy Conversations is a free, educational event for patients, families, medical professionals, researchers, and all those touched by or interested in learning more about epilepsy. Join us as doctors and researchers answer your questions on the latest research as it relates to new epilepsy treatment options, surgery, genetics, and more.

Day of Science: Epilepsy Conversations features:

- A panel of epilepsy experts discussing your questions on the latest in epilepsy research and what it means for patients and families.
- Q&A sessions and small roundtable discussions with epilepsy experts over lunch
- Information on cutting-edge therapies and treatments
- The opportunity to engage with other families and advocacy groups in the epilepsy community
- Morning refreshments and a provided lunch

8th Eilat International Educational Course: Pharmacological Treatment of Epilepsy

Sunday, September 8, 2019

The course is held under the auspices of the ILAE Europe. The program is designed for junior researchers and clinicians (45 years and younger) working in the field of epilepsy treatment and related basic research. It is open to young neurologists, neuropediatricians, pharmacists, pharmacologists, neuropsychologists and neuroscientists. A number of bursaries have been made available towards partially defraying the cost of accommodation expenses of bursary recipients, who will also have their registration fees waived.

Gordon Research Conference (GRC) on Inhibition in the Central Nervous System

Sunday, July 7, 2019

The 2019 GRC on Inhibition in the CNS aims to increase our understanding of the spatio-temporal control of inhibitory signaling in normal and pathological CNS function. The scientific sessions will focus on the developmental diversification of inhibition, synaptic plasticity, technical. The sessions will also discuss conceptual challenges to capturing GABAergic diversity, and inhibitory circuit control underlying normal behaviors and CNS disorders.

A New Focus Topic special emphasis session will explore the implications of recent discoveries that a large part of CNS myelin is on specific sets of GABAergic axons, with discussions encompassing bidirectional glia-interneuron communication and their relevance to pathological states.

The conference will feature an unusually high number of opportunities for graduate students and postdoctoral trainees to interact with the invited speakers and other conference participants. Such opportunities will include, in addition to the traditionally well-attended poster sessions, a new mentee-mentor pairing program offering pre-arranged meetings between individual trainees and assigned senior investigators during Monday lunch, and short talks every morning by junior investigators selected from abstract submissions. In addition, for the first time in the history of this GRC, a Power Hour will be held on Monday afternoon to provide an open forum to support the professional growth of women by discussing the challenges women face in science.

The conference will offer in-depth, high-quality scientific discussions aimed at deepening our understanding of the mechanisms of inhibition in CNS function and dysfunction in a collegial, inclusive atmosphere with substantial time for interactions among all participants to accelerate the forging of novel, impactful collaborations to test transformative new ideas.

STXBP1 Investigators and Family Meeting (SIFM)

Saturday, June 22, 2019

The inaugural STXBP1 Investigator and Family Meeting held on **June 21, 2019** and **June 22, 2019** will bring together researchers and families of individuals with STXBP1 encephalopathies, foster development of the STXBP1 community and accelerate the search for a cure.

STXBP1 has become one of the more commonly diagnosed genetic causes of epileptic encephalopathy in children, accounting for 5% of positive epilepsy cases in a recent study. This conference is designed to foster interaction and in-depth discussions among researchers and clinicians to further research and innovation in this field. The meeting will also provide opportunities for researchers and the patient community to connect. The goal is to develop a research strategy and scientific roadmap

for the STXBP1disorder, and to encourage collaborations and initiatives to support achievement of the roadmap and advancement in the field.

Friday, June 21 will be dedicated to Investigators ONLY and will be held at CHoP. This is where Investigators will have the opportunity to present STXBP1 research and interact with other scientists studying the gene. Investigators will have a chance to interact with our families during the banquet and poster session that night.

On Saturday, June 22, our sessions will be held at the Sheraton University Center and here is where parents, family, and other caregivers will have an opportunity to learn about research that is built and presented for the non-scientific community.

Your participation at the SIFM is invaluable to the STXBP1 Foundation as discussions and information gleaned will assist the Foundation and the Scientific Advisory Board to build a scientific roadmap. This output will inform future decisions and drive future investments by the STXBP1 Foundation. Through this interaction we hope to drive research in a manner that has the greatest potential to provide better therapies and ultimately, a cure.

Other 2019 CURE Focused Programs:

EDUCATION ENRICHMENT FUND SCHOLARSHIP

This program is a one-time scholarship (up to $5,000) for those living with epilepsy, family members, or caregivers. These scholarships support coursework in scholars' chosen fields, so they can use their knowledge and skills to become agents of change in the epilepsy community. In 2019, ten scholarships were awarded that are detailed on our website.

SEIZING LIFE

Seizing Life® is a CURE podcast and videocast aiming to inspire empathy, offer helpful stories, and give hope as we search for a cure for epilepsy. Listen as guests share stories and insights on living with and battling epilepsy. In 2019, 25 individual programs were completed. Please visit our website to see what topics were covered and watch items of interest.

WEBINARS

Epilepsy experts discuss cutting-edge discoveries, research, and treatments in this free webinar series.

Available 2019 Webinars (see our website for more details):

- Epilepsy Rescue Medication Delivery Methods and Future Therapies
- Epilepsy Emergencies and Current Rescue Medication
- Epilepsy Surgery: Advancements, Options and Considerations
- Epilepsy and Dietary Therapies: How What You Eat May Help Control Seizures
- Transitioning from Pediatric to Adult Epilepsy Care
- Epilepsy, Pregnancy and Contra