

## 2021 CURE Epilepsy Program Service Accomplishments:

### CURE Epilepsy Background:

Citizens United for Research in Epilepsy (CURE Epilepsy), is the leading nongovernmental agency fully committed to funding research in epilepsy. Our 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 Epilepsy has raised more than \$85 million to fund epilepsy research and other initiatives that will lead the way to cures for the epilepsies. CURE Epilepsy awards grants for novel research projects to prevent epilepsy related to pediatric epilepsy, post-traumatic epilepsy, treatment-resistant epilepsies, Sudden Unexplained Death in Epilepsy (SUDEP), Jeavons Syndrome and sleep and epilepsy advancing the search for a cure, eliminating treatment side effects, and reversing deficits caused by frequent seizures. CURE Epilepsy funds grants for young and established investigators and to date has awarded more than 270 cutting-edge projects in 17 countries around the world.

CURE Epilepsy 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.

### 2021 Financial Metrics:

|                  |                    |
|------------------|--------------------|
| Total Revenue    | \$6,349,208        |
| Total Expenses   | \$5,884,336        |
| Awareness        | \$962,652          |
| Scholarships     | \$50,000           |
| Research         | <u>\$4,070,075</u> |
| Program Expenses | \$5,082,727        |
| Fundraising      | \$495,928          |
| Administration   | \$305,681          |
| 12/31 Net Assets | \$7,371,739        |

## **CURE Officers:**

Beth Dean - Chief Executive Officer

Laura Lubbers – Chief Science Officer

John Anderluh – Chief Financial Officer

## **CURE Board of Directors:**

Kelly Cervantes – Chair

Stacey Pigott – Immediate Past Chair

Kathy McKenna – Treasurer

Mike Axelrod – Secretary

Other Board Members – Marilyn Gardner, David Reifman, Lisa Cotton, Shalee Cunneen, Kimberly Borden, Carrie Garman, Matt Schneider & Brian Gorczynski

## **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 Epilepsy, 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 Impact/Signature Programs" on our website for further details & findings*

### **Post-Traumatic Epilepsy:**

With the help of a \$10 million grant from the U.S. Department of Defense, CURE Epilepsy 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 Epilepsy'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 Epilepsy'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 Impact/Signature Programs” on our website for further details & findings*

#### **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 Epilepsy, in 2004, launched the first ever private US research program dedicated to advancing understanding of SUDEP and its prevention. Since this time, CURE Epilepsy has been the leading private funder of SUDEP research, supporting over 40 investigators who have dramatically changed our understanding of this phenomenon. Simultaneously, CURE Epilepsy, 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 Epilepsy 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 & findings*

#### **Infantile Spasms Initiative:**

Infantile spasms are a rare and particularly severe epilepsy syndrome that typically begins within the first year of life. Infantile spasms are 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 Epilepsy has made infantile spasms research an important part of our mission to address gaps in the field. Since 2011, CURE Epilepsy 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. Collectively, the investigators studied the basic biology underlying IS, searched for biomarkers as well as novel drug targets, and developed improved treatments.

*See “Our Impact/Signature Programs” on our website for further details & findings*

## 2021 Research Grant Awards

In 2021, CURE Epilepsy awarded \$3.0 million in 16 research grants across our portfolio of research opportunities.

**1) 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, 5) Treatment-resistant epilepsies and 6) Sleep and Epilepsy

### Cardiac and Autonomic Pathological Markers for Arrhythmias and Sudden Unexpected Death in Epilepsy Patients

David Auerbach, PhD

SUNY Upstate Medical University

People with epilepsy are at a high risk of sudden death (e.g., SUDEP). Current SUDEP risk factors are not linked to the proposed biological causes for SUDEP. There is a higher prevalence of cardiac electrical abnormalities in people with epilepsy, and arrhythmias or irregular heart rhythms are reported to precede cases that almost result in SUDEP.

Dr. Auerbach's team will use analytical tools that are well accepted in the cardiac field, but new to the field of epilepsy and SUDEP, to identify epilepsy patient populations at risk of cardiac arrhythmias. Additionally, his team will test whether these tools identify people with epilepsy who later died of SUDEP. The team's long-term goal is to develop a comprehensive SUDEP risk assessment tool based on markers for each of the proposed biological causes of SUDEP, including cardiac arrhythmias.

Dr. Auerbach's grant has been generously funded by The Cameron Boyce Foundation with The CURE Epilepsy Cameron Boyce SUDEP Research Award.

# Systems Biology-Derived Treatment of Status Epilepticus and Epileptogenesis After Traumatic Brain Injury

Asla Pitkänen, MD, PhD

University of Eastern Finland, Kuopio Campus

Traumatic brain injury (TBI) is a major cause of epilepsy in adults. Gene expression is the process a cell uses to produce the molecule it needs by reading the genetic code written in the DNA.

Dr. Pitkänen and her team studied changes in gene expression in brain tissue from an animal model of TBI. They identified potential drug-like compounds that might reverse or prevent these changes. The goal of this project is to assess whether the most promising of these compounds, either alone or in combination with an anti-seizure treatment, will prevent the development of epilepsy in an animal model of post-traumatic epilepsy. As the seizures in the animal model typically occur during sleep, the team will also assess whether alleviation of sleep disturbances will have an anti-epileptogenic effect.

## Sleep and Epilepsy Interactions – Uncovering Mechanisms

Nigel Pedersen, MD

Emory University

There is a long-recognized link between epilepsy and sleep-wake states. Many patients have seizures that occur at a specific time of day or in relation to sleep or the daytime.

Dr. Pedersen's team is studying whether brain regions that control sleep-wake also control seizures. For this project, the team will directly study electrical activity in parts of the brain that control sleep and wakefulness, and brain regions involved in seizures. They will utilize new methods to determine exactly which brain cell types are involved in this strong relationship between sleep-wake and epilepsy. This work will develop open-source tools for further studies by the epilepsy community, helping to uncover new strategies to treat epilepsy and its comorbidities.

## Finding new therapies for epileptic encephalopathies by employing knowledge from rare genetic diseases

Stefan Barakat, MD, PhD

Erasmus University Medical Center, Rotterdam, the Netherlands

Epileptic encephalopathies are severe genetic disorders resulting in intractable seizures and pronounced developmental delay. Current treatment is mainly supportive and aims to prevent symptoms. Tailored therapies that directly modulate the biological pathways leading to disease, instead of simply repressing symptoms, are urgently needed to improve therapies and possibly find future cures for epileptic encephalopathies.

Dr. Barakat's studies have identified a number of genes involved in biological pathways that were previously not implicated in epilepsy. For this project, his team will use human cell models and zebrafish to develop novel therapies for epileptic encephalopathy by targeting metabolic processes implicated in these pathways.

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**2) 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).

## Predicting Epileptogenesis with Invasive and Non-Invasive Brain Stimulation Evoked High Frequency Oscillations in Humans

Rina Zelman, PhD

Massachusetts General Hospital

Identification of individuals at risk of developing epilepsy remains a major challenge. Accurate prediction of who will develop epilepsy after a first seizure or brain injury could expedite treatment and prognosis might improve. High frequency oscillations (HFOs), a type of electrical activity in the brain, could potentially be used to identify brain regions responsible for seizure generation and might also be used to predict development of epilepsy. However, HFOs are hard to detect from the scalp and are not yet part of routine clinical diagnosis.

Dr. Zelman proposes to generate HFOs by repeated mild stimulation of the brain through the scalp, which may enhance the ability to detect HFOs. Ultimately, this could pave the way toward a quick and relatively easy test to generate scalp HFOs and help predict epilepsy in outpatient clinics.

## Harnessing Neuromodulation to Target Peri-ictal Dysfunction in Epilepsy

Joanna Mattis, MD, PhD

University of Pennsylvania

A seizure is a sudden burst of uncontrolled electric disturbance in the brain. How can this pattern arise abruptly from normal activity? In other words, how do seizures start? This fundamental question remains unanswered despite decades of research.

Dr. Joanna Mattis will study neuromodulatory neurons which are “master regulators” that control many functions in the brain. These neurons are located deep within the brain but connect with seizure-prone brain regions. Dr. Mattis will test whether these neurons coordinate the transition between normal brain activity and seizures, and whether activating these neurons can be therapeutic in epilepsy.

## The Gut Microbiota and Derived Metabolites Affect the Development of Epilepsy

Ana Beatriz DePaula-Silva, PhD

The University of Utah

Inflammation caused by viral infection of the central nervous system is associated with seizures and epilepsy but how inflammation can lead to seizures is not fully understood. Recent studies found that the various bacterial species in the gut, collectively called the gut microbiota, can impact inflammation as well as brain function.

In this project, Dr DePaula-Silva will study a mouse model of epilepsy caused by a viral infection to identify specific gut bacterial populations and molecules produced by the bacteria that may play a role in protecting the animals from seizure development.

If successful, the knowledge obtained from this study will allow for the development of novel therapies, including modification of gut microbiota or of specific molecules, to treat and possibly cure seizures/epilepsy.

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**3) Catalyst Awards:** The CURE Epilepsy Catalyst Award (2 years / \$250,000) supports nimble development of data necessary to attract larger commercialization funding opportunities and is not intended to replace those opportunities.

## Safety and Efficacy of a Novel MicroRNA-Based Therapy for Epilepsy in a Translational Animal Model

Rodrigo Gutierrez-Quintana, MVZ, MVM, DipECVN, MRCVS

University of Glasgow

Current treatments for epilepsy work mainly by reducing brain excitability. They fail to control seizures in many patients and must be taken repeatedly. Dr. Gutierrez-Quintana and his team propose to test a completely new class of drug targets for epilepsy called microRNAs. Instead of changing brain excitability, these naturally occurring molecules coordinate signaling processes inside brain cells by controlling expression of various genes. The team has previously found that, in brain tissue from people with temporal lobe epilepsy, there was a consistent increase in the level of one of these molecules called microRNA-134. The team developed an inhibitor of microRNA-134, called Ant-134, that when injected into mice and rats significantly suppressed seizures. Remarkably, Ant-134 has been shown to have potent and long-lasting anti-convulsant effects in numerous rodent models after a single dose.

Dr. Gutierrez-Quintana's team will now test the effects of Ant-134 in a population of dogs with naturally occurring drug-resistant epilepsy, an important step towards translating their findings into treatments for humans. If successful, this project will pave the way for human clinical trials for a treatment that has the potential of providing long-lasting seizure control after a single dose and may be even cure some forms of epilepsy.

## Action of Nav1.6 and Nav1.2-Specific Sodium Channel Blockers on Seizures in a Mouse Model of Pediatric Epilepsy

Ruth Westenbroek, PhD

University of Washington

Dravet syndrome (DS) is caused by mutations in a specific type of protein called a sodium channel, and specifically, a protein called Nav1.1. These mutations impair the function of inhibitory neurons and alter the balance of excitation to inhibition, in favor of excitation. Many of the symptoms of DS are replicated in a genetic mouse model of the syndrome including thermally-induced seizures, spontaneous seizures, premature death, hyperactivity, severe cognitive impairment, and autistic-like behaviors.

Using their genetic mouse model of DS, Dr. Westenbroek's lab plans to test newly developed inhibitors that act on sodium channels called Nav1.6 and Nav1.2. These drugs may be beneficial over traditional sodium channel blockers with fewer side effects because they would specifically block sodium channels in excitatory neurons and improve the excitation-inhibition imbalance. With this grant, Dr. Westenbroek's team will test these drugs for efficacy on specific symptoms of DS such as thermally induced seizures, spontaneous seizures, and premature death. If these findings are validated, they could transform treatment of pediatric epilepsies by permitting development of improved therapeutic strategies for control of intractable seizures.

**4) Federal Grant Research:** Investment continued with our U.S. Department of Defense research program focusing on post-traumatic epilepsy. In total, we invested an additional \$1.1 million in post-traumatic epilepsy as a result of traumatic brain injury.

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**5) 2020 CURE Sponsored Research Conferences:** 2021 marked the return to CURE Epilepsy sponsoring conferences that bring together epilepsy researchers and enable learning opportunities and information sharing. During 2021, CURE Epilepsy provided sponsorship to four individual epilepsy focused conferences with an investment of \$30,000. We expect our sponsorship level to return to historical levels in 2022

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## **Other 2020 CURE Epilepsy Program Service Accomplishments:**

### **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 2021, ten scholarships were awarded for a total of \$50,000 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 2021, 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 2021 Webinars (see our website for more details):

- Post-Traumatic Epilepsy and Cognitive Training: Improving Quality of Life Through HOBSCOTCH
- SUDEP & The Heart: A Multi-System Approach to Understanding Electrical Disturbances
- Non-epileptic Seizures: Diagnosis, Treatment, and Management Strategies for Patients and their Families
- Aging and Epilepsy: Consequences and Comorbidities to Consider in Older Individuals
- Siblings and Severe Childhood Epilepsy: The Impact of Seizures on the Family's Mental Health
- Women's Health: Complex Interactions of Epilepsy, Medications, and Hormones

- International Disparities in Epilepsy Care: Social & Economic Effects of Epilepsy in Sub-Saharan Africa
- Cenobamate: A New Treatment Option for Partial-Onset (Focal) Seizures

## **CURE Epilepsy CARES Events**

At CURE Epilepsy *CARES (Conversations Around Research in Epilepsy & Seizures)* events, leading experts answer your questions about epilepsy.

These free events happen across the country each year to give those impacted by epilepsy and their families the chance to learn from researchers and local physicians in an encouraging environment.

## **Awareness**

CURE Epilepsy invested over \$960,000 in 2021 on Epilepsy Awareness. CURE Epilepsy believes Epilepsy Awareness is a critical vehicle to increase the amount of funding available for Epilepsy research and to share key learnings and opportunities for those impacted by Epilepsy. CURE Epilepsy creates, sponsors and leverages our website, webinars, seminars, podcasts, educational events and other digital communication to drive this critical awareness.

In 2021, a specific focus was investing in the information insights available on our website for epilepsy patients. Understanding Epilepsy Basics is a new tool for the epilepsy community made possible with the financial support of SK Life Science. Details can be found on our website at [\*\*“for patients/understanding epilepsy”\*\*](#).

In 2021, CURE Epilepsy also created an on-line store to help us provide opportunities for those familiar with all CURE Epilepsy does the opportunity to drive increased awareness of our mission and our impact. Check out our new store on our website at [\*\*“get involved/shop”\*\*](#).