THE LGS FOUNDATION

MEETING OF THE MINDS

FINDING DISEASE-MODIFYING THERAPIES FOR LGS

September 13-14, 2021 - Research Discussion
September 18, 2021 - Family Discussion

LGSFoundation.org

LGS FOUNDATION
LENNOX-GASTAUT SYNDROME

MEETING OF THE MINDS

FOR RESEARCHERS - SEPT. 13TH

SESSION 1

10am EST	***Opening Remarks & Introductions*** Tracy Dixon-Salazar, PhD
10:15am EST	***What We Know about LGS & Ongoing Questions*** **Moderators:** Heather Mefford, MD, PhD Ann Poduri, MD, MPH
10:30am EST	***History, EEG Features, & Clinical Findings in LGS*** Elaine Wirrell, MD
11am EST	***Causes of LGS*** Anup Patel, MD
11:30am EST	***What does better look like? Identifying and Measuring Meaningful Outcomes for LGS*** Anne Berg, PhD
12pm EST	***Current and Emerging Treatments in LGS*** James Wheless, MD
12:30pm EST	***Panel Discussion:*** *Where are the gaps in our understanding of LGS and what do we need to do to bridge those gaps?*
1pm EST	***Break (1 hour)***

SESSION 2

2pm EST	***How do we advance clinical research to understand the LGS network?*** **Moderators:** Eric Marsh, MD, PhD Brenda Porter, MD, PhD
2:15pm EST	***How we might map network dysfunction in LGS: Early Developmental Changes in the EEG and MRI that portend LGS*** Jurriaan Peters, MD, PhD
2:45pm EST	***How we might modulate network dysfunction in LGS: Important findings in Mapping and Modulating Networks*** Jennifer Gelinas, MD, PhD
3:15pm EST	***Specific Network changes in LGS*** John Archer, MD, PhD
3:45pm EST	***How we might predict who will develop LGS: Potential Biomarkers of the LGS Phenotype*** Zach Grinspan, MD, MS
4:15pm EST	***Break (15 mins)***
4:30pm EST	***Developing Novel Approaches to Clincial Trials for LGS*** Dennis Dlugos, MD
5pm EST	***Panel Discussion:*** *Where are the gaps in our clinical understanding of LGS and what do we need to do to bridge those gaps?*
5:30pm EST	***Happy Hour***

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MEETING OF THE MINDS

FOR RESEARCHERS - SEPT. 14TH

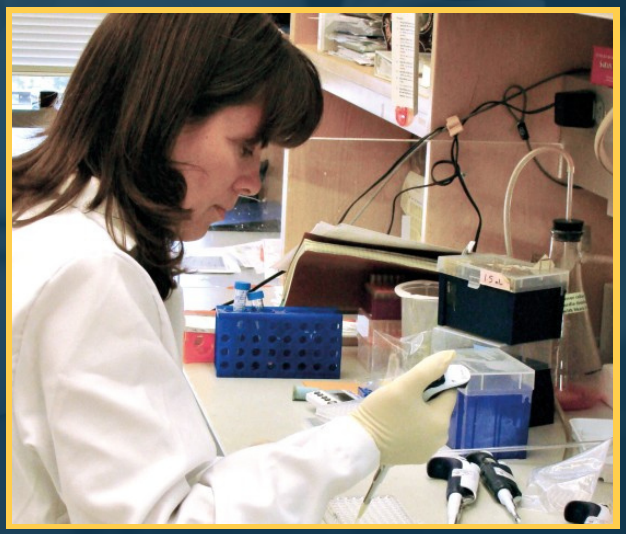
SESSION 3

10am EST	***Welcome Back*** Tracy Dixon-Salazar, PhD
10:15am EST	***Advancing Basic Research to Understand the LGS Network*** Scott Baraban, PhD
10:30am EST	***Organoids Modeling of Networks*** Allyson Muotri, PhD
11am EST	***Zebrafish Modeling of Networks and Relevance to LGS*** Megan Dennis, PhD
11:30am EST	***Rodent Modeling of Networks and Relevance to LGS*** Mingshan Xue, PhD
12pm EST	***Panel Discussion:*** *Where are the gaps in our understanding of LGS and what do we need to do to bridge those gaps?*
1pm EST	***Break (1 hour)***

SESSION 4

2pm EST	***What do we know? Where are the gaps? What can researchers, clinicians, families do to fill those gaps?*** **Moderators:** Eric Marsh, MD, PhD
2:15pm EST	***Clinical Research Needs on the LGS Network*** Comments by Martina Bebin, MD, MPA
3pm EST	***Basic Research Needs on the LGS Network*** Comments by Ivan Soltesz, PhD
3:45pm EST	***Translating LGS Network Research to Patients*** Comments by Jeff Noebels, MD, PhD
4:30pm EST	***Wrap-up and the Role of the LGS Foundation in Funding Research*** Tracy Dixon-Salazar, PhD

"This meeting is critical! This meeting will not only bring the research and family communities together but will help guide the LGS Foundation's research funding strategy as we seek disease-modifying therapies for LGS."
Tracy Dixon-Salazar, PhD



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MEETING OF THE MINDS

FAMILY DAY - SEPT. 18TH

What does a Disease-Modifying Therapy look like? The Patient Family Perspective

11am - 11:15am EST	***Welcome*** Natalie Gilmore *President, LGS Foundation*
11:15am - 12:15pm EST	***What we learned from the scientists at the LGS Research Meeting of the Minds*** Tracy Dixon-Salazar, PhD
12:15pm - 1:00pm EST	***Ask the Experts Breakout Session:*** Patient Family Experts
1:00pm EST	***Break (15 mins)***
1:15pm - 2:00pm EST	***Ask the Experts Breakout Session:*** Patient Family Experts
2:00pm - 2:30pm EST	***LGS Research: Next Steps*** Tracy Dixon-Salazar, PhD
2:30pm - 2:45pm EST	***Closing Remarks*** Natalie Gilmore *President, LGS Foundation*

MEET OUR MODERATORS

Heather Mefford, MD, PhD
St. Jude Children's Research Hospital
Heather Mefford is a Full Member of the Center for Pediatric Neurological Disease Research at St. Jude Children's Research Hospital. She runs a research laboratory dedicated to gene discovery in pediatric disease, with a major focus on pediatric epilepsies. Her work uses cutting-edge genomic technologies and has helped define the genetic landscape of epileptic encephalopathies with studies reporting novel copy number variants and numerous novel disease-causing genes. She identified and characterized several novel deletion and duplication syndromes due to recurrent CNVs. She was a co-PI for several of the Epi4K consortium projects and co-chairs the ClinGen Neurodevelopmental Disorder Clinical Domain Working Group and Epilepsy Gene Curation Working Group. She serves on the Professional Advisory Board for LGSF.

Ann Poduri, MD, MPH
Associate, Department of Neurology; Director, Epilepsy Genetics Program Professor of Neurology, Harvard Medical School
Boston Children's Hospital
Dr. Annapurna Poduri is a clinician-scientist focused on understanding the genetic causes of human epilepsy. She is a pediatric neurologist and the director of the Programs in Neurogenetics and Epilepsy Genetics at Boston Children's Hospital. Dr. Poduri's role is to evaluate the contribution of epilepsy and its genetics to sudden death. Dr. Poduri serves as an expert for the Department of Neurology for Boston Children's Hospital Precision Medicine Service.

Eric Marsh, MD, PhD
Pediatric Neurologist
Children's Hospital of Philadelphia (CHOP)
Dr. Marsh specializes in diagnosing and treating children with developmental epilepsies, epilepsy, infantile spasm, and malformations of cortical development. In addition to his role at CHOP, Dr. Marsh is an associate professor of neurology at the Perelman School of Medicine at the University of Pennsylvania. He serves on the Professional Advisory Board for LGSF.

Brenda Porter, MD, PhD
Professor of Neurology and of Pediatrics
Stanford University
Dr. Porter received her MD and Ph.D. from Washington University in St. Louis. She traveled east to complete her child neurology fellowship at the Children's Hospital of Philadelphia. She went on to complete a combined clinical and research fellowship in epilepsy. Dr. Porter developed an interest in difficult-to-treat epilepsy, with a special focus on children with neuronal developmental disorders leading to epilepsy such as tuberous sclerosis and focal cortical dysplasia. Her clinical research focuses on improving outcomes in epilepsy surgery, increasing parental understanding of epilepsy and the role epilepsy surgery plays in treatment. She serves on the Professional Advisory Board for LGSF.

Scott C. Baraban, PhD
Professor, Department of Neurological Surgery
University of California, San Francisco
Scott C. Baraban, Ph.D. is a Professor of Neurological Surgery and William K. Bowes Jr. Endowed Chair in Neuroscience Research at the University of California, San Francisco (UCSF). He obtained his Bachelor's degree from Johns Hopkins University (1983-87) and a Ph.D. in Pharmacology from the University of Virginia (1990-94). He trained as a postdoctoral fellow (1994-1997) with Phil Schwartzkroin at the University of Washington. A faculty member at UCSF since 1999, he directs the Epilepsy Research Laboratory in the Department of Neurological Surgery; a research program continuously funded by NIH for over 20 years.

MEET OUR SPEAKERS – DAY 1

Tracy Dixon-Salazar, PhD
Executive Director
LGS Foundation
Dr. Tracy Dixon-Salazar is a neuroscientist, geneticist, and patient advocate. Her desire to get her Ph.D. was inspired by her daughter, Savannah, who developed intractable seizures at the age of 2, which evolved into LGS by the age of 5. She did her Ph.D. and postdoctoral work at UC, San Diego, and during her research tenure, and after 16 years of watching daily, unrelenting seizures in her child, she uncovered the driver of her daughter's illness and identified a novel precision therapy that improved her child's life.

Elaine Wirrell, MD, FRCPC
Professor, Child and Adolescent Neurology
Mayo Clinic
Dr. Wirrell is the Director of Pediatric Epilepsy at Mayo Clinic. She focuses on early-onset epilepsies and epileptic encephalopathies, such as LGS. Her research activities include early diagnosis and treatment, prediction of medical intractability, and understanding common comorbidities of epilepsy. She is co-founder of the Pediatric Epilepsy Research Consortium, a multicenter U.S. group of clinicians that focuses on epilepsy in children.

Anup Patel, MD
Associate Medical Director
Nationwide Children's Hospital
Anup Patel, M.D. is board certified in neurology with special qualifications in child neurology. He is the President-Elect for the Child Neurology Foundation. He is an associate medical director for quality improvement at Nationwide Children's Hospital and the director of quality improvement for neurology. He is an associate professor for neurology and pediatrics at Nationwide Children's Hospital and The Ohio State University Medical Center in Columbus, Ohio. He has publications and clinical research interests in the field of pediatric epilepsy, health care utilization, learning healthcare systems, and quality improvement.

Anne T. Berg, PhD
Research Professor
Northwestern Feinberg School of Medicine
Dr. Berg's research has focused on the "natural" history of seizures and epilepsy with a specific emphasis on seizure outcomes, developmental and cognitive consequences of epilepsies in children and the impact all of these have on quality of life for patients and families. She was also a lead investigator in the Multicenter Study of Epilepsy Surgery and with the PI, Susan Spencer, and Barbara Vickrey contributed to the literature defining the seizure, psychiatric, cognitive, and quality of life outcomes of patients who have undergone epilepsy surgery.

James W. Wheless, BScPharm, M.D., FAAP, FACP, FAAN, FAES
Professor and Chief of Pediatric Neurology
University of Tennessee Health Science Center
Dr. Wheless is a Diplomate of the American Board of Pediatrics, and the American Board of Psychiatry and Neurology with special qualifications in Child Neurology, Clinical Neurophysiology, and Epilepsy. He is a fellow of the American Academy of Pediatrics, the American College of Pediatrics; the American Academy of Neurology & the American Epilepsy Society. Dr. Wheless is a member of the Editorial Board of Journal of Child Neurology, Formulary, and Epilepsy.com and serves as a reviewer of a number of journals including Neurology; Epilepsia; Pediatrics; and Epilepsy and Behavior.

MEET OUR SPEAKERS – DAY 1

Jurriaan Peters, MD, PhD
Principal epileptologist at the Multidisciplinary Tuberous Sclerosis Clinic at Boston Children's Hospital
Jurriaan M. Peters MD, Ph.D., is the principal epileptologist at the Multidisciplinary Tuberous Sclerosis Clinic at Boston Children's Hospital. His research in the Laboratory of Translational Neuroimaging and in the Computational Radiology Laboratory focuses on novel MRI and EEG modeling techniques in the localization of the seizure onset zone in children with medically refractory epilepsy, on how focal lesions give rise to a generalized epileptic encephalopathy, and on early medical and surgical treatment of epilepsy to mitigate detrimental effects on neurodevelopment.

Jennifer Gelinas, MD, PhD
Assistant Professor of Neurology, Columbia University
Jennifer Gelinas, MD, Ph.D. is an assistant professor of neurology (in the Institute for Genomic Medicine and the Gertrude H. Sergievsky Center) at Columbia University Irving Medical Center. Dr. Gelinas obtained her medical doctorate and doctorate degrees at the University of Alberta, Canada. She subsequently completed a pediatric neurology residency at the University of British Columbia, followed by an epilepsy fellowship at New York University Langone Medical Center. Dr. Gelinas' clinical practice focuses on infantile and childhood epilepsy, with a special interest in epilepsy surgery and intracranial electroencephalography (iEEG).

John Archer, MD, PhD
Senior Lecturer in Medicine
University of Melbourne
Dr. John Archer obtained his medical degree through the University of New South Wales in 1990. He trained in General Neurology in Sydney and Oxford and subsequently completed a Ph.D. in Epilepsy and Neuroimaging through Austin Hospital and The University of Melbourne in 2002. From 2002-7 he initiated and managed the neurology service at Cairns Base Hospital, whilst helping establish the medical program of James Cook University. In 2007 he was appointed Senior Lecturer in Medicine at the University of Melbourne, Neurologist and Head of EEG laboratory Austin Health, and Research Fellow The Florey Institute of Neuroscience and Mental Health.

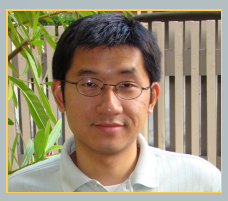
Zach Grinspan, MD, MS
Associate Professor and Director of Pediatric Epilepsy
New York-Presbyterian Hospital-Weill Cornell Medicine
Dr. Grinspan graduated from Yale University in 1996, taught high school through the Teach for America Program, then attended and graduated medical school from the Albert Einstein College of Medicine in 2004. He completed pediatrics training at the Mass General Hospital for Children, neurology training at Columbia University Medical Center, and epilepsy training at Montefiore Medical Center, then joined Weill Cornell Medicine in 2011. At Cornell, he obtained a master's degree in biostatistics and completed a postdoctoral fellowship in quality of care and medical informatics.

Dennis J. Dlugos, MD
Director, Pediatric Epilepsy Program
Children's Hospital of Philadelphia
Dr. Dlugos is Professor of Neurology and Pediatrics in the Perelman School of Medicine at the University of Pennsylvania; and Director, Pediatric Epilepsy Program at Children's Hospital of Philadelphia (CHOP). He received his MD from Columbia University College of Physicians and Surgeons, New York. He went on to complete his internship in Pediatrics at the National Naval Medical Center, Bethesda, Maryland; a residency in Neurology / Child Neurology at the University of Pennsylvania Medical Center and CHOP; and his fellowship in Epilepsy at CHOP. Dr. Dlugos serves as Vice-President of The Epilepsy Study Consortium (TESC) and is a member of the Pediatric Epilepsy Research Consortium (PERC).

MEET OUR SPEAKERS – DAY 2

Allyson Muotri, PhD
Professor
University of California, San Diego
Dr. Muotri is a professor at the Departments of Pediatrics and Cellular and Molecular Medicine at UC San Diego. He is also the Director of the Stem Cell Program and Archealization Center. Dr. Muotri earned a BSc in Biological Sciences from the State University of Campinas in 1995 and a Ph.D. in Genetics in 2001 from the University of Sao Paulo, in Brazil. He moved to the Salk Institute as Pew Latin America Fellow in 2002 for postdoctoral training in the fields of neuroscience and stem cell biology. His research focuses on brain evolution and modeling neurological diseases using human induced pluripotent stem cells and brain organoids. He has received several awards, including the prestigious NIH Director's New Innovator Award, NARSAD, Emerald Foundation Young Investigator Award, Surugadai Award, Rock Star of Innovation, NIH EUREKA Award, Telly Awards among several others.

Megan Dennis, PhD
Assistant Professor
University of California, Davis
Megan Dennis studies disease genetics, human genomics, and evolution. Her main interests lie in identifying previously unexplored genes and variants that contribute to human-specific neurological traits and diseases, developing next-generation sequencing methods to assay regions of the genome that are difficult to study with traditional techniques, and identifying genetic variants associated with neurological disorders.



Mingshan Xue, PhD
Assistant Professor
Baylor College of Medicine
Dr. Mingshan Xue is an Assistant Professor in the Department of Neuroscience at Baylor College of Medicine and the Caroline DeLuca Scholar in the Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital. The long-term research goal of his lab is to understand the neural circuit dysfunctions in neurodevelopmental disorders and harness this knowledge to explore new therapeutic strategies for these disorders. His lab currently uses mouse models to study STXBP1 dysfunction, one of the genetic causes of LGS, and develop therapeutic interventions.

SPECIAL THANKS TO MEETING ADVISOR:

Vicky Holets Whittemore, PhD,
Program Director
National Institute of Health (NIH)
Vicky Holets Whittemore, PhD., is a program director of the Channels, Synapses and Circuits Cluster in the National Institute of Neurological Disorders and Stroke (NINDS) at the National Institutes of Health (NIH) in Bethesda, Maryland, United States. She represents NINDS on the Trans-NIH Working Group on myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).
While the committee was still active, she served as the NIH Representative to the U.S.Department of Health and Human Services (HHS) CFS Advisory Committee, CFSAC, as an ex officio member.

LGS FOUNDATION RESEARCH INITIATIVES

LGS Research Roundtable at AES

The LGS Foundation organizes a Research Roundtable every year at the American Epilepsy Society (AES) meeting in an effort to bring researchers together to share the latest findings on LGS Foundation-funded research with the community.

Meeting of the Minds Seminars

This meeting will kick off the Meeting of the Minds (MoM) Seminar Series, which will continue the conversations started here. Future seminars will focus on making current clinical trials in LGS better, research and discovery in pre-LGS, the evolution of LGS from etiology to SSW/GPFA, and more. If you would like to host a seminar, please email us at info@lgsfoundation.org.

Voice of the Community Reports

The LGS Foundation is the leading voice of patients and families living with LGS. We are members of, hold regular meetings with, and conduct surveys in our global LGS community and relay what we learn to researchers. We have also convened the Voices of Experience: DEE and LGS Patient-Focused Drug Development (PFDD) meeting to benefit the FDA. You can check out all of our learning from our community on our website. Reports include:

- Voice of the LGS Community Report *NEW*
- LGS Characteristics and Caregiver Concerns Survey
- DEE and LGS Voices of Experience PFDD Video & Transcript
- Lurie Children's Hospital Patient Family Survey on Impact of LGS

LGS Research Grant Program

The 2021 LGS Foundation seed grant program awarded one-year and two-year grants up to $50,000 to young investigators, physician residents, and clinicians interested in studying LGS. Seed grants help researchers explore novel ideas and answer questions related to the clinical aspects, therapies, causes, and evolution of LGS. The 2022 LGS Grants Program will be designed based on outcomes of this meeting. Look for the RFA in early 2022!

LGS FOUNDATION 2021 RESEARCH GRANT RECIPIENT

RNA Modulation in KCNB1 Model of LGS

Jennifer A. Kearney, Ph.D.

Lennox-Gastaut Syndrome (LGS) is a severe pediatric epilepsy syndrome that includes a characteristic EEG pattern, some degree of cognitive impairment, and multiple seizure types that respond poorly to available treatments. New therapies are needed to both better control seizures and improve other issues seen in LGS. Up to 35% of LGS cases have no obvious cause and are presumed to result from a genetic mutation. Heterozygous mutations in KCNB1 have been identified as a genetic cause in some patients with LGS. In genetic disease resulting from a heterozygous mutation, the individual has one good copy and one bad copy of the gene. A major unanswered question for KCNB1-associated LGS is whether the LGS results because one good copy is not enough, or from harmful effects of the bad copy of the gene. Based on our current understanding, we think that the bad copy exerts harmful effects and poisons the good copy. To formally investigate this, we will use a mouse model with a Kcnb1-associated LGS mutation and evaluate the effects of turning off the bad copy using a tool called antisense oligonucleotide (ASO). If we see improvement in neurological and behavioral symptoms in Kcnb1 LGS mice, it will provide evidence that harmful effects of the bad copy are responsible for the seizures and LGS. Addressing this critical gap in our knowledge will improve our understanding of LGS and pave the way for the development of an RNA-based disease-modifying therapy.

FAMILY COMMUNITY PROGRAMS

The challenges of LGS are tough! So are we!

While there is no cure for LGS there is a hopeful path forward. The LGS Foundation fights every day to support and empower families living with LGS. Our mission is to improve the lives of individuals impacted by LGS through research, family support programs, and education. We are making a difference! You are making a difference! LGSF families are at the heart of what we do. We bring families together! If you need support or have questions, or know someone who does, please check out our Families First Programs:

Family First Programs

- Global Online Private Support Groups
- LGS Family Ambassador Program
- New Family Welcome & Resource Referral Program
- Bereavement Support Program
- Siblings Support Program
- Elevate Patient Assistance Program
- Local MeetUps for Families Living with LGS

Education & FUNraising

- Biennial LGS Foundation Family Conference
- Biennial LGS Foundation Research Meeting of the Minds Conference
- LGS Research Meeting of the Minds Seminars
- LGS Research Roundtable at AES Presenting our LGSF Grantees
- "Navigating the LGS Maze" Video Educational Series
- LGS Foundation Research Revolution Online Family MeetUps & Webinars
- LGS Online Learning and Resource Center *NEW*
- LGS Foundation Monthly Newsletter
- International LGS Awareness Day Events
- LGS Walk 'n' Wheel
- Infantile Spasms Action Awareness Week
- Seizure Action Plan Awareness Week

Thank You CZI Rare As One for Supporting This Meeting!

Rare As One

Rare disease is anything but rare. As many as 7,000 rare diseases affect 400 million people globally. The vast majority are not well understood, and less than 5 percent have approved treatments. Yet worldwide, patients are meeting these challenges head-on. The Rare As One project is committed to uniting these communities in their quest for cures.

The LGS (Lennox-Gastaut Syndrome) Foundation is one of 30 patient-led disease organizations chosen to join the Rare As One Project, launched by the Chan Zuckerberg Initiative (CZI) to help rare disease communities accelerate research and drive progress against rare disease.

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