GRIN Genes Roundtable Summary

October 29, 2020

CureGRIN

Funding Research for GRIN Disorder

Total Participants

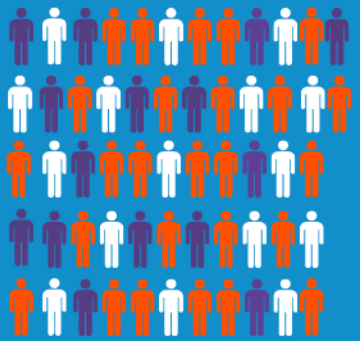
Collaboration

Our goal is to promote collaboration to accelerate the path to therapies and cures for GRIN disorder.

CureGRIN

57

Participants



13

Countries

Presentations from researchers and many more global attendees

7

Researcher and doctor presentations

Next meeting is Thursday, December 10, 2020.

If you are a GRIN / NMDA researcher or clinician, please reach out to keith@curegrin.org to be added.

CureGRIN Foundation hosted our second GRIN Genes Roundtable on October 29, 2020. Our goal is to **promote collaboration so that we can accelerate the path to treatments and cures for GRIN Disorder.**

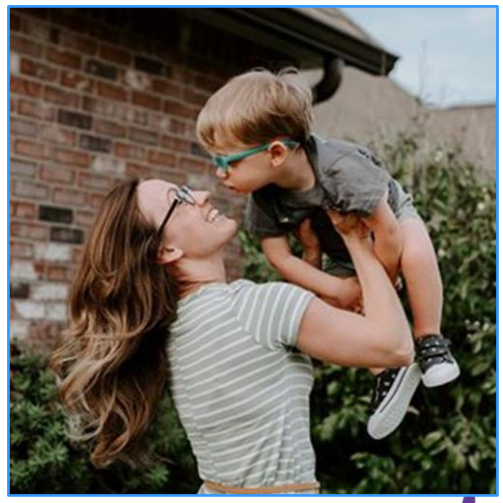
We brought together researchers and clinicians studying GRIN Disorder, GRIN genes, NMDA receptors, and other ionotropic receptors to **share research updates and exchange new ideas.**

We asked Lauren Williams to share her family story about her son Carter, and we asked researchers to give three-minute presentations on their work. Following the presentations, we also had an open discussion which covered several topics. This document summarizes these presentations.

Presentation Summaries: Family Story

Lauren Williams, United States

- Mother of Carter (GRIN1 patient)
  - Carter was born in 2016.
  - Carter experienced the following symptoms: Seizures, Hypotonia, Strabismus, Esotropia, Failure to Thrive, Continuous Random Vomiting (all day), Hypermobility, Hyperkinetic Movements, GERD, Chronic Constipation and Severe Feeding Issues.
  - At 18 months, Whole Exome Sequencing revealed a variant in GRIN1 and prompted Carter's diagnosis with GRIN Disorder.
  - Carter currently attends Pre-Kindergarten and has continued with Physical, Occupational, Vision, Speech/Feeding and Play Therapies.
  - Carter and the Williams family are beloved members of our GRIN Disorder community and CureGRIN family.



Presentation Summaries

Dr. Stephen Traynelis, Emory University, United States

- Functional analysis of NMDA receptor variants by CFERV
  - Dr. Traynelis' lab is working to collaborate with clinicians and generate functional datasets through the evaluation of rare variants in order to stratify phenotype.
  - Dr. Traynelis is a member of the CureGRIN Scientific Advisory Board.

Dr. Zhexing Wen, Emory University, United States

- Modeling GRIN disorder with human brain organoids
  - Dr. Wen's lab is working to generate patient IPSCs by reprogramming somatic cell samples and create 3D mini-brains to characterize structure and function and assess synaptic activity and neural differentiation.

Dr. Simone Chiola, Shcheglovitov Lab, University of Utah, United States

- Studying GRIN2B-related neurodevelopmental disorders in human cortical organoids
  - Dr. Chiola's work in Dr. Alex Shcheglovitov's lab is focused on studying synaptic genes in cortical development.
  - Dr. Chiola has created 3D culture of human stem cell-derived cortical organoids, and he plans to perform scRNAseq to assess cell types and bulk RNAseq to assess gene expression.

Dr. Andrew Fry, Cardiff University, United Kingdom

- NMDA receptor mutations and brain malformations
  - Dr. Fry's lab is working to study brain MRI findings in GRIN disorder patients (normal, atrophy/volume loss, simplified gyral pattern, dysgyria) and assess genotype-phenotype.
  - Dr. Fry's lab is working to facilitate UK involvement in GRIN studies.

Presentation Summaries

Dr. Laetitia Mony, Dr. Pierre Paoletti Research Team, Institut de Biologie de l'Ecole Normale Supérieure, France

- Glutamate Receptors and Excitatory Synapses
  - Dr. Mony's work in Dr. Pierre Paoletti's lab is focused on studying NMDAR functional diversity, using molecular, cellular, and in vivo approaches. Dr. Mony is assessing the structural mechanisms and pharmacology of NMDA receptors (allosteric modulation), as well as developing photopharmacological tool to control specific NMDARs with light.
  - The team of Dr. Paoletti is also assessing the molecular mechanisms and physiology of GluN1/GluN3 NMDARs, as well as the role of the synaptic microenvironment of NMDARs.

Dr. Antonio Sanz-Clemente, Northwestern University, United States

- NMDAR-dependent synapse unsilencing and Rett Syndrome
  - Dr. Sanz-Clemente's lab is working to assess the effects of phosphorylation in GluN2B, as well as assessing synapse unsiliencing and BDNF-dependent glutamate receptor plasticity in the pathogenesis of Rett Syndrome.

Dr. Ladislav Vyklicky, Institute of Physiology, Czech Republic

- Function and pharmacology of disease-associated mutations in the NMDA receptors
  - Dr. Vyklicky's lab is working on structure-function studies of endogenous neurosteroid modulation of NMDAR channel activity in GluN2B mice and in zebrafish.

Open Discussion Summary

- Animal and Cell Models
  - Mouse models
  - GRIN2B brain organoids
- Brain banks
  - Collaborations between clinicians, scientists, and families to capture postmortem data
- Registries
  - Gaps in Asia
    - Expand our reach with collaborators and parents/families in Asia
- Clinical trials
  - L-Serine
  - Need for international protocols for capturing data on clinical trials and outcome measures

At our next meeting, we will have an open discussion on the topic of animal and cell models.

Our next GRIN Genes Research Roundtable is scheduled for:
Thursday, December 10, 2020

If you are a GRIN / NMDA researcher or clinician, please reach out to keith@curegrin.org to be added to the next meeting invitation.