GRIN Genes Roundtable Summary

December 10, 2020

CureGRIN

Funding Research for GRIN Disorder

CureGRIN Foundation hosted our third GRIN Genes Roundtable on December 10, 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 discuss and exchange ideas on **animal and cell models.** There were 54 participants present for the meeting.

We asked Sandra Silva and Christian Brander to share their family story about their daughter with a variant in GRIN2B. We also asked Steve Rockwood from Jackson Labs to share information about the JAX repository and their mouse line donation program. Additionally, a panel of five researchers presented on their work with animal and cell models. Following the presentations, we also had an open discussion on this topic. This document summarizes these presentations.

Presentation Summaries: Family Story

Sandra Silva (Peru) and Christian Brander (Switzerland)

- Parents to a daughter with a variant in GRIN2B
  - Family currently lives in Spain.
  - Received a diagnosis with the help of Dr. Àngels García-Cazorla and Dr. Judith Armstrong.
  - Recruited Dr. Xavier Altafaj, Dr. David Soto, and Dr. Mireia Olivella to help the doctors understand their child's variant and the resulting structural changes.
  - Sandra and Christian hope that we can promote cooperative work between the GRIN families, physicians, researchers, and associations so that we can improve the quality of care for GRIN children.

Presentation Summaries: Jackson Labs

Steve Rockwood, Associate Director, Mouse Repository at The Jackson Laboratory

JAX GRIN Holdings

JAX #	Name	Type	Donor
5246	B6.129S4-*Grin1*^{tm2Stl}/J	Floxed	Dr. Susumu Tonegawa, Massachusetts Institute of Technology
7808	B6.129P2-*Grin3b*^{tm1Yaha}/J	KO	Yasunori Hayashi, Brain Science Institute, RIKEN
18825	B6(Cg)-*Grin1*$^{tm1c(EUCOMM)Wtsi}$/ZwzJ	floxed	Zhong-wei Zhang, The Jackson Laboratory
23538	B6;129S-*Grin2b*$^{tm1.1(Grin2a)Bjha}$/J	KO	Benjamin J Hall, Tulane University
27998	B6.129S4(FVB)-*Grin2a*$^{tm1.1Lpleo}$/J	conditional , S1991A, Y1292F, S1312A and Y1472F	John P Leonard, University of Illinois at Chicago
29151	STOCK Tg(Camk2a-Grin2a/Grin2b)1Jzt/J	Transgeneic	Joe Z Tsien, Augusta University - Georgia Regents University
29152	STOCK Tg(Camk2a-Grin2b/Grin2a)1Jzt/J	Transgeneic	Joe Z Tsien, Augusta University - Georgia Regents University
29974	B6;129X1-*Grin3a*^{tm1Nnk}/J	KO	Nobuki Nakanishi, Scintillon Institute
30460	57BL/6-Tg(tetO-EGFP/Grin2a)38Jplo/J	Transgeneic	Jonathan Ploski, University of Texas at Dallas
32664	C57BL/6J-*Grin2b*^{em5Lutzy}/J	floxed	Cathleen Lutz, The Jackson Laboratory
33730	B6(Cg)-*Grin1*$^{tm1.1Zwz}$/J	KO	Zhong-wei Zhang, The Jackson Laboratory
34737	STOCK *Grin1*^{tm1Zwz}/J	Floxed	Zhong-wei Zhang, The Jackson Laboratory

- If you have additional questions about the Mouse Repository at Jackson Labs, please email sfr@jax.org.
- If you are interested in donating a GRIN mouse line for broad use by other researchers, please email meagan@curegrin.org for CureGRIN to cover shipping costs and also fill out the form at: https://www.jax.org/jax-mice-and-services/cryo-and-strain-donation/donate-a-strain

Presentation Summaries: Animal/Cell Models Panel

Dr. Wayne Frankel, Columbia University, United States

- GRIN2A and GRIN2D mouse models
  - Dr. Frankel's lab is working to develop new mouse models of Developmental and Epileptic Encephalopathy (DEE) to interpret phenotypes and assess possible interventions/therapies.

Dr. Amy Ramsey, University of Toronto, Canada

- GRIN1 mouse models
  - Dr. Ramsey's lab is using mouse models of genetic diseases to understand how NMDARs work in specific cell types and at certain points of time during development.
  - Dr. Ramsey's team has developed a GRIN1 rescue mouse which demonstrates the potential for recovery.

Dr. Ladislav Vyklicky, Institute of Physiology, Czech Republic

- GRIN2B mouse model and zebrafish
  - Dr. Vyklicky's lab is working on structure-function studies to assess how NMDARs are influenced by steroids in GluN2B mice and in zebrafish.

Dr. Lonnie P. Wollmuth, Stony Brook University, United States

- Using zebrafish as a model organism to express GRIN variants and perform drug screens to reverse deficits
  - Dr. Wollmuth's lab is working in partnership with Dr. Howard Sirotkin's lab to knockout GRIN genes and characterize phenotypes, humanize NMDAR signaling in zebrafish, and express NMDAR variants, as well as perform small molecule screenings to reverse deficits.

Dr. Zhexing Wen, Emory University, United States

- Disease modeling and drug development with human brain organoids
  - Dr. Wen's lab is working to generate patient IPSCs and create 3D mini-brains to characterize structure and function, assess synaptic activity and neural differentiation, and perform drug discovery studies.

Animal/Cell Models Discussion Summary

- Zebrafish Models
  - Behavioral testing
- Mouse Models
  - KO mice are good to use to perform therapy screens
  - Develop new mouse lines as needed to clarify cell testing
  - Expand the scope of study to assess other systems outside of the nervous system
- Discussion Platform
  - CureGRIN is in the process of developing a discussion platform for researchers to communicate with one another

At our next meeting, we will have an open discussion on the topic of clinical trials.

Our next GRIN Genes Research Roundtable is scheduled for:
Thursday, January 21, 2021

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