

- **Animal models generated and phenotype description/characterization (not with patient-specific variants)**
 - Jackson Labs (<https://www.jax.org/>) mouse strains:
 - *Grin1^{tm2Stl}*
 - Floxed NR1 mice allow deletion of the GluN1 subunit of the N-methyl-D-aspartate receptor in Cre recombinase expressing cells/tissues (Tsien et al., 1996).
 - JAX stock #005246
 - *Grin1^{tm1Zwz/J}*
 - *Grin1^{floxedEx5}* mice carry loxP sites flanking *Grin1* (glutamate receptor, ionotropic, NMDA1 (zeta 1)) exon 5. Deletion of exon 5 disrupts the maturation of excitatory synapses in the thalamus and cortex, and increases seizure susceptibility. This allele does not enable the production of complete gene knock-outs
 - JAX stock #034737
 - *Grin1^{ΔEx5}*
 - Carry targeted deletion of *Grin1* exon 5.
 - Interrupts the maturation of excitatory synapses in the thalamus and cortex, increases seizure predisposition (Li et al., 2013).
 - JAX stock #033730
 - *Grin1^{2lox}*
 - *loxP* sites flanking exon 6 of the *Grin1* gene (Zhang et al., 2013).
 - JAX stock #018825
 - *Grin2a^{S644G}*
 - CRISPR/Cas9 generated mutant of the NMDA2A (epsilon 1) gene carrying the S644G missense mutation that is associated with human DEE phenotype (Amador et al., 2020).
 - JAX stock #028785
 - *Grin2aΔPKC*
 - B6.129S4(FVB)-*Grin2a^{tm1.1Jpleo/J}*
 - Amino acid substitutions resulting in nonphosphorylatable PKC sites (Balu D et al., 2016)
 - May be useful in studies related to synaptic plasticity, memory and learning.
 - JAX stock #027998
 - Tg-GluN2A^{2B(CT)}
 - Forebrain excitatory neuron overexpression of GluN2A^{2B(CTR)} (Jacobs et al., 2014).
 - JAX stock #029151
 - Tg-GluN2B^{2A(CT)}

- Forebrain excitatory neuron over-expression of GluN2B^{2A(CTR)} (Jacobs et al., 2014).
 - JAX stock #029152
- B6;129S-*Grin2b*^{tm1.1(Grin2a)Bjha/J}
 - Rat *Grin2a* cDNA replaces most of the first coding exon (exon 4) of the mouse *Grin2b* gene, including the initial ATG site.
 - eliminates endogenous GluN2B expression and targets rat GluN2A expression from the endogenous mouse GluN2B promoter/enhancer elements.
 - earlier onset of GluN2A expression
 - May be useful in studying the NMDAR and downstream signaling molecules/pathways (including alpha-CaMKII and mTOR), synaptic plasticity, social behavior, etc., (Wang CC et al., 2011).
 - JAX stock #023538
- *Grin3b*^{tm1Yaha}
 - NR3B (*Grin3b*) homozygotes are viable and fertile, with no RNA expression from the targeted allele in the adult spinal cord (Niemann et al., 2007).
 - JAX stock #007808
- B6.129(Cg)-*Gria1*^{tm4Rlh/J}
 - Five alanine substitutions (S831A, T838A, S839A, T840A, and S845A) that permit experiments on phosphorylation (Lee et al., 2007).
 - JAX stock #024420
- B6.129-*Gria1*^{tm1Rsp/J}
 - GluA1 knockout mice show behavioral, social, and cognitive deficits (Zamanillo et al., 1999; Resnik E , et al., 2012).
 - JAX stock #019011
- *Gria1*^{tm8.1Rlh/J}
 - SEP-GluA1 KI is useful for studying synaptic strength and plasticity with fluorescence imaging (Graves AR , et al., 2021)
 - JAX stock #037254
- C57BL/6-*Gria1*^{tm3Rlh/J}
 - Deletion of exon 11 (Kim CH , et al., 2005)
 - JAX stock #024422
- B6.129-*Gria1*^{tm1Rlh/J}
 - S831A and S845A phosphorylation site mutations (Lee HK , et al., 2003)
 - JAX stock #008892

- B6.129-Gria1^{tm5Rlh/J}
 - Serine 831 phosphorylation site (Crombag HS , et al., 2008)
 - JAX stock #012612
- B6.129S6-Gria1^{tm7Rlh/J}
 - S831D and S845D amino acid substitutions in the mouse *Gria1* gene that are phosphomimetic (mimic a phosphorylated protein). Phosphorylation at these amino acids is sufficient to lower the threshold for LTP induction, increasing the probability of synaptic plasticity.
 - JAX stock #024418
- B6.129-Gria1^{tm6Rlh/J}
 - The serine 845 phosphorylation site was mutated to alanine in this *Gria1* (glutamate receptor, ionotropic, AMPA1 (alpha 1)) targeted mutation strain. Normal GRIA3 protein expression is replaced by the mutant form in the brain. Young (3 week old) and adult (more than 3 month old) homozygous mutants display a specific deficit in long-term depression of synaptic transmission in the central nervous system. This strain may be useful in studies of synaptic plasticity
 - JAX stock #012613
- B6N.129-Gria1^{tm2Rsp/J}
 - The GluA1^{fl} floxed exon 11 allele allows deletion of the sequences encoding the glutamate receptor transmembrane domain ion channel pore in cells/tissues expressing Cre recombinase. These mice are useful in applications related to the study of behavioral, social and cognitive abnormalities, hippocampal synaptic transmission/plasticity, nociception and short and long term memory, as well as neuropsychiatric disorders such as schizophrenia and depression/mania
 - JAX stock #019012
- B6.129-Gria1^{tm2Rlh/J}
 - Lacking the last seven amino acid residues of Gria1 (Kim CH , et al., 2005)
 - JAX stock #012614
- Gria2^{tm1Rod/J}
 - These *Gria2* knock-out mice exhibit an increase in Ca²⁺ permeability and enhanced long-term potentiation in neurons. They are suitable for use in applications related to the study of Ca²⁺ permeability and plasticity of neurons in the central nervous system
 - JAX stock #002913

- B6.129-Gria2^{tm1Rlh/J}
 - This mutation of *Gria2* (glutamate receptor, ionotropic, AMPA2 (alpha 2); GluR2) incorporates a deletion of the last seven transcribed amino acids, eliminating the C-terminal type II PDZ ligand and disrupting the interaction with PICK1 and GRIP1/2. This strain may be useful for further characterization of the targeted gene's synaptic function
 - JAX stock #012615
- B6.129(Cg)-Gria2^{tm2Rlh/J}
 - A K882A mutation was introduced to *GluA2/Gria2* to prevent PKC α -mediated phosphorylation at serine 880 (S880). This eliminates cerebellar long-term depression (LTD), reported to be critical for certain types of motor learning
 - JAX stock #024419
- B6.129-Gria2^{tm1Rod/J}
 - These *Gria2* knock-out mice exhibit an increase in Ca²⁺ permeability and enhanced long-term potentiation
 - JAX stock #003143
- B6.129S6(Cg)-Gria2^{tm3.1Rlh/J}
 - These mice possess a Y876F mutation in the *GluA2* gene, a phosphorylation site which plays an important role in synaptic plasticity. These mice may have applications in studies related to synapse-specific Hebbian plasticity and network-level homeostatic plasticity
 - JAX stock #037072
- B6.129-Gria3^{tm2Rlh/J}
 - Expression of *Gria3* (glutamate receptor, ionotropic, AMPA3 (alpha 3)) is ablated in homozygous (female) and hemizygous (male) targeted mutation mice as demonstrated by Western blot analysis of whole brain samples. This strain may be useful for further characterization of the targeted gene's synaptic function
 - JAX stock #012617
- B6.129-Gria3^{tm1Rlh/J}
 - This mutation of X-linked *Gria3* (glutamate receptor, ionotropic, AMPA3 (alpha 3); GluR3) incorporates a deletion of the last seven transcribed amino acids. This strain may be useful for further characterization of the targeted gene's synaptic function
 - JAX stock #012616
- B6.129-Gria4^{tm1Rlh/J}

- Expression of *Gria4* (glutamate receptor, ionotropic, AMPA4 (alpha 4); GluR4) is ablated in homozygous targeted mutation mice as demonstrated by Western blot analysis of whole brain samples. This strain may be useful for further characterization of the targeted gene's synaptic function
 - JAX stock #012619
- B6.129(Cg)-*Gria4*^{tm2.1Rlh}/J
 - This mutation of *Gria4* (glutamate receptor, ionotropic, AMPA4 (alpha 4); GluR4) incorporates a deletion of the last seven transcribed amino acids. Normal GRIA4 protein expression is replaced by the mutant form in the brain. This strain may be useful for further characterization of the targeted gene's synaptic function
 - JAX stock #012618
- C3Fe.C3-Pcnx2^{em1Frk}, *Gria4*^{spkw1}/FrkJ
 - These mice, on a congenic C3HeB/FeJ background, carry the absence-seizure-associated *Gria4*^{spkw1} mutation in addition to a 1 bp insertion in exon 16 of the mitigating *Pcnx2* modifier/suppressor gene. This is founder line A+1/FS2
 - JAX stock #029994
- C3Fe.C3-Pcnx2^{em4Frk}, *Gria4*^{spkw1}/FrkJ
 - These mice, on a congenic C3HeB/FeJ background, carry the absence-seizure-associated *Gria4*^{spkw1} mutation in addition to a 2 bp deletion in exon 29 of the mitigating *Pcnx2* modifier/suppressor gene. This is founder line B-2/FS3
 - JAX stock #029997
- C57BL/6-Tg(*Grik4-cre*)G32-4Stl/J
 - Cre recombinase expression in these transgenic mice is driven by the endogenous promoter/enhancer elements of the glutamate receptor, ionotropic, kainate 4 (*Grik4*) gene, and is observed primarily in the CA3 region of the hippocampus. These *cre*-expressing mice may be useful in neurological studies involving hippocampal function, learning and memory, and pyramidal cell function and physiology
 - JAX stock #006474
- B6.129P2-*Grik5*^{tm1Dgen}/J
 - This targeted mutant was created and characterized by Deltagen, Inc. [View phenotypic data](#) developed by Deltagen

- JAX stock #005813
- C57BL/6NJ-*Grid1*^{em1(IMPC)J}/Mmjax
 - This CRISPR/cas9-mediated knock-out mutant of the gene glutamate receptor, ionotropic, delta 1 (*Grid1*) was generated by the [Knockout Mouse Phenotyping Program](#) at The Jackson Laboratory
 - JAX stock #037994
- FVB/NJ-*Grid1*^{em1Mpan/J}
 - *Grid1* floxed mice carry a CRISPR/Cas9 generated mutation resulting in *loxP* sites surrounding exon 4 of the (*Grid1*) gene. This strain may be useful for studying heightened aggression found in a subset of autism spectrum disorder (ASD) cases
 - JAX stock #036630
- C57BL/6J-*Grid2*^{ho-16J/J}
 - These mice carry an ENU-induced mutation characterized by body tremors and muscle spasms.
 - JAX stock #005447
- C57BL/6J-*Grid2*^{ho17J/J}
 - These mice carry a spontaneous mutation of the *Grid2* gene and exhibit body tremors and abnormal gait.
 - JAX stock #005718
- C57BL/6J-*Grid2*^{ho-19J/GrsrJ}
 - This recessive mutation is useful for characterizing the function of *Grid2* in Purkinje cells and cerebellar ataxia
 - JAX stock #017687
- C57BL/6J-*Grid2*^{ho-21J/GrsrJ}
 - This strain is useful as part of an allelic series in the *Grid2* gene for assessing the impact of genetic variation and distinct molecular mutations on the phenotypic outcome
 - JAX stock #024577
- C57BL/6J-*Grid2*^{ho-5J/J}
 - The glutamate receptor delta2 (*Grid2*) gene is predominantly expressed in the postsynaptic densities of parallel fiber-Purkinje cell synapses and plays a crucial role in cerebellar function. Many mutations have been found for this gene, and while several hotfoot spontaneous mutations involve deletions of one or more exons in the *Grid2* gene, the *Grid2*^{ho-5J} hotfoot mutation has been shown to be a point mutation
 - JAX stock #000527
- DBA/2J-*Grid2*^{ho-4J/J}

- These mice carry a spontaneous mutation at the *Grid2* locus characterized by ataxia
 - JAX stock #000548
 - B6(Cg)-*Grid2*^{ho-20J}/GrsrJ
 - This strain is useful as part of an allelic series in the *Grid2* gene for assessing the impact of genetic variation and distinct molecular mutations on the phenotypic outcome
 - JAX stock #024550
 - B6CBACa A^{W-J}/A-*Grid2*^{Lc}/J
 - These mice carry a spontaneous mutation at the *Grid2* locus characterized by a swaying of the hindquarters and a jerky up and down movement. The mutation induces apoptotic programmed death of the cerebellar cortical Purkinje cells
 - JAX stock #001046
 - B6.Cg-*Grid2*^{ho-18J}/GrsrJ
 - This recessive mutation is useful for characterizing the function of *Grid2* in Purkinje cells and cerebellar ataxia
 - JAX stock #021782
 - B6 x BALB/cByJ-*Grid2*^{Lc-J}/J
 - These mice carry a spontaneous mutation at the *Grid2* locus characterized by an early loss of Purkinje cells in the cerebellum and ataxia
 - JAX stock #002440

- **Zebrafish animal models generated and phenotype description reported in ZFIN**
 - *grin1b*^{s3020/s3020}
 - <https://zfin.org/ZDB-FISH-231019-8#summary>
 - Griffin A, Carpenter C, Liu J, Paterno R, Grone B, Hamling K, Moog M, Dinday MT, Figueroa F, Anvar M, Ononuju C, Qu T, Baraban SC. Phenotypic analysis of catastrophic childhood epilepsy genes. *Commun Biol.* 2021 Jun 3;4(1):680. doi: 10.1038/s42003-021-02221-y. PMID: 34083748; PMCID: PMC8175701.
 - ID ZDB-FISH-231019-8
 - *grin1b*^{s3020/+}
 - <https://zfin.org/ZDB-FISH-231024-11#summary>
 - Griffin A, Carpenter C, Liu J, Paterno R, Grone B, Hamling K, Moog M, Dinday MT, Figueroa F, Anvar M, Ononuju C, Qu T, Baraban SC. Phenotypic analysis of

catastrophic childhood epilepsy genes. *Commun Biol.* 2021 Jun 3;4(1):680. doi: 10.1038/s42003-021-02221-y. PMID: 34083748; PMCID: PMC8175701.

- ID ZDB-FISH-231024-11
- **grin1b**^{sbu93/sbu93}
 - <https://zfin.org/ZDB-FISH-230822-11#summary>
 - Zoodsma JD, Keegan EJ, Moody GR, Bhandiwad AA, Napoli AJ, Burgess HA, Wollmuth LP, Sirotkin HI. Disruption of *grin2B*, an ASD-associated gene, produces social deficits in zebrafish. *Mol Autism.* 2022 Sep 22;13(1):38. doi: 10.1186/s13229-022-00516-3. PMID: 36138431; PMCID: PMC9502958.
 - ID ZDB-FISH-230822-11
- **grin1b**^{sbu94/sbu94}
 - <https://zfin.org/ZDB-FISH-210716-3#summary>
 - Zoodsma JD, Chan K, Bhandiwad AA, Golann DR, Liu G, Syed SA, Napoli AJ, Burgess HA, Sirotkin HI, Wollmuth LP. A Model to Study NMDA Receptors in Early Nervous System Development. *J Neurosci.* 2020 Apr 29;40(18):3631-3645. doi: 10.1523/JNEUROSCI.3025-19.2020. Epub 2020 Apr 3. PMID: 32245827; PMCID: PMC7189761.
 - ID ZDB-FISH-210716-3
- WT + CRISPR1-*grin1a* + CRISPR1-*grin1b*
 - <https://zfin.org/ZDB-FISH-190218-4#summary>
 - Gao J, Stevenson TJ, Douglass AD, Barrios JP, Bonkowsky JL. The Midline Axon Crossing Decision Is Regulated through an Activity-Dependent Mechanism by the NMDA Receptor. *eNeuro.* 2018 Apr 17;5(2):ENEURO.0389-17.2018. doi: 10.1523/ENEURO.0389-17.2018. PMID: 29766040; PMCID: PMC5952305.
 - ID ZDB-FISH-190218-4
- **grin1a**^{sbu90/sbu90}; **grin1b**^{sbu94/sbu94}
 - <https://zfin.org/ZDB-FISH-210716-4>
 - Zoodsma JD, Chan K, Bhandiwad AA, Golann DR, Liu G, Syed SA, Napoli AJ, Burgess HA, Sirotkin HI, Wollmuth LP. A Model to Study NMDA Receptors in Early Nervous System Development. *J Neurosci.* 2020 Apr 29;40(18):3631-3645. doi: 10.1523/JNEUROSCI.3025-19.2020. Epub 2020 Apr 3. PMID: 32245827; PMCID: PMC7189761.
 - ID ZDB-FISH-210716-4
- **zc69Tg** + CRISPR1-*grin1a* + CRISPR1-*grin1b*

- <https://zfin.org/ZDB-FISH-190218-3>
- Gao J, Stevenson TJ, Douglass AD, Barrios JP, Bonkowsky JL. The Midline Axon Crossing Decision Is Regulated through an Activity-Dependent Mechanism by the NMDA Receptor. *eNeuro*. 2018 Apr 17;5(2):ENEURO.0389-17.2018. doi: 10.1523/ENEURO.0389-17.2018. PMID: 29766040; PMCID: PMC5952305.
- ID ZDB-FISH-190218-3
- grin2Aa SBU99; grin2Ab SBU300
 - Zoodsma JD, Keegan EJ, Moody GR, Bhandiwad AA, Napoli AJ, Burgess HA, Wollmuth LP, Sirotkin HI. Disruption of grin2B, an ASD-associated gene, produces social deficits in zebrafish. *Mol Autism*. 2022 Sep 22;13(1):38. doi: 10.1186/s13229-022-00516-3. PMID: 36138431; PMCID: PMC9502958.
- grin2Ba SBU310; grin2Bb SBU311
 - Zoodsma JD, Keegan EJ, Moody GR, Bhandiwad AA, Napoli AJ, Burgess HA, Wollmuth LP, Sirotkin HI. Disruption of grin2B, an ASD-associated gene, produces social deficits in zebrafish. *Mol Autism*. 2022 Sep 22;13(1):38. doi: 10.1186/s13229-022-00516-3. PMID: 36138431; PMCID: PMC9502958.
- grin2Da SBU329; grin2Db SBU330
 - Zoodsma JD, Keegan EJ, Moody GR, Bhandiwad AA, Napoli AJ, Burgess HA, Wollmuth LP, Sirotkin HI. Disruption of grin2B, an ASD-associated gene, produces social deficits in zebrafish. *Mol Autism*. 2022 Sep 22;13(1):38. doi: 10.1186/s13229-022-00516-3. PMID: 36138431; PMCID: PMC9502958.

Animal models with patient variants

Gene	Variant	Domain	LOF/GOF	Institution	Country
GRIN1	Q536R	S1	LOF	University of Toronto	Canada
GRIN1	G620R	M2	LOF	University of Toronto	Canada
GRIN1	Y647S	M3	GOF	University of Toronto	Canada
GRIN1	L655Q	M3	GOF	Zhejiang People's Hospital of	China

				Hangzhou	
GRIN1	M813T	M4	LOF	University of Toronto	Canada
GRIN1	G827R	M4	LOF	University of Toronto	Canada
GRIN2A	S644G	M3	GOF	Columbia University	United States
GRIN2B	E413G	S1	LOF	Emory University	United States
GRIN2B	C456Y	S1	-	Institute for Basic Science	Korea
GRIN2B	M818T	M4	GOF	National University of Singapore	Singapore
GRIN2B	L825V	M5	-	Institute of Physiology	Czech Republic
GRIN2B*	S1415L	CTD	LOF	National Institute of Health	United States
GRIN2D	V667I	M3	GOF	Columbia University	United States
GRIN2D	V667I	M3	GOF	Tel Aviv University	Israel

- GRIN3A A762T Emory University, United States
- GRIN2A NM_01134407.3:c.1936A>G - p.Thr646Ala (third transmembrane domain (M3) of the GluN2A subunit of the NMDA receptor);GOF. University of Bologna, Italy.
- GRIN2A p.A243V, University of Maryland, United States.
- GRIA2 p.Pro528Thr (heterozygous/homozygous viable)
- GRIA2 p.Asn812Ser (heterozygous/homozygous viable)
- GRIA2 p.Gly792Val (in flip exon, heterozygous/homozygous viable)
- GRIA2 p.Glu776Asp (heterozygous/homozygous viable)
- GRIA2 p.Asp611Asn (heterozygous/homozygous viable)
- GRIA2 p.Phe644Leu (heterozygous lethal)