GRI Update 2023

GRIN publications

Clinical Investigations

↗ **Strehlow et al. (2022)** reported the first observation of autosomal recessive *GRIN2A*-related disorder

↗ **Brock et al. (2022)** outlined similarties of *GRIN1*- and *GRIN2B*-related cortical malformations

↗ **Platzer, Krey, Lemke (2022)** wrote a GeneReviews® on *GRIN2D*-related disorder (based on findings from the registry)

In silico and in vitro Research

↗ **Brünger et al. (2022)** showed conserved patters across ion channels correlate with variant pathogenicity and clinical phenotypes

↗ **Han et al. (2022)** explored opportunities for precision treatment of *GRIN2A* and *GRIN2B* GoF variants in triheteromeric NMDARs

Treatment Investigations

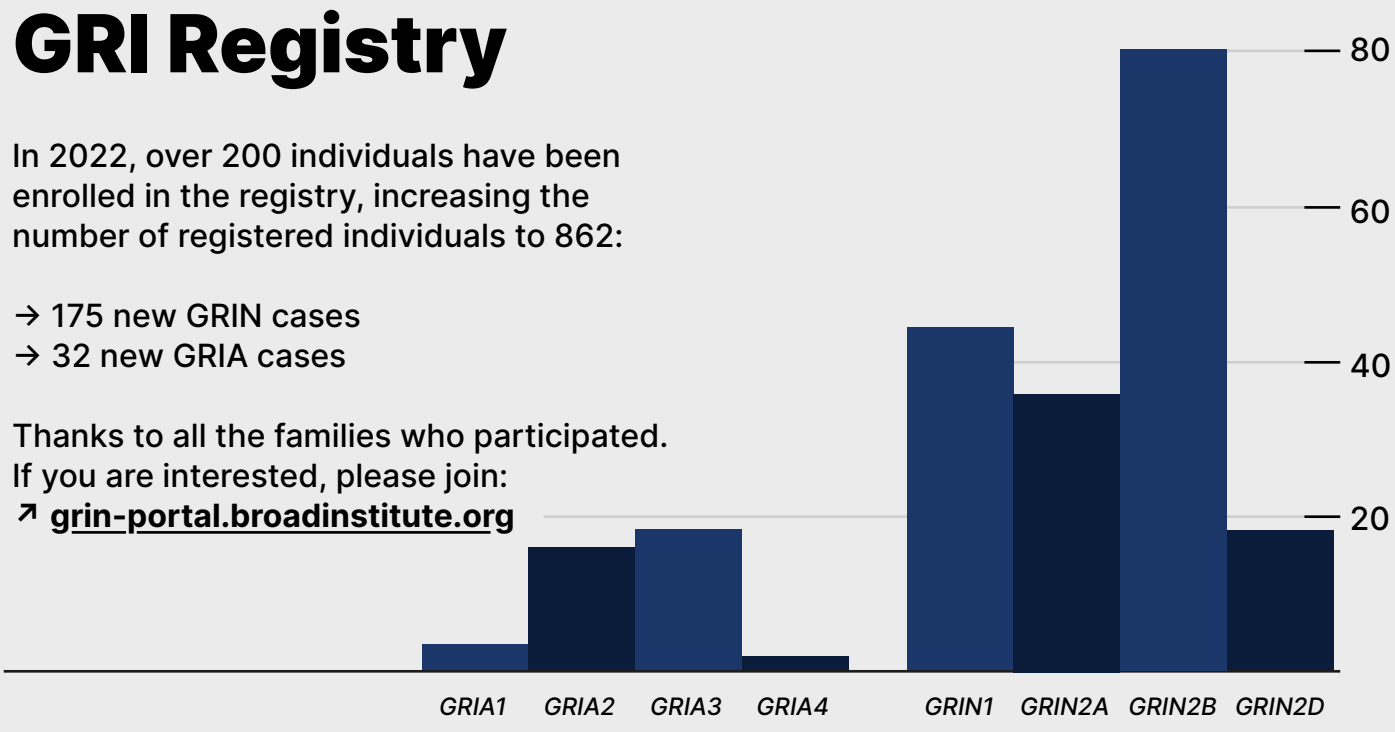
↗ **Krey et al. (2022)** identified improvements in behaviour, development, seizure frequency and EEG due to L-serine therapy in individuals with *GRIN2A* or *GRIN2B* null variants.

GRI Registry

In 2022, over 200 individuals have been enrolled in the registry, increasing the number of registered individuals to 862:

→ 175 new GRIN cases
→ 32 new GRIA cases

Thanks to all the families who participated.
If you are interested, please join:
↗ **grin-portal.broadinstitute.org**



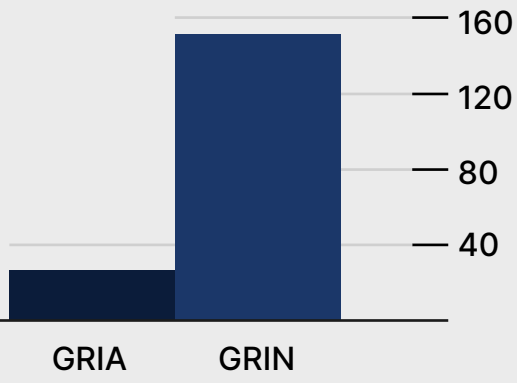
GRIN Portal

Variants of individuals newly enrolled in the ↗ **GRI Registry** will be forwarded to CFERV for functional testing on a monthly basis. After prioritization, CFERV will process the functional workup and report back bi-annually. Novel data will be updated on the ↗ **GRIN Portal** bi-annually, as well *(latest update: 15.12.2022)*.

functional investigations

In 2022, we performed functional investigations on

→ 152 GRIN variants
→ 30 GRIA variants



outlook on 2023

Our ongoing projects to be finalised very soon

→ The largest and most comprehensive genotype-electrotype-phenotype correlation study on *GRIN1* (based on ~200 cases from our joint registry)

→ The conclusions of the ClinGen GRIN Variant Curation Expert Panel to define international standards for classification of GRIN variants

→ Description of memantine responses in over 20 individuals

→ Functional investigations of over 50 GRIA variants

→ Novel mouse line (*GRIN2B* Ser810Arg)

We will get involved in novel endeavours

→ Start of an international clinical trial on radiprodil in GRIN gain-of-function cases

→ Investigation of blood counts in GRIN-related disorders: if you have reports and are willing to share → please provide to the ↗ **GRI Registry**

Johannes Lemke and team, Leipzig/Germany — GRI@medizin.uni-leipzig.de
Stephen Traynelis and team, Atlanta/US
Tim Benke and team, Denver/US — grinresearch@cuanschutz.edu
Dennis Lal and team, Cleveland/US