

Article

Distinct Functional Alterations and Therapeutic Options of Two Pathological De Novo Variants of the T292 Residue of GABRA1 Identified in Children with Epileptic Encephalopathy and Neurodevelopmental Disorders

Supplementary Materials:

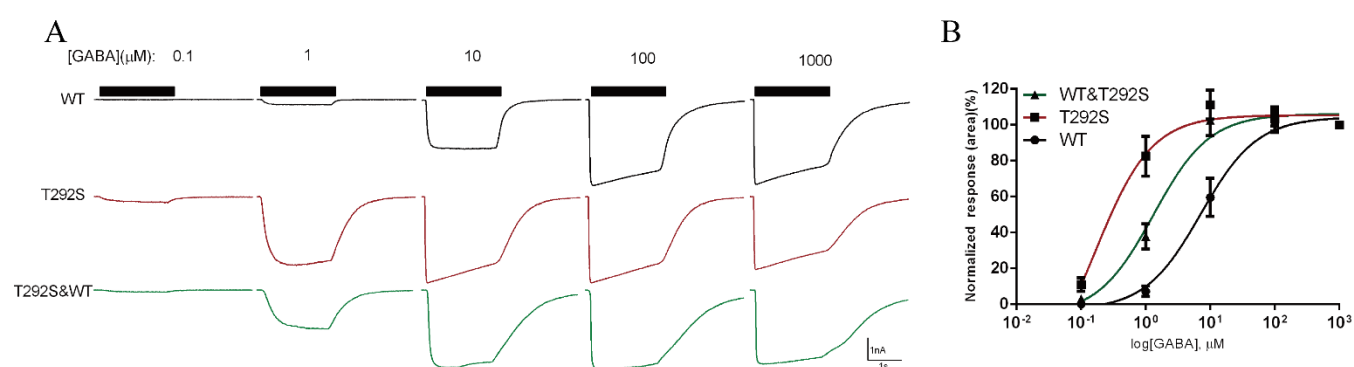


Figure S1. Overexpressing mixed GABRA1 subunits ($\alpha 1_{T292} : \alpha 1_{T292S} : \beta 2 : \gamma 2 = 1:1:2:1$) in HEK293 cells to mimic heterozygous status in patient. **(A)** Representative trace of GABA-evoked currents of WT (black), $\alpha 1_{T292S}$ GABA_AR (red) and mixed expression of $\alpha 1_{T292}\alpha 1_{T292S}\beta 2\gamma 2$ (green). **(B)** Dose-response curve of WT ($n = 10$), $\alpha 1_{T292S}$ GABA_AR ($n = 8$) and mixed expression of $\alpha 1_{T292}\alpha 1_{T292S}\beta 2\gamma 2$ ($n = 8$).

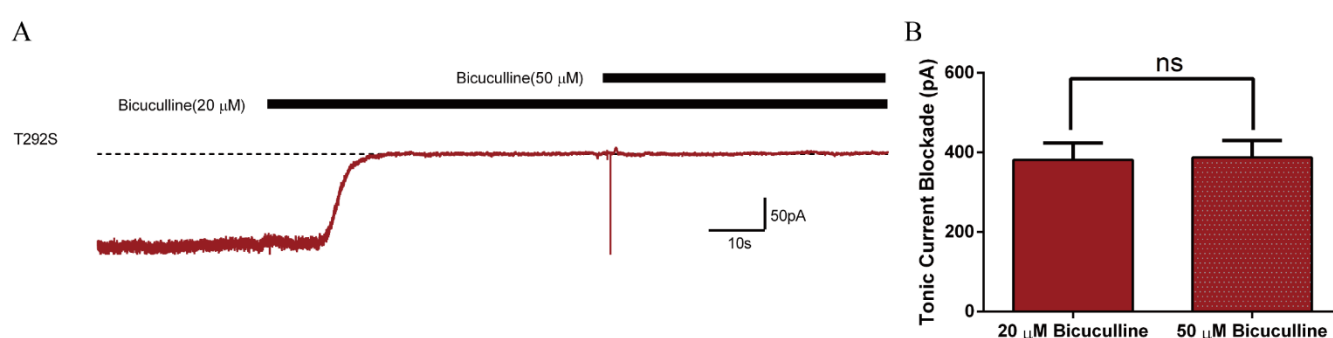


Figure S2. Higher concentration bicuculline could not further block tonic current of $\alpha 1_{T292S}$ GABA_AR **(A)** Representative trace of 20 μM and 50 μM bicuculline blocked tonic current of $\alpha 1_{T292S}$ GABA_AR. **(B)** Quantification of tonic current blocked by 20 μM and 50 μM bicuculline of $\alpha 1_{T292S}$ ($n = 7$) of GABA_AR. Statistical differences were determined using unpaired t-test (ns = not significant).

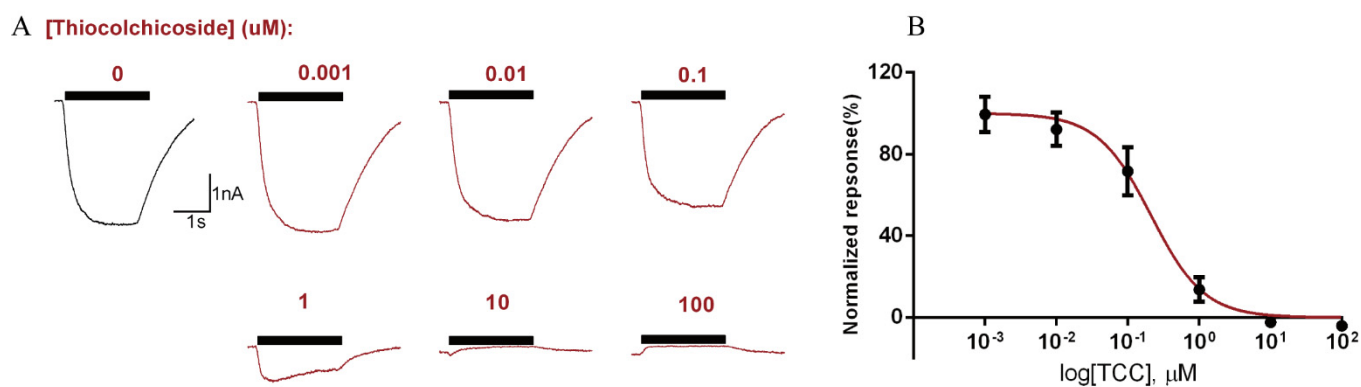


Figure S3. (A) Representative trace and (B) dose-response curve of TCC on $1\mu\text{M}$ GABA-evoked current to determine the optimal concentration of thiocolchicoside to restore the GABA-evoked currents of T292S GABA A Rs to the wild-type level.