CSNK2B Phenotypes Include Infantile Epilepsy with Myoclonic Seizures

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De novo variants in the *CSNK2B* gene have been suggested as a novel genetic cause for intellectual disability with or without epilepsy based on three cases reported in the literature. Here we describe an additional 17 individuals with a neurodevelopmental phenotype who carry a variant in *CSNK2B*. The cases included in our series had genetic testing on a research or clinical basis, and the respective institutions were connected via GeneMatcher.

Of the 20 identified cases, including those newly described in this series and the three previously reported, there were 16 males and four females. Epilepsy was reported in 15 cases (75%), all of whom had seizure onset in the first three years of life. Half of the patients with seizures had onset in infancy, and all but one of these infants had myoclonic seizures. All cases had some degree of developmental delay and/or intellectual disability, ranging from mild developmental delay to severe intellectual disability. Some degree of speech impairment was also described in every case, and motor delay or impairment was reported in most (16/20). Additional findings included hypotonia (10/20), behavioral issues (10/20), autism/autistic features (6/20), endocrine abnormalities (3/20), cardiac issues (3/20), hearing loss (3/20) and genitourinary issues (3/20). More than half (11/20) had dysmorphic features, most of which were reported to be minor. The types of variants reported included: four stop-gain, four frameshift, four splice site, seven missense, and one start-loss. Eighteen of the 20 variants were *de novo*, and two had unknown inheritance (one stop-gain and one splice site). Individuals with a loss-of-function variant were more likely to have epilepsy than those who carried a missense variant, representing a potential genotype-phenotype correlation.

This robust series of patients solidifies the association between *CSNK2B* and neurodevelopmental disease and allows for further characterization of the phenotypic spectrum seen in this condition, including infantile onset epilepsy with myoclonic seizures.