KCNB1

Potassium voltage-gated channel, Shab-related subfamily, member 1, also known as KCNB1 or Kv2.1, is a protein that, in humans, is encoded by the KCNB1 gene.

Potassium voltage-gated channel subfamily B member one, or simply known as KCNB1, is a delayed rectifier and voltage-gated potassium channel found throughout the body. The channel has a diverse number of functions. However, its main function, as a delayed rectifier, is to propagate current in its respective location. It is commonly expressed in the central nervous system, but may also be found in pulmonary arteries, auditory outer hair cells, stem cells, the retina, and organs such as the heart and pancreas. Modulation of K+ channel activity and expression has been found to be at the crux of many profound pathophysiological disorders in several cell types.

Developmental and epileptic encephalopathies (DEE) refer to a heterogeneous group of devastating neurodevelopmental disorders. Variants in KCNB1 have been recently reported in patients with early-onset DEE. KCNB1 encodes the alpha subunit of the delayed-rectifier voltage-dependent potassium channel Kv 2.1. We review the 37 previously reported patients carrying 29 distinct KCNB1 variants and significantly expand the mutational spectrum describing 18 novel variants from 27 unreported patients. Most variants occur de novo and mainly consist of missense variants located on the voltage sensor and the pore domain of Kv 2.1. We also report the first inherited variant (p.Arg583*). KCNB1-related encephalopathies encompass a wide spectrum of neurodevelopmental disorders with predominant language difficulties and behavioral impairment. Eighty-five percent of patients developed epilepsies with variable syndromes and prognosis. Truncating variants in the C-terminal domain are associated with a less severe epileptic phenotype. Overall, this report provides an up-to-date review of the mutational and clinical spectrum of KCNB1, strengthening its place as a causal gene in DEEs and emphasizing the need for further functional studies to unravel the underlying mechanisms [1].

De novo KCNB1 missense variants in the ion channel domain and loss-of-function variants in this domain and the C-terminal likely cause neurodevelopmental disorders with or without seizures. Patients with presumed pathogenic variants in KCNB1 have a variable phenotype. However, the type and position of the variants in the protein are (imperfectly) correlated with the severity of the disorder [2].

1)
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