Potassium Channel, Voltage-Gated, Shaker-Related Subfamily, Member 2

Alternative Names
KCNA2
MK2, Mouse, Homolog of
KV1.2

Record Category
Gene locus

WHO-ICD
N.B.: Classification not applicable to gene loci.

Incidence per 100,000 Live Births
N/A to gene loci

OMIM Number
176262

Mode of Inheritance
N/A

Gene Map Locus
1p13.3

Description
The Potassium Channel, Voltage-Gated, Shaker-Related Subfamily, Member 2 (KCNA2) gene encodes a member of the voltage-gated potassium channel family that regulates neurotransmitter release, heart rate, neuronal excitability, smooth muscle contraction, epithelial electrolyte transport, insulin secretion, and cell volume. KCNA2 belongs to the KV1 subfamily of voltage-gated potassium channels and can form functional homotetrameric and heterotetrameric channels with variable proportions of KCNA1, KCNA4, KCNA5, KCNA6, KCNA7, and other family members. These channels contribute towards the repolarization of the neuronal membrane following an action potential. They thus play a presynaptic role, prevent hyperexcitability and aberrant action potential firing, prevent random spontaneous calcium spikes, suppressing dendritic hyperexcitability, and play a significant role in motor coordination.

Reduced KCNA2 expression plays a role in the perception of neuropathic pain after peripheral nerve injury. Defects in this gene are the cause of infantile epileptic encephalopathy 32 (EIEE32), a condition characterized by refractory seizures, and neurodevelopmental impairment.

Molecular Genetics
The KCNA2 gene has been mapped to 1p13.3 chromosome and is clustered with KCNA3 and KCNA10 gene. It has only one coding exon spanning approximately 38 kb. The encoded protein comprises 499 amino acids with a molecular mass of 57 kDa. The encoded protein has six membrane-spanning helices with a shaker-type repeat in the fourth helix. The first four of these helices constitute a voltage sensing domain while the last two make up the pore domain.

Mutations in this gene have been associated with early infantile epileptic encephalopathy 32 (EIEE32). To date, only nine patients have been reported with mutations in the KCNA2 gene. Two dominant negative loss-of-function (c.1214C>T and c.788T>C) mutations associated with less severe phenotype, and three dominant gain-of-function (c.894G>T, c.890G>A, and c.890C>A) mutations associated with more severe phenotypes have been reported in this gene.

Epidemiology in the Arab World

Saudi Arabia
See: [Sudan > Hundallah et al., (2016)]

Sudan
Hundallah et al., (2016) described an infant who had seizures on the first day of life in the form of clonic and myoclonic jerks, with frequent daily attacks. He was born to healthy non-consanguineous Sudanese parents living in Saudi Arabia. Whole-exome sequencing revealed a novel de novo (c.1120A>G) gain-of-function mutation in the KCNA2 gene, which was not found in both parents.

References

Hundallah K, Alenizi A, AlHashem A, Tabarki B. Severe early-onset epileptic encephalopathy due to mutations in the KCNA2 gene: Expansion of the genotypic and phenotypic spectrum. Eur J Paediatr Neurol. 2016; 20(4):657-60. PMID: 27117551

Related CTGA Records

Epileptic Encephalopathy, Early Infantile, 32

External Links

https://ghr.nlm.nih.gov/gene/KCNA2#conditions
http://www.genecards.org/cgi-bin/carddisp.pl?gene=KCNA2

Contributors

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