SK channel

SK channels (small conductance calcium-activated potassium channels) are a subfamily of Ca2+-activated K+ channels.

They are so called because of their small single channel conductance in the order of 10 pS.

SK channels are a type of ion channel allowing potassium cations to cross the cell membrane and are activated (opened) by an increase in the concentration of intracellular calcium through N-type calcium channels. Their activation limits the firing frequency of action potentials and is important for regulating afterhyperpolarization in the neurons of the central nervous system as well as many other types of electrically excitable cells. This is accomplished through the hyperpolarizing leak of positively charged potassium ions along their concentration gradient into the extracellular space. This hyperpolarization causes the membrane potential to become more negative.

SK channels are thought to be involved in synaptic plasticity and therefore play important roles in learning and memory.

Loss of function in the Scn1a gene leads to Dravet syndrome (DS). Reduced excitability in cortical inhibitory neurons is thought to be the major cause of DS seizures.

Ritter-Makinson et al., showed enhanced excitability in thalamic inhibitory neurons that promotes the non-convulsive seizures that are a prominent yet poorly understood feature of DS. In a mouse model of DS with a loss of function in Scn1a, reticular thalamic cells exhibited abnormally long bursts of firing caused by the downregulation of calcium-activated potassium SK channels. The study supports a mechanism in which loss of SK activity causes the reticular thalamic neurons to become hyperexcitable and promote non-convulsive seizures in DS. They propose that reduced excitability of inhibitory neurons is not global in DS and that non-GABAergic mechanisms such as SK channels may be important targets for treatment [1].

1)
Ritter-Makinson S, Clemente-Perez A, Higashikubo B, Cho FS, Holden SS, Bennett E, Chkaidze A, Eelkman Rooda OHJ, Cornet MC, Hoebeek FE, Yamakawa K, Cilio MR, Delord B, Paz JT. Augmented Reticular Thalamic Bursting and Seizures in Scn1a-Dravet Syndrome. Cell Rep. 2019 Jan 2;26(1):54-64.e6. doi: 10.1016/j.celrep.2018.12.018. PubMed PMID: 30605686.