Maxi-K channels: structure, characteristics, biological process and principal blockers and activators. A general overview.

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Maxi-K also known as BK channels, Slo1 or KCa1.1 channels, are one type of calcium-activated potassium channels that have large single channel conductance of 100–300 pS. Their most important physiological property is dual regulation through membrane voltage and intracellular Ca^{2+}. [1] The complexity of this channel function mirrors the complexity of its protein structure. The amino acid sequence includes the integral membrane pore shared by all K^+ channels, the integral membrane voltage sensor domains present in voltage-dependent channels, and a cytoplasmic domain (CTD) consisting of approximately 800 amino acids per subunit, which accounts for the C-terminal two thirds of the entire channel. The CTD structure confers upon the BK channel its ability to respond to changes in intracellular Ca^{2+}. [2-5] It is also the source of functional heterogeneity through alternate splicing, polymorphisms, phosphorylation, and protein interactions, which modulate BK channel activity. [5-8] These channels modulate several physiological events, like blood pressure, smooth muscle relaxation or electrical tuning of hair cells in the cochlea and have a leading role in many pathophysiological conditions such as epilepsy, ischemic stroke, cognitive disorders, and the behavioral response to alcohol, to give only a few examples.[9, 10] Studies involving activation and inactivation with pharmacological and genetic tools, including global, and tissue-specific knockouts, have implicated Maxi-K channels in cardiac function, neuroprotection, and cardio-protection from ischemia-reperfusion (IR) injury, in addition to IR-induced inflammation and mucosal barrier disruption in the small intestine. [11] It is also known that Maxi-K channels function as neuronal calcium sensors and contribute to the control of cellular excitability and the regulation of neurotransmitter release.[9] Numerous Maxi-K channel blockers and activators are used to identify these channels and study their functions. Some of the most common Maxi-K channel modulators include tetraethylamonium (TEA), paxilline, penitrem A, charybdotoxin, iberiotoxin, indoles, benzimidazolones, biarylthioureas, anthraquinone analogs, tetrahydroquinolines, terpenes, benzofuroindoles, anilinoanthraquinones and quinoline. [9, 12-15] Both, the structural variety presented by the main modulators of the Maxi-K channel and the large number of pathophysiological conditions in which they are involved open a powerful research niche for the treatment of multiple pathologies.

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