Calcium-Sensitive Potassium Channels

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Introduction

The calcium-activated potassium channels can be divided in two functionally different groups. The first group belongs to the family of potassium channels that consists of one pore region (1P) with six putative transmembrane segments (6T) per alpha subunit (1P6T). These channels are potassium selective and are opened by an increase in $[Ca^{++}]_i$ via calmodulin. The opening of the channel is independent from the applied voltage. The single channel conductance of these calcium-activated potassium channels range from small (SK channels; ~ 5 pS) to intermediate (IK channels; 1060 pS) conductances Hille (2001). In addition to the different single-channel conductance, they seem to have a specific pharmacology; i.e., IK channels are blocked by charybdotoxin (ChTX), a peptide toxin isolated from scorpion venom, and are blocked by clotrimazole, and SK channels are blocked by apamin. Both channel types can be activated by 1-EBIO (1-ethyl-benzimidazolinone). The second group of calcium-activated potassium channels are the so-called MaxiK or BK channels. They also have 1P region, however, with 7-transmembrane segments (S0–S6) per alpha-subunit. These channels are also potassium selective and can be opened by either membrane depolarization and an increase in $[Ca^{++}]_i$. The single-channel conductance is very large (in the range ~ 250 pS), therefore, the name MaxiK channel or BK channel (for big conductance). BKchannels are also blocked by ChTX, more specifically, by Iberiotoxin (IbTX) and paxilline Sanchez and McManus (1996). BKchannels can also be activated by a variety of substances, for example, NS1608 and NS1619 Stroebaek et al (1996).

Nomenclature

Superfamily	1P6T potassium channels
Family	Ca^{++}-activated potassium channels
Type	SK1-3, IK1, BK (Slo)
Subtypes	
Classification Numbers	KCNN1-3,KCNN4, KCNMA1
Alternate or Previous Names	
Comments	

Target Structure

Protein Information

SK1-3, IK1, and Slo are pore-forming subunits. The functional channel consists of four identical subunits (homotetramer), each with one pore region (1P) and six (Sk, IK) or seven (BK) putative transmembrane segments (6T). The Ca^{++} sensor for SK and IK seems to be calmodulin bound to each subunit at a region between the S6 segment and the C-terminal end of the channel. Slo is associated with beta-subunits Jiang et al (1999), Weiger et al (2000).

Ligands, Substrates, Ions

Ligands

Ca^{++}, calmodulin (SK, IK), beta-subunits (BK)

Substrates

Name	Km value	Km units	Reference	Remarks
Ca++ (SK, IK)	300	nM	Kohler et al (1999)	
Ca++ (BK)	1, 10	μM	Nimigean et al (1999)	Beta-subunit changes calcium-sensitivity from 10 to 1μM; $[Ca^{++}]_i$ shifts the voltage dependence of the BK channel toward more hyperpolarized potentials.
Calmodulin (SK, IK)			Xia et al (1998), Fanger et al (1999)	

Ions

	Value	Units	Reference	Remarks
K^+ Voltage Dependence	only BK			Calcium and/or the beta subunit shift the voltage dependence of activation of the BK channel toward more hyperpolarized potentials.

Effectors, Products

Establishing a link between Ca^{++}-based second messenger systems and the membrane potential of cells.

Endogenous Regulation

Protein Partners

Calmodulin (SK, IK), beta-subunits (BK)

Pharmacological Regulation

Different blockers and openers (see individual targets). Common openers for SK and IK are 1-ethyl-benzimidazolinone (1-EBIO) Devor et al (1996), Pedarzani et al (2001) and 5,6 dichloro-1-ethyl-benzimidazolinone (DC-EBIO) with different affinities for IK and SK; see individual targets. Openers for BK include NS1608, NS1619, BMS204352 Gribkoff et al (2001), DHS-1 McManus et al (1993), and estradiol Valverde et al (1999).

Research Tools

Probes

Antibodies and Other Probes

Antibodies against calcium-activated potassium channels are available from Alamone and Chemicon.

Assays

Molecular / Cellular	Calcium-activated potassium channels are mainly investigated by electrophysiological techniques, e.g., patch-clamping, conventional voltage-clamp, and two electrode voltage-clamping. These methods have been used for heterologously expressed channels as well as for endogenous channels in tissue preparations. Imaging with membrane potential sensitive fluorescent dyes and flux measurements using radioactive Rb^+ were also used.
Genetically Engineered Organisms	Transgenic mice with targeting the SK3 allele have been generated Bond et al (2000).

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