SK-Ca2 Small Conductance Calcium Activated Potassium Channel

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Introduction

The SK2 small conductance calcium-activated potassium channel belongs to the family of potassium channels that consist of one pore region (1P) with 6 putative transmembrane segments (6T) per alpha subunit (1P6T). It is a potassium selective ion channel that is opened by an increase in $[Ca^{++}]_i$. The opening of the channel is independent from the applied voltage, and the single channel conductance is of small size compared to calcium-activated potassium channels with intermediate and large single channel conductances Hille (2001). This channel type is usually thought to underlie the slow after hyperpolarization seen in neuronal cells. In addition to the different single channel conductance, these channels do also have a specific pharmacology, i.e., they are blocked by apamin, a peptide toxin isolated from bee venom, as well as blocked by Scyllatoxin (Leiurustoxin I), a peptide toxin isolated from scorpion venom. In addition, the channels are also blocked selectively by several bis-quinolinium cyclophanes (UCL 1530, UCL 1684, UCL 1848, UCL 2079). The channels can be activated by 1-EBIO (1-ethyl-benzimidazolinone), similar to the calcium-activated potassium channels with intermediate conductance.

Nomenclature

Superfamily	1P6T potassium channels
Family	Voltage independent Ca^{++}-activated potassium channels
Type	SK2
Subtypes	
Classification Numbers	KCNN2
Alternate or Previous Names	SK2, SKCa2
Comments	

Target Structure

Protein Information

SK2 is a pore forming subunit. The functional channel consists of four identical subunits (homotetramer), each with one pore region (1P) and 6 putative transmembrane segments (6T). The Ca^{++} sensor seems to be calmodulin bound to each subunit at a region between the S6 segment and the C-terminal end of the channel.

Protein Sequence Information

	Number or Name	Comments
Subunit Name	hKCNN2	
Organism Name	Human	
Gene Accession #	NM_021614	AF239613 Desai et al (2000), AF397175, XM_011226
SwissProt Accession #	Q9H2S1	
# of Amino Acid Residues	579	
Protein Sequence Motifs		hKCNN2 contains 3 consensus sites for N-glycosylation site, 3 consensus sites for cAMP- and cGMP-dependent protein kinase phosphorylation, 12 consensus sites for Protein kinase C phosphorylation, 7 consensus sites for Casein kinase II phosphorylation, 20 consensus sites for N-myristoylation site, 1 glycine-rich and 1 serine-rich region.
Chromosomal Localization	5q23.1-23.2	Ganshani et al (2000) NT_006899 chromosome 5 reference genomic contig.

	Number or Name	Comments
Subunit Name	rKCNN2	Kohler et al (1996)
Organism Name	Rat	Kohler et al (1996)
Gene Accession #	NM_019314	
SwissProt Accession #	P70604	
# of Amino Acid Residues	581	
Protein Sequence Motifs		rKCNN2 contains 3 consensus sites for N-glycosylation, 3 consensus sites for cyclic AMP- and cyclic GMP-dependent protein kinase phosphorylation, 13 consensus sites for Protein kinase C phosphorylation site, 8 consensus sites for casein kinase II phosphorylation, 24 consensus sites for N-myristoylation site, 1 glycine-rich and 1 serine-rich region.
Chromosomal Localization		

	Number or Name	Comments
Subunit Name	mKCNN2	
Organism Name	Mouse	
Gene Accession #	NM_080465	AF357240, AY123778
SwissProt Accession #	P58390	
# of Amino Acid Residues	575	
Protein Sequence Motifs		mKCNN2 contains 3 consensus sites for N-glycosylation, 3 consensus sites for cyclic AMP- and cyvlic GMP-dependent protein kinase phosphorylation, 13 consesnus sites for Protein kinase C phosphorylation, 8 consensus sites for Casein kinase II phosphorylation, 18 consensus sites for N-myristoylation, 1 glycine-rich and 1 serine-rich region.
Chromosomal Localization	18	NW_000134 mus musculus WGS supercontig Mm18_WIFeb01_311

	Number or Name	Comments
Subunit Name	cKCNN2	
Organism Name	Gallus gallus (chicken)	
Gene Accession #	AF079372	
SwissProt Accession #		
# of Amino Acid Residues	554	
Protein Sequence Motifs		cKCNN2 contains 3 consensus sites for N-glycosylation site, 3 consensus sites for cAMP- and cGMP-dependent protein kinase phosphorylation, 10 consensus sites for Protein kinase C phosphorylation, 5 consensus sites for Casein kinase II phosphorylation, and 5 consensus sites for N-myristoylation.
Chromosomal Localization		

Localization

Protein

Neurons Hille (2001); Jurkat T lymphocytes Grissmer et al (1992), Jager et al (2000).

mRNA

Hippocampus (CA3), dentate gyrus, subiculum, anterior olfactory nucleus, olfactory tubercle, cerebellum, and cortex Stocker et al (2000).

Ligands, Substrates, Ions

Ligands

Ca^{++}, calmodulin

Substrates

Name	Km value	Km units	Reference	Remarks
Ca++ Calmodulin	300	nM	Kohler et al (1996), Grissmer et al (1992) Xia et al (1998), Schuhmacher et al (2001)	

Ions

	Value	Units	Reference	Remarks
Potassium Conductance	4-20	pS	Hille (2001)	The higher conductance is measured with elevated external potassium concentrations.
Voltage Dependence				none

Effectors, Products

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

Endogenous Regulation

Protein Partners

calmodulin

Pharmacological Regulation

Selective peptide blockers are apamin and scyllatoxin Hille (2001). Highly selective non-peptide blockers are different bis-quinolinium cyclophanes Stroebaek et al (2000), Shah et al (2000). Non-selective, more unspecific blockers are d-tubocurarine, verapamil, diltiazem, and tetraethylammonium. Openers are 1-ethyl-benzimidazolinone (1-EBIO, (Pedarzani et al., 2001)); EBIO activates also IK channels Devor et al (1996) but not BK channels.

Agonist / Activator / Substrate

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: 1-ethyl-benzimidazolinone (1-EBIO)							
Ki:	650	μM	Rat KCNN2		Xenopus oocytes	Pedarzani et al (2001)	1-EBIO activates directly the channel and requires the presence of intracellular Ca^{++} method: electrophysiology (whole cell).

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: UCL1684							
IC50:	0.4	nM	Rat KCNN2		HEK-293	Stroebaek et al (2000)	Method used: electrophysiology (whole cell).

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: Apamin							
IC50:	0.3	nM	Human	T-cell carcinoma; endogeneously expressed	Jurkat	Grissmer et al (1992)	Method used: electrophysiology (whole cell).

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: Apamin							
IC50:	0.1	nM	Rat KCNN2		HEK-293	Stroebaek et al (2000)	Method used: electrophysiology (whole cell).

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: Leiurutoxin / scyllatoxin							
IC50:	0.3	nM	Human	T-cell carninoma; endogeneously expressed	Jurkat	Hanselmann and Grissmer (1996)	Method used: electro-physiology (whole cell).

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: Leiurutoxin / scyllatoxin							
IC50:	0.3	nM	Rat KCNN2		HEK-293	Stroebaek et al (2000)	Method used: electrophysiology (whole cell).

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/Type	Reference	Comments
Agent: Lei-Dab7							
IC50:	4	nM	Rat KCNN2		COS-7	Shakkotai et al (2001)	

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: Dequalinium							
IC50:	160	nM	Rat KCNN2		HEK-293	Stroebaek et al (2000)	Method used: electrophysiology (whole cell).

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: Tubocurarine							
IC50:	2	μM	Rat KCNN2		Xenopus oocytes; HEK-293	Kohler et al (1996), Jager et al (1997), Stroebaek et al (2000)	Method used: electrophysiology (whole cell).

Antagonist / Inhibitor

	Value	Units	Organism	Organ Tissue	Cell Line/ Type	Reference	Comments
Agent: Bicuculline							
IC50:	1	μM	Rat KCNN2		Xenopus oocytes	Khawaled et al (1999)	Method used: electrophysiology (whole cell).

Journal Citations

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