

International Union of Pharmacology. LIII. Nomenclature and Molecular Relationships of Voltage-Gated Potassium Channels

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Introduction

Potassium-selective channels are the largest and most diverse group of ion channels, represented by some 70 known loci in the mammalian genome. The first cloned potassium channel gene was the *Drosophila* voltage-gated *shaker* channel, and this was rapidly followed by the identification of other voltage- and ligand-gated potassium channel genes in flies, mammals, and many other organisms. The voltage-gated K_v channels, in turn, form the largest family of some 40 genes among the group of human potassium channels, which also includes the Ca^{2+} -activated (K_{Ca}), inward-rectifying (K_{IR}), and two-pore (K_{2P}) families described in the following articles of this compendium. K_v and K_{Ca} channels together constitute the six/seven-transmembrane group of potassium-selective channels, made up of subunits containing six or seven membrane-spanning domains, including the positively charged S4 segment, which confers on some of these channels their voltage sensitivity.

Table 1 lists the International Union of Pharmacology (IUPHAR¹) names assigned to the members of the K_v family of channels, as well as the gene names established by the HUGO Gene Nomenclature Committee (HGNC). Two new sequences, $K_v6.4$ and $K_v8.2$, have been added to this list since the earlier edition of this compendium. Figures 1 and 2 show two phylogenetic tree reconstructions, one for the K_v1-9 families and the other for the K_v10-12 families, based on amino acid sequence alignments of the entire hydrophobic core of the proteins.

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¹ Abbreviations: IUPHAR, International Union of Pharmacology; HGNC, HUGO Gene Nomenclature Committee.

TABLE 1

K_v channel families

Gene names shown are those assigned by the IUPHAR (Catterall et al., 2002) and HGNC (<http://www.gene.ucl.ac.uk>) in addition to some other commonly used names.

IUPHAR	HGNC	Other
$K_v1.1$	<i>KCNA1</i>	<i>Shaker</i> -related family
$K_v1.2$	<i>KCNA2</i>	
$K_v1.3$	<i>KCNA3</i>	
$K_v1.4$	<i>KCNA4</i>	
$K_v1.5$	<i>KCNA5</i>	
$K_v1.6$	<i>KCNA6</i>	
$K_v1.7$	<i>KCNA7</i>	
$K_v1.8$	<i>KCNA10</i>	
$K_v2.1$	<i>KCNB1</i>	<i>Shab</i> -related family
$K_v2.2$	<i>KCNB2</i>	
$K_v3.1$	<i>KCNC1</i>	<i>Shaw</i> -related family
$K_v3.2$	<i>KCNC2</i>	
$K_v3.3$	<i>KCNC3</i>	
$K_v3.4$	<i>KCNC4</i>	
$K_v4.1$	<i>KCND1</i>	<i>Shal</i> -related family
$K_v4.2$	<i>KCND2</i>	
$K_v4.3$	<i>KCND3</i>	
$K_v5.1$	<i>KCNF1</i>	Modifier
$K_v6.1$	<i>KCNG1</i>	Modifiers
$K_v6.2$	<i>KCNG2</i>	
$K_v6.3$	<i>KCNG3</i>	
$K_v6.4$	<i>KCNG4</i>	
$K_v7.1$	<i>KCNQ1</i>	<i>KVLQT</i> <i>KQT2</i>
$K_v7.2$	<i>KCNQ2</i>	
$K_v7.3$	<i>KCNQ3</i>	
$K_v7.4$	<i>KCNQ4</i>	
$K_v7.5$	<i>KCNQ5</i>	
$K_v8.1$	<i>KCNV1</i>	Modifiers
$K_v8.2$	<i>KCNV2</i>	
$K_v9.1$	<i>KCNS1</i>	Modifiers
$K_v9.2$	<i>KCNS2</i>	
$K_v9.3$	<i>KCNS3</i>	
$K_v10.1$	<i>KCNH1</i>	<i>eag1</i> <i>eag2</i>
$K_v10.2$	<i>KCNH5</i>	
$K_v11.1$	<i>KCNH2</i>	<i>erg1</i> <i>erg2</i> <i>erg3</i> <i>elk1, elk3</i> <i>elk2</i> <i>elk1</i>
$K_v11.2$	<i>KCNH6</i>	
$K_v11.3$	<i>KCNH7</i>	
$K_v12.1$	<i>KCNH8</i>	
$K_v12.2$	<i>KCNH3</i>	
$K_v12.3$	<i>KCNH4</i>	

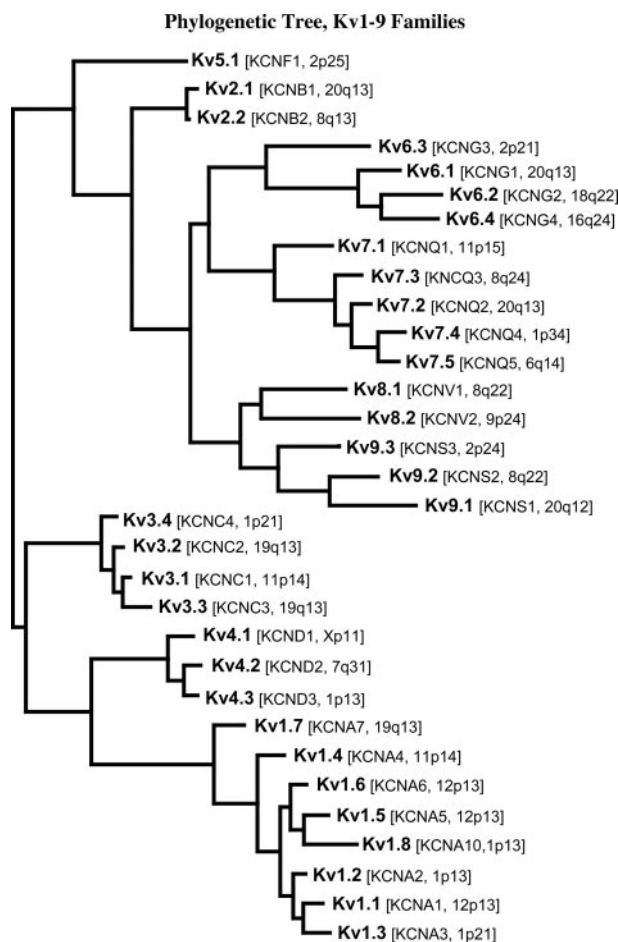


FIG. 1. Phylogenetic tree for the K_v 1–9 families. Amino acid sequence alignments of the human channel K_v proteins were created using CLUSTALW, and analysis by maximum parsimony using PAUP* resulted in unrooted trees comprising the K_v 1– K_v 6 and K_v 8– K_v 9 families that appeared in the previous edition of this compendium. Sequences of K_v 7.1–7.5, K_v 6.4, and K_v 8.2 were added to the existing alignment, and these new sequences were incorporated into the existing tree topology by use of a combination of maximum parsimony and neighbor-joining analysis. Only the hydrophobic cores (S1–S6) were used for analysis. The IUPHAR and HGNC names are shown together with the genes' chromosomal localization and other commonly used names.

K_v channels form an exceedingly diverse group, much more so than one would predict simply based on the number of distinct genes that encode them. This diversity arises from several factors. 1) *Heteromultimerization*. Each K_v gene encodes a peptide subunit, four of which are required to form a functional channel. K_v channels may be homotetramers but may also be heterotetramers formed between different subunits within the same family (in the case of the K_v 1, K_v 7, and K_v 10 families), and these diverse heterotetramers express properties that may be considerably different from those of any of the homotetramers. 2) *“Modifier” subunits*. Four of the K_v families (K_v 5, 6, 8, and 9) encode subunits that act as modifiers. Although these do not produce functional channels on their own, they form heterotetramers with K_v 2 family subunits, increasing the functional diversity within this family. 3) *Accessory proteins*. A variety of other peptides has also been shown to

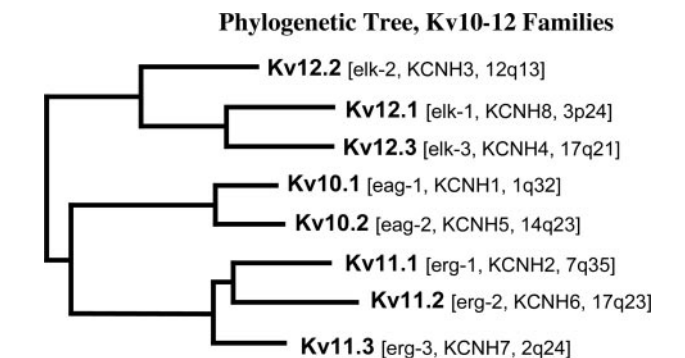


FIG. 2. Phylogenetic tree for the K_v 10–12 families. This unrooted tree was created as described in Fig. 1 and appeared in the previous edition of this compendium. The IUPHAR and HGNC names are shown together with the genes' chromosomal localization and other commonly used names.

associate with K_v tetramers and modify their properties, including several β subunits (which associate with K_v 1 and K_v 2 channels), KCHIP1 (K_v 4), calmodulin (K_v 10), and minK (K_v 11), as well as many others identified in the tables that follow the text of this article. 4) *Alternate mRNA splicing*. A number of K_v channel genes are known to contain intronless coding regions, including all of the K_v 1 family genes (with the sole exception of K_v 1.7) and K_v 9.3. Although alternate splicing of noncoding exons may be important in regulating the expression of these channels, one gene can produce only a single kind of protein subunit. However, various members of the K_v 3, 4, 6, 7, 9, 10, and 11 gene families have coding regions made up of several exons that are alternately spliced, providing yet another significant source of K_v channel functional diversity. 5) *Post-translational modification*. Many K_v channels can be post-translationally modified by phosphorylation (Jerng et al., 2004), ubiquitinylation (Henke et al., 2004), and palmitoylation (Gubitosi-Klug et al., 2005), which in turn modifies channel function.

Our current understanding of the roles of this family of channels is catalogued in Tables 2 through 41, including recent developments in the pharmacology, regulation of expression, and disease associations of its various members (Misonou and Trimmer, 2004; Norton et al., 2004; Wua and Dworetzky, 2005).

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TABLE 2
K_V1.1 channels

Channel name	K _V 1.1 ¹⁻⁶
Description	Voltage-gated potassium channel, delayed rectifier
Other names	HuK (I), MBK1, MK1, RCK1, RBK1, HBK1
Molecular information	Human: 494 aa, NM_000217, chr. 12p13.3, ^{7,8} <i>KCNA1</i> , GeneID: 3736, PMID: 1349297 ³⁵ Mouse: 495aa, NM_010595, chr. 6 Rat: 495aa, NM_173095, chr. 4q42
Associated subunits	K _V β ₁ , K _V β ₂ , PSD95, synapse-associated protein 97 (SAP97), SNAP25 ⁹⁻¹⁹
Functional assays	Voltage-clamp
Current	Voltage-gated potassium channel in neurons and skeletal muscle
Conductance	10pS ²⁰
Ion selectivity	K ⁺ (1) > Rb ⁺ (0.8) > NH ₄ ⁺ (0.1)
Activation	V _a = -32 mV; k _a = 8.5 mV; τ _n = 5 ms (-32 mV) ^{20,21}
Inactivation	V _h = -51 mV; k _h = 3 mV; τ _h = 11 s (40 mV) ^{20,21}
Activators	None
Gating inhibitors	None
Blockers	Tetraethylammonium (0.3 mM), DTX (20 nM), DTX-K, ShK (16 pM), 10- <i>N</i> -methylcarbamoyl-3,7-bis(dimethylamino)phenothiazine (490 nM), 4-aminopyridine (290 μM), capsaicin (29 μM), resiniferatoxin (9 μM), flecainide (209 μM), nifedipine (96 μM), diltiazem (144 μM), kaliotoxin (41 nM), hongotoxin-1, margatoxin ^{20,22-24}
Radioligands	¹²⁵ I-DTX, ¹²⁵ I-BgK ^{25,26}
Channel distribution	Brain, heart, retina, skeletal muscle, islets ²⁷⁻³¹
Physiological functions	Maintaining membrane potential, modulating electrical excitability in neurons and muscle
Mutations and pathophysiology	Episodic ataxia/myokymia syndrome type 1 ^{8,32-34}
Pharmacological significance	Not established
Comments	K _V 1.1 can coassemble with others in the K _V 1 family members in heteromultimers, but not with members of other K _V families; intronless coding region; mammalian <i>Shaker</i> -related family

aa, amino acids; chr., chromosome; DTX, dendrotoxin; ShK, *Stychoactyla helianthus* toxin; BgK, *Bundosoma granulifera* toxin.

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TABLE 3
K_v1.2 channels

Channel name	K _v 1.2
Description	Voltage-gated potassium channel, delayed rectifier
Other names	HuK (IV), MK2, BK2, RCK5, RAK, BGK5, XSha2, NGK1, HBK5 ^{1–8}
Molecular information	Human: 499aa, NM_004974, chr. 1p13, <i>KCNA2</i> , GeneID: 3737, PMID: 2251283 ³³ Mouse: 499aa, NM_008417, chr. 3 Rat: 499aa, NM_012970 chr. 2q34
Associated subunits	K _v β ₁ , K _v β ₂ , PSD95, synapse-associated protein 97 (SAP97), SNAP25, Caspr2, RhoA ^{9–17}
Functional assays	Voltage-clamp
Current	Delayed rectifier
Conductance	14–18pS ¹⁸
Ion selectivity	K ⁺ -selective
Activation	Voltage-dependent, V _a between 5 and 27 mV; k _a = 13 mV; τ _n = 6 ms (60 mV) ^{6,18}
Inactivation	V _n between –33 and –15 mV; k _n ~ 8 mV ^{6,18}
Activators	None
Gating inhibitors	None
Blockers	4-Aminopyridine (590 μM), capsaicin (45 μM), resineratoxin (31 μM), flecainide (217 μM), nifedipine (18 μM), diltiazem (187 μM), 10-N-methylcarbamoyl-3,7-bis(dimethylamino)phenothiazine (0.44 μM), DTX (17 nM), charybdotoxin (14 nM), margatoxin, natrexone (2 nM), tetraethylammonium (560 mM), H37 (18 μM), picrotoxin-Kα (32 pM), OsK2 (97 nM), BgK (25 nM), HgTx (pM), anandamide (2.7 μM) ^{18–23}
Radioligands	¹²⁵ I-DTX, ¹²⁵ I-HgTX1-A19Y/Y37F ²²
Channel distribution	Brain (pons, medulla, cerebellum, inferior colliculus > hippocampus, thalamus, cerebral cortex, superior colliculus > midbrain, corpus striatum, olfactory bulb; neurons associated with mechanoreception and proprioception), spinal cord, Schwann cells, atrium, ventricle, islet, retina, smooth muscle, PC12 cells ^{1–8,24–30}
Physiological functions	Maintaining membrane potential, modulating electrical excitability in neurons and muscle
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	Delayed rectifier potassium channel; can coassemble with other K _v 1 family members in heteromultimers but not with members of other K _v families ^{19,22,25,29,31} ; intronless coding region ⁵ ; T1 domain in N terminus required for multimerization ³² ; mammalian <i>Shaker</i> -related family

aa, amino acids; chr., chromosome; DTX, dendrotoxin; HgTX, hongotoxin.

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TABLE 4
K_v1.3 channels

Channel name	K _v 1.3 ^{1–8}
Description	Voltage-gated potassium channel, delayed rectifier
Other names	MK3, MBK3, RCK3, hPCN3, HuK (III), HLK3, RKG5, KV3, HGK5, <i>n</i> -channel
Molecular information	Human: 523aa, NM_002232, chr. 1p13.3, ^{7,9} <i>KCNA3</i> , GeneID: 3738, PMID: 22512834 Mouse: 528aa, NM_008418, chr. 3 Rat: 525aa, NM_019270, chr. 2q34
Associated subunits	K _v β, hDlγ, β ₁ integrin, KChaP ^{10–12}
Functional assays	Voltage-clamp
Current	Type N voltage-gated potassium channel in lymphocytes ^{3,4}
Conductance	13pS ⁴
Ion selectivity	K ⁺ (1) > Rb ⁺ (0.77) > NH ₄ ⁺ (0.1) > Cs ⁺ (0.02) > Na ⁺ (<0.01) ¹³
Activation	Voltage, V _a = –35 mV; k _a = 6 mV; τ _n = 3 ms at 40 mV ^{4,13}
Inactivation	C-type inactivation, V _h = –63 mV; k _h = 7.7 mV; τ _h = 250 ms (40 mV) ⁴
Activators	None
Gating inhibitors	None
Blockers	4-Aminopyridine (195 μM), tetraethylammonium (10 mM), charybdotoxin (3 nM), naltrexone (1 nM), MgTX (110 pM), kaliotoxin (650 pM), AgTX2 (200 pM), Pi1 (11 nM), Pi2 (50 pM), Pi3 (500 pM), HsTx1 (12 pM), ShK (11 pM), BgK (39 nM), ShK-Dap22 (52 pM), quinine (14 μM), diltiazem (60 μM), verapamil (6 μM), CP339818 (150 nM), UK78282 (200 nM), correolide (90 nM), sulfamid-benzamidoindane (100 nM), capsaicin (26 μM), resiniferatoxin (3 μM), nifedipine (5 μM), H37 (23 μM) ^{14,15}
Radioligands	¹²⁵ I-HgTx1-A19Y/Y37F mutant (0.1–0.25 pM); ¹²⁵ I-MgTx (0.3 pM) ^{16,17}
Channel distribution	Brain (inferior colliculus > olfactory bulb, pons/medulla > midbrain, superior colliculus, corpus striatum, hippocampus, cerebral cortex), lung, islets, thymus, spleen, lymph node, fibroblasts, B lymphocytes, T lymphocytes, pre-B cells, tonsils, macrophages, microglia, oligodendrocytes, osteoclasts, platelets, testis ^{1–8,18–21}
Physiological functions	Regulation of membrane potential and calcium signaling in lymphocytes and oligodendrocytes ^{14,21–23}
Mutations and pathophysiology	Not established
Pharmacological significance	Therapeutic target for immunosuppressants; K _v 1.3 inhibitors suppress T-cell activation in vitro and delayed type hypersensitivity in vivo and have proven effective for multiple sclerosis in an animal ^{24,25} ; K _v 1.3 expression is dramatically and exclusively increased in effector memory T cells
Comments	Can coassemble with other K _v 1 family members in heteromultimers but not with members of other K _v families; intronless coding region; mammalian <i>Shaker</i> -related family

aa, amino acids; chr., chromosome; MgTX, margatoxin; HgTX, hongotoxin; CP339818, *N*-[1-(phenylmethyl)-4(1*H*)-quinolinylidene]-1-pentamine monohydrochloride; UK78282, 4-[(diphenylmethoxy)methyl]-1-[3-(4-methoxyphenyl)propyl]-piperidine.

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TABLE 5
K_V1.4 channels

Channel name	K _V 1.4 ^{1–7}
Description	Voltage-gated potassium channel, A-type, fast-inactivating
Other names	HuK (II), hPCN2, HK1, RCK4, RHK1, RK4, RK8, MK4
Molecular information	Human: 653aa, NM_002233, chr. 11p14.3–15.2, ⁷ KCNA4, GeneID: 3739, PMID: 2263489 ³² Mouse: 654aa, NM_021275, chr. 2 Rat: 654aa, NM_012971, chr. 3q33
Associated subunits	K _V β , PSD95, synapse-associated protein 97 (SAP97), SAP90, α -actinin-2, KChAP, σ receptor ^{8–18}
Functional assays	Voltage-clamp
Current	K _V 1.4/K _V 1.2 heteromultimers may underlie the presynaptic A-type K ⁺ channel ¹⁹
Conductance	5pS ¹
Ion selectivity	K ⁺ -selective (50 times more selective for K ⁺ than Na ⁺) ²⁰
Activation	Voltage, V _a = –22 mV ¹ ; –34 mV ²⁰ ; K _a = 5 ²¹
Inactivation	N-type inactivation, V _h = –62 mV ²⁰ ; τ_h = 47 ms (0 mV) ²⁰
Activators	CaMKII/calcineurin regulation through phosphorylation/dephosphorylation makes inactivation Ca ²⁺ -dependent ²²
Gating inhibitors	None
Blockers	4-Aminopyridine (13 μ M), ¹ tetraethylammonium (>100 mM), ³ UK78282 (170 nM), ²³ riluzole (70 μ M), ²⁴ quinidine (10 μ M–1 mM), ²⁵ nifedipine (0.8 μ M) ²⁶
Radioligands	None
Channel distribution	Brain (olfactory bulb, corpus striatum > hippocampus, superior and inferior colliculus > cerebral cortex, midbrain basal ganglia > pons/medulla), lung-carcinoid, skeletal muscle, heart, pancreatic islet ^{1,6,27–29}
Physiological functions	Neuronal afterhyperpolarization
Mutations and pathophysiology	K _V 1.4 expression increases in rat ventricular myocytes after myocardial infarction and induction of diabetes ^{30,31}
Pharmacological significance	Not established
Comments	Can coassemble with other K _v 1 family members in heteromultimers but not with members of other K _v families; intronless coding region; mouse K _v 1.4 mRNA contains an internal ribosome entry site in its 5'-noncoding region and may be translated by cap-independent mechanisms ^{33,34} ; mammalian <i>Shaker</i> -related family

aa, amino acids; chr., chromosome.

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TABLE 6
K_v1.5 channels

Channel name	K _v 1.5
Description	Voltage-gated potassium channel, delayed rectifier
Other names	HpCN1, HK2, HCK1, KV1, fHK, RK3, RMK2, HuK (II) ¹⁻⁸
Molecular information	Human: 613aa, NM_002234, chr. 12p13.3, ⁸⁻¹⁰ KCNA5, GeneID: 3741, PMID: 1986382 ³ Mouse: 602aa, NM_002234, chr. 6 Rat: 602aa, NM_012972, chr. 4q42-44
Associated subunits	K _v β ₁ , K _v β ₂ , KCNA3B, Src tyrosine kinase, fyn, KChAP, α-actinin-2, caveolin, synapse-associated protein 97 (SAP97) ¹¹⁻²¹
Functional assays	Voltage-clamp
Current	Ultrarapid-activating K ⁺ current in heart (IK _{ur}) ^{22,23}
Conductance	8pS ²⁴
Ion selectivity	K ⁺
Activation	Voltage, V _a = -14 mV; k _a = 6-12 mV ^{22,24}
Inactivation	V _h = -25 to -10 mV; k _h = 3-5 mV; τ _{h1} = 460 ms; τ _{h2} = 5 s (40 mV) ^{22,24}
Activators	None
Gating inhibitors	None
Blockers	S9947 (420 nM), 4-aminopyridine (270 μM), capsaicin (23 μM), resiniferatoxin (26 μM), flecainide (101 μM), nifedipine (81 μM), diltiazem (115 μM), tetraethylammonium (330 mM), clofilium inside (140 nM), bupivacaine (4.1 μM), propafenone (4.4 μM), ²⁴⁻²⁶ quinidine (0.6 μM) ²⁷
Radioligands	None
Channel distribution	Aorta, colon, kidney, pooled colon, kidney, stomach, smooth muscle, whole embryo, hippocampus and cortex (oligodendrocytes, microglia, Schwann cells), pituitary, pulmonary artery ^{1-7,28-33}
Physiological functions	K _v 1.5 has properties similar to the ultrarapidly activating IK _{ur} current in the heart, and antisense-targeting K _v 1.5 suppresses IK _{ur} currents almost 50% ^{22,23} ; maintains membrane potential that modulates electrical excitability in neurons
Mutations and pathophysiology	Not established
Pharmacological significance	Potential use in management of atrial fibrillation via blockade of IK _{ur} ^{34,35}
Comments	Can coassemble with other K _v 1 family members in heteromultimers but not with members of other K _v families; intronless coding region; mammalian <i>Shaker</i> -related family.

aa, amino acids; chr., chromosome.

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TABLE 7
K_v1.6 channels

Channel name	K _v 1.6 ^{1–5}
Description	Voltage-gated potassium channel, delayed rectifier
Other names	HBK2, MK1.6, RCK2, KV2
Molecular information	Human: 528aa, NM_002235, chr. 12p13.3, ⁶ <i>KCNA6</i> , GeneID: 3742, PMID:2347305 ¹ Mouse: 529aa, NM_013568, chr. 6 Rat: 530 aa, XM_575671 (predicted), chr. 4q42
Associated subunits	K _v β ₁ , K _v β ₂ , ^{7,8} Caspr2 ¹⁸
Functional assays	Voltage-clamp
Current	Delayed rectifier
Conductance	9pS ¹
Ion selectivity	K ⁺ -selective
Activation	V _a = -20 mV; k _a = 8 mV ¹
Inactivation	K _h = -43 ² ; τ_h = > 3 s ¹
Activators	None
Gating inhibitors	None
Blockers	α -Dendrotoxin (20 nM), ¹ 10-N-methylcarbamoyl-3,7-bis(dimethylamino)phenothiazine (10 nM, ¹ 200 nM ³), 4-aminopyridine (1.5 mM), ^{1,3} tetraethylammonium (7 mM), ^{1,3} ShK (160 pM), ⁹ HgTX (9.6 pM), ¹⁰ BgK (W5Y/F6A/Y26F) ¹¹ ¹²⁵ I-BgK (W5Y/F6A/Y26F), ¹¹ ¹²⁵ I-HgTX
Radioligands	
Channel distribution	Brain, colon, germ cell, heart, lung, ovary, testis, astrocytes, pulmonary artery smooth muscle cells, oligodendrocytes ^{1,3–5,8,12–16}
Physiological functions	Regulator of membrane potential in neurons
Mutations and pathophysiology	No K ⁺ channel clustering in optic nerves of hypomyelinating Shiverer mice
Pharmacological significance	Not established
Comments	Can coassemble with other K _v 1 family members in heteromultimers but not with members of other K _v families; intronless coding region; N terminus contains an N terminus inactivation prevention (NIP) domain; ¹⁷ mammalian <i>Shaker</i> -related family

aa, amino acids; chr., chromosome; HgTx, hongotoxin.

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TABLE 8
K_v1.7 channels

Channel name	K _v 1.7 ¹⁻³
Description	Voltage-gated potassium channel, delayed rectifier
Other names	None
Molecular information	Human: 456aa, NM_031886, chr. 19q13.3 ¹⁻³ , <i>KCNA7</i> , GeneID: 3743, PMID: 11368907 ⁶ Mouse: 532aa, NM_010596, chr. 7 Rat: 457, XM_344889 (predicted), chr. 1q22
Associated subunits	None identified
Functional assays	Voltage-clamp
Current	Possibly a component of I _{K_{ur} in the heart³}
Conductance	21pS ¹
Ion Selectivity	K ⁺
Activation	Voltage, V _a = -8 mV; τ _n = 6 ms (30 mV) ³
Inactivation	Very slow inactivation
Activators	None
Gating inhibitors	None
Blockers	Flecainide (8 μM), quinidine (15 μM), verapamil (16 μM), amiodarone (35 μM), 4-aminopyridine (150 μM), tetraethylammonium (150 mM) ³
Radioligands	None
Channel distribution	Placenta, amnion, islets (mouse), skeletal muscle, heart, pulmonary arteries ^{4,5}
Physiological functions	K _v 1.7 has properties similar to the ultrarapidly activating I _{K_{ur} current in the heart³}
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	Can coassemble with other K _v 1 family members in heteromultimers but not with members of other K _v families; only member of this family that has an intron in the coding region ¹⁻³ ; mammalian <i>Shaker</i> -related family

aa, amino acids; chr., chromosome.

1. Kalman K, Nguyen A, Tseng-Crank J, Dukes ID, Chandy G, Hustad CM, Copeland NG, Jenkins NA, Mohrenweiser H, Brandriff B, et al (1998) Genomic organization, chromosomal localization, tissue distribution, and biophysical characterization of a novel mammalian *Shaker*-related voltage-gated potassium channel, K_v1.7. *J Biol Chem* **273**:5851-5857.

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4. UniGene Cluster Hs0.306973; OMIM no. 176268.

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TABLE 9
K_v1.8 channels

Channel name	K _v 1.8
Description	Voltage-gated potassium channel, delayed rectifier
Other names	K _v 1.10, Kcn1 ¹⁻⁵
Molecular information	Human: 511aa, NM_005549, chr. 1p13.1, <i>KCNA10</i> , GeneID: 3744, PMID: 9177773 ¹ Mouse: 503aa, XM_143471 (predicted), chr. 3 Rat: 511aa, XM_227577 (predicted), chr. 2q34
Associated subunits	KCNA4B
Functional assays	Voltage-clamp
Current	Possibly a component of I _{K_{ur} in the heart²}
Conductance	10-12pS ²
Ion selectivity	K ⁺ /Na ⁺ > 70:1 ²
Activation	V _a = 3.6 mV (oocytes); τ _a = 18 ms at +60 mV (oocytes) ²
Inactivation	τ _h = 10 s
Activators	cGMP
Gating inhibitors	None
Blockers	Barium (5 mM), tetraethylammonium (50 mM), 4-aminopyridine (1.5 mM), charybdotoxin (100 nM), ketoconazole (500 nM), pimozone (300 nM), verapamil (45 μM) ²
Radioligands	None
Channel distribution	Kidney (cortex > medulla), brain, heart, skeletal muscle, adrenal gland ^{1-3,6}
Physiological functions	Regulation of membrane potential in renal proximal tubule
Mutations and pathophysiology	None
Pharmacological significance	Not established
Comments	Can coassemble with other K _v 1 family members in heteromultimers but not with members of other K _v families; intronless coding region; mammalian <i>Shaker</i> -related family

aa, amino acids; chr., chromosome.

1. Orias M, Bray-Ward P, Curran ME, Keating MT, and Desir GV (1997) Genomic localization of the human gene for KCNA10, a cGMP-activated K channel. *Genomics* **42**:33-37.

2. Lang R, Lee G, Liu W, Tian S, Rafi H, Orias M, Segal AS, and Desir GV (2000) KCNA10: a novel ion channel functionally related to both voltage-gated potassium and CNG cation channels. *Am J Physiol* **278**:F1013-F1021.

3. Yao X, Segal AS, Welling P, Zhang X, McNicholas CM, Engel D, Boulpaep EL, and Desir GV (1995) Primary structure and functional expression of a cGMP-gated potassium channel. *Proc Natl Acad Sci USA* **92**:11711-11715.

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6. UniGene Cluster Hs0.306973; OMIM no. 176268.

TABLE 10
K_v2.1 channels

Channel name	K _v 2.1 ¹⁻³
Description	Voltage-gated potassium channel, delayed rectifier
Other names	hDRK1, DRK1
Molecular information	Human: 858aa, NM_004975, chr. 20q13.2, ^{4,5} <i>KCNB1</i> , GeneID: 3745, PMID: 8081723 ³⁵ Mouse: 857aa, NM_008420, chr. 2 Rat: 853aa, NM_013186, chr. 3q42
Associated subunits	K _v 5.1, K _v 6.1–K _v 6.3, K _v 8.1, K _v 9.1–K _v 9.3, KChAP (binds to N terminus of K _v 2.1), Fyn SH2 domain ⁶⁻¹⁵
Functional assays	Voltage-clamp
Current	K _v 2.1/K _v 9.3 (delayed rectifier in oxygen-sensitive pulmonary artery), ⁹ delayed rectifier current in hippocampal and globus pallidus neurons ^{16,17}
Conductance	8pS; on removal of K ⁺ , K _v 2.1 displays a large Na ⁺ conductance that is inhibited by low concentrations of K ^{+2,18}
Ion selectivity	K ⁺ > Rb ⁺
Activation	Voltage, V _a = 12 mV; k _a = 3 mV ³
Inactivation	Noninactivating
Activators	Linoleic acid ¹⁹
Gating inhibitors	Hanatoxin (42 nM) ^{20,21}
Blockers	Internal tetraethylammonium and tetrapentylammonium, internal Ba ²⁺ (13 μM), external Ba ²⁺ (30 mM), internal Mg ²⁺ , 4-AP (18 mM), halothane ²²⁻²⁵
Radioligands	None
Channel distribution	Brain (cerebral cortex > hippocampus > cerebellum > olfactory bulb; restricted to neurons, where staining is present on dendrites and cell bodies but not on axons; Schwann cells), atria, ventricle, skeletal muscle, retina, cochlea, eye, germ cell, lung, PC12 cells, pulmonary arteries, insulinomas ^{1,3,9,14,16,17,26-33}
Physiological functions	Maintaining membrane potential and modulating electrical excitability in neurons and muscle ^{9,16,17}
Mutations and pathophysiology	K _v 2.1 expression is reduced in chronic hypoxic pulmonary hypertension. ^{30,32}
Pharmacological significance	Not established
Comments	Ser857Asn polymorphism in 0–3% in different ethnic populations ⁵ ; two other single nucleotide polymorphisms have been identified ³⁴ ; the 4-AP binding site is in the S6 inner vestibule. ²³ Mammalian <i>Shab</i> -related family.

aa, amino acids; chr., chromosome; 4-AP, 4-aminopyridine.

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5. Mazzanti CM, Bergen A, Enoch MA, Michelini S, and Goldman D (1996) Identification of a Ser857-Asn857 substitution in DRK1 (KCNB1), population frequencies and lack of association to the low voltage α EEG trait. *Hum Genet* **98**:134–137.
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12. Kramer JW, Post MA, Brown AM, and Kirsch GE (1998) Modulation of potassium channel gating by co expression of Kv2.1 with regulatory Kv5.1 or Kv6.1 α-subunits. *Am J Physiol* **274**:C1501–C1510.
13. Chiara MD, Monje F, Castellano A, and Lopez-Barneo J (1999) A small domain in the N terminus of the regulatory α-subunit Kv23 modulates Kv2.1 potassium channel gating. *J Neurosci* **19**:6865–6873.
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TABLE 11
K_v2.2 channels

Channel name	K _v 2.2 ^{1–3}
Description	Voltage-gated potassium channel, delayed rectifier
Other names	CDRK
Molecular information	Human: 911 aa, NM_004770, chr. 8q13.2, <i>KCNB2</i> , GeneID: 9312, PMID: 9612272 ¹⁵ Mouse: 758 aa, XM_136482 (predicted), chr. 1 Rat: 802 aa, NM_054000, chr. 5q11
Associated subunits	Mouse K _{vβ} 4 associates with K _v 2.2 and enhances expression level, K _v 8.1, K _v 9, KChAP ^{4–7}
Functional assays	Voltage-clamp
Current	None determined
Conductance	15pS ⁸
Ion selectivity	K ⁺ -selective
Activation	Voltage
Inactivation	Noninactivating
Activators	None
Gating inhibitors	None
Blockers	Quinine (13.7 μM), tetraethylammonium (2.6 mM), 4-aminopyridine (1.5 mM), phencyclidine (μM) ^{8,9}
Radioligands	None
Channel distribution	Brain [olfactory bulb (granule cell layer > olfactory tubercle) > cortex > hippocampus > cerebellum; hypothalamus], ventricle, tongue, sympathetic neurons, gastrointestinal smooth muscle, mesenteric artery smooth muscle ^{1–3,10–14}
Physiological functions	Maintaining membrane potential, modulating electrical excitability in neurons
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	The angiotensin II type 1 receptor mediates inhibition of K _v 2.2 in brainstem and hypothalamic neurons ¹² ; mammalian <i>Shab</i> -related family

aa, amino acids; chr., chromosome.

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TABLE 12
K_v3.1 channels

Channel name	K _v 3.1
Description	Voltage-gated potassium channel, delayed rectifier
Other names	Kv3.1, ¹ NGK2, ² KV4, ³ KShIIIB, ¹⁵ Raw2, ⁴ type <i>l</i> channel in T cells ⁵
Molecular information	Human: 511aa, NM_004976, chr. 11p15, ^{1-4,16} <i>KCNC1</i> , GeneID: 3746, PMID: 1400413 ¹ Mouse: 511aa, NM_008421, chr. 7 Rat: 585aa, NM_012856, chr. 1q22
Associated subunits	Not established
Functional assays	Electrophysiology
Current	Delayed rectifier
Conductance	27pS ^{1,5}
Ion selectivity	K ⁺ (1) > Rb ⁺ (0.76) > NH ₄ ⁺ (0.12) = Cs ⁺ (0.12) > Na ⁺ (0.004) ⁶
Activation	V _a = 16 mV; k _a = 10 mV; τ _a = 2 ms (40 mV) ⁷
Inactivation	τ _h = 630 ms (40 mV) ¹
Activators	None
Gating inhibitors	None
Blockers	4-Aminopyridine (29 μM), capsaicin (158 μM), resiniferatoxin (46 μM), flecainide (108 μM), nifedipine (131 μM), diltiazem (97 μM), cromakalim (237 μM), tetraethylammonium (0.2 mM) ⁸
Radioligands	None
Channel distribution	Brain (cerebellum > globus pallidus, subthalamic nucleus, substantia nigra > reticular thalamic nuclei, cortical and hippocampal interneurons > inferior colliculi, cochlear and vestibular nuclei), skeletal muscle, human Louckes B cells, germ cell, lung, testis, AtT20 cell line ^{9-13,19,20}
Physiological functions	Important for the high-firing frequency of auditory ⁸ and fast-spiking GABAergic interneurons ^{11,21} ; regulation of action potential duration in presynaptic terminals ^{17,18}
Mutations and pathophysiology	Kv3.1 ^{-/-} mice exhibit impaired motor skills and reduced muscle contraction force ¹³ ; Kv3.1/Kv3.3 double knockout mice display severe ataxia, myoclonus, and hypersensitivity to ethanol ¹⁴
Pharmacological significance	Not established
Comments	H-ras oncogene switches anterior pituitary-derived cells (AtT20) to a more neuron-like phenotype in parallel with the induction of expression of K _v 3.1 ¹² ; mammalian <i>Shaw</i> -related family

aa, amino acids; chr., chromosome.

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TABLE 13
K_v3.2 channels

Channel name	K _v 3.2
Description	Voltage-gated potassium channel, delayed rectifier
Other names	RKShIIIa, ¹ Raw1, ² Kv3.2a, ³ rKv3.2b and rKv3.2c ⁴
Molecular information	Human: 613aa, NM_139136 (transcript variant 1), chr. 12q14.1, ⁵ <i>KCNK2</i> , GeneID: 3747, PMID: 8111118 ²¹ Mouse: AC121610 (genomic), chr. 10 Rat: 613aa, NM_139216 (transcript variant a), chr. 7q12–22
Associated subunits	None
Functional assays	Electrophysiology
Current	Delayed rectifier
Conductance	16–20pS ¹⁶
Ion selectivity	K ⁺
Activation	V _a = 13 mV; k _a = 7–7.5 mV ¹ ; t _{on} = 10–90% (40 mV) 4 ms; τ _{off} 2.9 ms (–60 mV) ¹⁶
Inactivation	Very slow ¹⁶
Activators	None
Gating inhibitors	None
Blockers	Tetraethylammonium (0.1 mM), ⁶ 4-aminopyridine (0.1 mM), ⁶ 8-bromo-cGMP, ⁷ 3-isobutyl-1-methylxanthine, ⁶ D-NONOate, ⁷ verapamil (11 μM), ⁸ ShK ¹⁹
Radioligands	None
Channel distribution	Brain (fast-spiking GABAergic interneurons of the neocortex, hippocampus, and caudate; terminal fields of thalamocortical projections), ^{9–12} islets, ¹³ mesenteric artery, Schwann cells ¹⁴
Physiological functions	Probably in heteromeric complexes with K _v 3.1; important for the high-frequency firing of fast spiking GABAergic interneurons ¹⁷ and GABA release via regulation of action potential duration in presynaptic terminals ¹⁸ ; modulated by protein kinase A in vitro and in vivo ^{10,20}
Mutations and pathophysiology	See “Comments”
Pharmacological significance	Not established
Comments	Fast deactivation; knockout mice show specific alterations in their cortical electroencephalographic patterns and an increased susceptibility to epileptic seizures consistent with an impairment of a cortical inhibitory mechanism ¹⁵ ; mammalian <i>Shaw</i> -related family

aa, amino acids; chr., chromosome; D-NONOate, 1,1-diethyl-2-hydroxy-2-nitrosodiazine; ShK, *Stichodactyla helianthus* toxin.

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TABLE 14
K_v3.3 channels

Channel name	K _v 3.3 ¹⁻⁴
Description	Voltage-gated A-type potassium channel ²
Other names	hKv3.3, mKv3.3, ¹ RKShIID, ³ Kv3.3b ⁴
Molecular information	Human: 757aa, NM_004977, chr. 19q13.3-4, ¹⁻³ <i>KCNK3</i> , GeneID: 3748, PMID: 1740329 ¹ Mouse: 679aa, NM_008422, chr. 7 Rat: 770aa, NM_053997, chr. 1q22
Associated subunits	None
Functional assays	Electrophysiology
Current	A-type
Conductance	Not established
Ion selectivity	K ⁺
Activation	$V_a = 7 \text{ mV}$; $k_a = 6 \text{ mV}^2$
Inactivation	$\tau_h \sim 200 \text{ ms}$ (40 mV) ²
Activators	None
Gating inhibitors	None
Blockers	Tetraethylammonium (0.14 mM), ² 4-aminopyridine (1.2 mM) ² ; blocked by hypoxia ⁵
Radioligands	None
Channel distribution	Brain, Purkinje cells, central nervous system motoneurons; auditory brainstem ¹² ; electrosensory, cerebellar neurons, central auditory nuclei ⁶⁻⁸ ; mesenteric artery ⁹ ; lens and corneal epithelium ¹⁰
Physiological functions	Not established
Mutations and pathophysiology	See "Comments"
Pharmacological significance	Not established
Comments	Alcohol hypersensitivity, ataxia, increased locomotion and myoclonus occur in mice lacking K _v 3.3 and K _v 3.1 ¹¹ ; mammalian <i>Shaw</i> -related family

aa, amino acids; chr., chromosome.

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TABLE 15
K_v3.4 channels

Channel name	K _v 3.4
Description	Voltage-gated potassium channel, A-type, fast-inactivating
Other names	Raw3, ¹ HKShIIIC, ² mKv3.4 ³
Molecular information	Human: 635 aa, NM_004978 (transcript variant 1), chr. 1p21 ^{1,2} , <i>KCNC4</i> , GeneID: 3749, PMID: 1920536 ² Mouse: 628 aa, NM_145922, chr. 3
Associated subunits	Rat: MiRP2 forms potassium channels in skeletal muscle with K _v 3.4 ⁴
Functional assays	Electrophysiology
Current	A-type
Conductance	14pS ^{1,5}
Ion selectivity	K ⁺
Activation	$V_a = 3.4 \text{ mV}^5$, $+14 \text{ mV}^1$; $k_a = 8.4 \text{ mV}^5$
Inactivation	N-type inactivation, $V_h = 53 \text{ mV}$; $k_h = 7.4 \text{ mV}$; $\tau_h = 15.9 \text{ ms (50 mV)}^{1,2,5}$
Activators	None
Gating inhibitors	None
Blockers	BDS-I (47 nM), ⁶ tetraethylammonium (0.3 mM) ^{1,5} ; the specificity of BDS-I for K _v 3.4 has been questioned ¹²
Radioligands	None
Channel distribution	Parathyroid, prostate, brain ⁷ (brainstem, hippocampal granule cells), ⁸ skeletal muscle, ^{4,8,9} pancreatic acinar cells ^{10,11}
Physiological functions	Together with MiRP2 forms low-voltage-activating potassium channels that regulate skeletal muscle resting potential ⁴
Mutations and pathophysiology	Mutations of MiRP2, which associates with K _v 3.4 in skeletal muscle, are associated with periodic paralysis ⁴
Pharmacological significance	Not established
Comments	Mammalian <i>Shaw</i> -related family

aa, amino acids; chr., chromosome.

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5. Rettig J, Wunder F, Stocker M, Lichtinghagen R, Mastiaux F, Beckh S, Kues W, Pedarzi P, Schroter KH, Ruppersberg JP, et al. (1992) Characterization of a Shaw-related potassium channel family in rat brain. *EMBO J* **11**:2473–2486.

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10. Kalman K, Nguyen A, Tseng-Crank J, Dukes ID, Chandy G, Hustad CM, Copeland NG, Jenkins NA, Mohrenweiser H, Brandriff B, et al. (1998) Genomic organization, chromosomal localization, tissue distribution, and biophysical characterization of a novel mammalian Shaker-related voltage-gated potassium channel, Kv1.7. *J Biol Chem* **273**:5851–5857.

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12. Yeung SYM, Thompson D, Wang Z, Fedida D, and Robertson B (2005) Modulation of Kv3 subfamily potassium currents by the sea anemone toxin BDS: significance for CNS and biophysical studies. *J Neurosci* **25**:8735–8745.

TABLE 16
K_v4.1 channels

Channel name	K _v 4.1
Description	Voltage-gated potassium channel, A-type potassium current
Other names	mShal ¹
Molecular information	Human: 647aa, NM_004979, chr. Xp11.23, ² <i>KCND1</i> (see 'Comments'), GeneID: 3750, PMID: 10729221 ¹² Mouse: 651aa, NM_008423, chr. X Rat: 650aa, XM_217601 (predicted), chr. Xq13
Associated subunits	KCHIP1 increases K _v 4.1 current densities, accelerates inactivation time course and recovery from inactivation, and shifts steady-state inactivation to more depolarized potentials ^{3,4}
Functional assays	Patch-clamp, two-electrode voltage-clamp
Current	Somatodendritic depolarization-activated potassium currents in rat neostriatal cholinergic interneurons are predominantly of the A-type and attributable to coexpression of K _v 4.2 and K _v 4.1 subunits ⁵ ; subthreshold transient A currents in rat brain ⁶
Conductance	~6pS (main unitary conductance under physiological conditions) ^{4,7}
Ion selectivity	$P_{Na}/P_K < 0.01$
Activation	Voltage, $V_a = -47.9$ mV; $k_a = 24.2$ mV (assuming a fourth-order Boltzmann function) ⁷
Inactivation	$V_h = -69$ mV; $k_h = 4.8$ mV; $\tau_{h1} = 22$ ms (20 mV); $\tau_{h2} = 86$ ms (20 mV); $\tau_{h3} = 368$ ms (20 mV) ⁷ (see "Comments")
Activators	None
Gating inhibitors	None
Blockers	4-Aminopyridine (9 mM) ^{1,7} , tetraethylammonium (>10 mM) ¹
Radioligands	None
Channel distribution	Fetal, infant, and adult brain; colon, heart, lung, stomach, testis, liver, kidney, thyroid gland, pancreas, pulmonary artery ⁸⁻¹⁰
Physiological functions	Not established
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	The <i>K_v4.1 (KCND1)</i> gene is encoded by at least 6 exons ² —the first exon encodes the protein from the N terminus through S5 into the P-region, whereas the remainder of the protein is encoded by exons 2–6; kinetic properties depend on the expression system, recording configuration, and the presence of auxiliary subunits (KChIPs) ^{4,11} ; mammalian <i>Shal</i> -related family

aa, amino acids; chr., chromosome.

1. Pak MD, Baker K, Covarrubias M, Butler A, Ratcliffe A, and Salkoff L (1991) mShal, a subfamily of A-type K⁺ channel cloned from mammalian brain. *Proc Natl Acad Sci USA* **88**:4386–4390.
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3. Nakamura TY, Nandi S, Pountney DJ, Artman M, Rudy B, and Coetzee WA (2001) Different effects of the Ca²⁺-binding protein, KCHIP1, on two Kv4 sub-family members, Kv4.1 and Kv4.2. *FEBS Lett* **499**:205–209.
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11. Beck E, and Covarrubias M (2001) Preferential modulation of closed-state inactivation in Kv4 K⁺ channels. *Biophys J* **81**:867–883.
12. Isbrandt D, Leicher T, Waldschutz R, Zhu X, Luhmann U, Michel U, Sauter K, and Pongs O (2000) Gene structures and expression profiles of three human KCND (Kv4) potassium channels mediating A-type currents I_{TO} and I_{SA}. *Genomics* **64**:144–154.

TABLE 17
K_v4.2 channels

Channel name	K _v 4.2
Description	Voltage-gated potassium channel, A-type potassium current
Other names	Shal1, RK5 ¹⁻³
Molecular information	Human: 630aa, NM_012281, chr. 7q31, <i>KCND2</i> (see "Comments"), GeneID: 3751, PMID: 10551270 ²⁴ Mouse: 630aa, NM_019697, chr. 6 Rat: 490aa, NM_031730, chr. 4q22
Associated subunits	Coexpression of KChIP1 results in increased current densities, slowed onset of inactivation, and accelerated recovery from inactivation ⁴ ; KChIP4/CALP interacts with K _v 4.2 and presenilin 2 ⁵ ; frequenin, a calcium-binding protein, enhances K _v 4.2 current amplitudes, slows inactivation time course and accelerates recovery from inactivation ⁶ ; PSD95, a PDZ domain protein, associates with K _v 4.2 and is involved in trafficking of the channel ⁷ ; a number of proteins have been shown to interact and modify K _v 4 proteins, including KChIPs, DPPX, DPP10, frequenin, PSD95, and filamin—most of these studies have used K _v 4.2 and sometimes K _v 4.3 proteins, but it is likely that these interactions also occur with Kv4.1; the physiological role of these proteins in native channels remains to be studied in most cases
Functional assays	Patch-clamp, two-electrode voltage-clamp
Current	I _{to} current in the heart is a heteromultimer of K _v 4.2 and K _v 4.3 subunits and KChIP2 ⁸ ; I _{SA} current in somatic recordings from neurons ⁹
Conductance	Not established
Ion selectivity	P _{Na} /P _K < 0.01
Activation	Midpoint of activation = 1 mV ²
Inactivation	Rapid inactivation with time constants of 15 and 60 ms ²
Activators	None
Gating inhibitors	None
Blockers	4-Aminopyridine (5 mM) ^{1,10} heteropodatoxins, ¹¹ PaTX1,2 (2–70 nM), arachidonic acid (2 μM) ¹²
Radioligands	None
Channel distribution	Brain [cerebellum (granular cells) > hippocampus, thalamus, medial habenular nucleus > cerebral cortex; basal ganglia and forebrain ¹³ ; concentrated in dendrites and soma ¹⁴], cochlear nucleus, ¹⁵ atrium, ventricle ^{1-3,16} ; in situ hybridization has shown that many neuronal populations preferentially express K _v 4.2 or K _v 4.3 ²³ —for example, CA1 hippocampal neurons express K _v 4.2 but not K _v 4.3—on the other hand, Purkinje cells and cortical interneurons express K _v 4.3 preferentially; in cerebellar granule cells, there is a reciprocal anterior-posterior gradient of expression
Physiological functions	Repolarization of the cardiac action potential (notch phase), dampening back-propagating action potentials in CA1 hippocampal neurons
Mutations and pathophysiology	KChIP2 ^{-/-} mice lack the I _{to} current and are susceptible to ventricular tachycardia ¹⁷ ; seizure activity reduces K _v 4.2 expression in the dentate granule cells of the hippocampus ¹⁸
Pharmacological significance	Not established
Comments	The <i>K_v4.2</i> (<i>KCND2</i>) gene, like <i>KCND1</i> and <i>KCND3</i> , contains six exons— however, the introns are significantly longer ¹⁹ ; kinetic properties depend on the expression system, recording configuration, and the presence of auxiliary subunits (KChIPs) ^{20,21} ; K _v 4.2 currents expressed in <i>Xenopus</i> oocytes are suppressed in response to protein kinase C activation ²² ; mammalian <i>Shal</i> -related family

aa, amino acids; chr., chromosome.

- Roberds SL and Tamkun MM (1991) Cloning and tissue-specific expression of five voltage-gated potassium channel cDNAs expressed in rat heart. *Proc Natl Acad Sci USA* **88**:1798–1802.
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20. An WF, Bowlby MR, Betty M, Cao J, Ling HP, Mendoza G, Hinson JW, Mattsson KI, Strassle JS, Trimmer BW, et al. (2000) Modulation of A-type potassium channels by a family of calcium sensors. *Nature (Lond)* **403**:553–556.
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22. Nakamura T, Coetzee WA, Vega-Saenz de Miera E, Artman M, and Rudy B (1997) Modulation of Kv4 channels, key components of rat ventricular transient K⁺ current, by PKC. *Am J Physiol* **273**:H1775–H1786.
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24. Zhu XR, Wulf A, Schwarz M, Isbrandt D, and Pongs O (1999) Characterization of human Kv4.2 mediating a rapidly-inactivating transient voltage-sensitive K⁺ current. *Receptors Channels* **6**:387–400.

TABLE 18
K_v4.3 channels

Channel name	K _v 4.3 ^{1–6}
Description	Voltage-gated potassium channel, A-type potassium current
Other names	None
Molecular information	Human: 655aa, NM_004980 (transcript variant 1), chr. 1p13.3, <i>KCND3</i> (see “Comments”), GeneID: 3752, PMID: 8734615 ² Mouse: 655aa, NM_019931, chr. 3 Rat: 636aa, NM_031739, chr. 2q34
Associated subunits	KChIP1 increases K _v 4.3 current densities, accelerates inactivation time course and recovery from inactivation, and shifts steady-state inactivation to more depolarized potentials; KChIP4a abolishes fast inactivation ⁷ ; expression of K _{vβ} 2 in brain increases current density and protein expression ⁸ ; KChAP acts as a chaperone for K _v 4.3 ⁹ ; K _v 4.3 may associate preferentially with DPP10 in native neurons that predominantly express this subunit ²⁰
Functional assays	Patch-clamp, two-electrode voltage-clamp
Current	I _{to} current in the heart is a heteromultimer of K _v 4.2 and K _v 4.3 subunits and KChIP2 ¹⁰
Conductance	~5pS (main unitary conductance under physiological conditions) ⁷ ; association with DPPX increases single channel conductance ²¹
Ion selectivity	P _{Na} /P _K < 0.01
Activation	Threshold for activation –30 mV, time course for activation 1.71 ms at 60 mV ¹¹
Inactivation	Time course for inactivation fit by a biexponential function; τ _{h1} = 27 ms at 60 mV, τ _{h2} = 142 ms at 60 mV ¹¹ (see “Comments”)
Activators	None
Gating inhibitors	None
Blockers	4-Aminopyridine, bupivacaine (31 μM), ¹¹ PaTX1,2, (2–70 nM), nicotine (40 nM) ¹²
Radioligands	None
Channel distribution	Heart, brain, smooth muscle ^{1–6,13,14}
Physiological functions	Repolarization of the cardiac action potential (notch phase)
Mutations and pathophysiology	K _v 4.3 mRNA levels are decreased in patients with paroxysmal atrial fibrillation ¹⁵
Pharmacological significance	Not established
Comments	The K _v 4.3 (<i>KCND3</i>) gene contains six exons analogous to those found in <i>KCND1</i> and <i>KCND2</i> and an additional exon L between exons 4 and 5—relative to <i>KCND1</i> , the introns are significantly longer; kinetic properties depend on the expression system, recording configuration, and the presence of auxiliary subunits (KChIPs) ^{16–18} ; K _v 4.3 currents expressed in <i>Xenopus</i> oocytes are suppressed in response to protein kinase C activation ¹⁹ ; mammalian <i>Shal</i> -related family

aa, amino acids; chr., chromosome.

1. Serodio P, Kentros C, and Rudy B (1994) Identification of molecular components of A-type channels activating at subthreshold potentials. *J Neurophysiol* **72**:1516–1529.
2. Serodio P, Vega-Saenz de Miera E, and Rudy B (1996) Cloning of a novel component of A-type K⁺ channels operating at subthreshold potentials with unique expression in heart and brain. *J Neurophysiol* **75**:2174–2179.
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4. Tsaour ML, Chou CC, Shih YH, and Wang HL (1997) Cloning, expression and CNS distribution of Kv4.3, an A-type K⁺ channel α subunit. *FEBS Lett* **400**:215–220.
5. Ohya S, Tanaka M, Oku T, Asai Y, Watanabe M, Giles WR, and Imaizumi Y (1997) Molecular cloning and tissue distribution of an alternatively spliced variant of an A-type K⁺ channel α-subunit, Kv4.3 in the rat. *FEBS Lett* **420**:47–53.
6. Dilks D, Ling HP, Cockett M, Sokol P, and Numann R (1999) Cloning and expression of the human Kv4.3 potassium channel. *J Neurophysiol* **81**:1974–1977.
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18. Beck E and Covarrubias M (2001) Preferential modulation of closed-state inactivation in Kv4 K⁺ channels. *Biophys J* **81**:867–883.
19. Nakamura T, Coetzee WA, Vega-Saenz de Miera E, Artman M, and Rudy B (1997). Modulation of Kv4 channels, key components of rat ventricular transient K⁺ current, by PKC. *Am J Physiol* **273**:H1775–H1786.
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TABLE 19
K_v5.1 channels

Channel name	K _v 5.1 ^{1–4}
Description	Modifier of the K _v 2 family of channels
Other names	KH1, IK8
Molecular information	Human: 494aa, NM_002236, chr. 2p25, ⁵ <i>KCNF1</i> , GeneID: 3754, PMID: 9434767 ⁵ Mouse: 493aa, NM_201531, chr. 12 Rat: 505aa, XM_216678 (predicted), chr. 6
Associated subunits	Associates with K _v 2.1 and K _v 2.2
Functional assays	Voltage-clamp
Current	None
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Brain, heart, skeletal muscle, liver, kidney pancreas, ^{1,2,6} cardiac myocytes ⁷
Physiological functions	Modifies the gating properties of K _v 2.1 and K _v 2.2 channels
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	K _v 5.1 has no function on its own, but it has important modulatory actions on K _v 2 channels

aa, amino acids; chr., chromosome.

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- Brahmajothi MV, Morales MJ, Liu S, Rasmusson RL, Campbell DL, and Strauss HC (1996) In situ hybridization reveals extensive diversity of K⁺ channel mRNA in isolated ferret cardiac myocytes. *Circ Res* **78**:1083–1089.

TABLE 20
K_v6.1 channels

Channel name	K _v 6.1 ¹⁻⁶
Description	Modifier/silencer of K _v 2 family channels
Other names	KH2, K13
Molecular information	Human: 513aa, NM_002237, chr. 20q13, ^{6,7} <i>KCNGL1</i> , GeneID: 3755, PMID: 9434767 ⁶ Mouse: 534aa, XM_141545 (predicted), chr. 2 Rat: 514aa, XM_215951 (predicted), chr. 3
Associated subunits	Associates with K _v 2 family channels
Functional assays	Electrophysiology
Current	None
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Skeletal muscle, brain, uterus, ovary, kidney, pancreas, placenta, bone, germ cell, prostate, skin, testis, ^{6,7} cardiac myocytes (sinoatrial node) ⁸
Physiological functions	K _v 6.1 subunits when expressed alone are unable to elicit any current— however, K _v 6.1 can suppress K _v 2.1 current (less effectively than K _v 5.1), and to a lesser extent it can suppress K _v 2.2; the K _v 2.1 currents are strongly modified by K _v 6.1, which increases the time constant of activation and slows down inactivation
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	K _v 6.1 has no function on its own, but it has important modulatory actions on K _v 2 channels

aa, amino acids; chr., chromosome.

1. Drewe JA, Verma S, Frech G, and Joho RH (1992) Distinct spatial and temporal expression patterns of K⁺ channel mRNAs from different subfamilies. *J Neurosci* **12**:538–548.
2. Post MA, Kirsch GE, and Brown AM (1996) Kv2.1 and electrically silent Kv6.1 potassium channel subunits combine and express a novel current. *FEBS Lett* **399**:177–182.
3. Verma-Kurvari S, Border B, and Joho RH (1997) Regional and cellular expression patterns of four K⁺ channel mRNAs in the adult rat brain. *Brain Res Mol Brain Res* **46**:54–62.
4. Salinas M, Duprat F, Heurteaux C, Hugnot JP, and Lazdunsk, M (1997) New modulatory α subunits for mammalian *Shab* K⁺ channels. *J Biol Chem* **272**:24371–24379.
5. Kramer JW, Post MA, Brown AM, and Kirsch GE (1998) Modulation of potassium channel gating by coexpression of Kv2.1 with regulatory Kv5.1 or Kv6.1 α -subunits. *Am J Physiol* **274**:C1501–C1510.
6. Su K, Kyaw H, Fan P, Zeng Z, Shell BK, Carter KC, and Li Y (1997) Isolation, characterization, and mapping of two human potassium channels. *Biochem Biophys Res Commun* **241**:675–681.
7. UniGene Cluster Hs0.118695; OMIM no. *603788.
8. Brahmajothi MV, Morales MJ, Liu S, Rasmusson RL, Campbell DL, and Strauss HC (1996) In situ hybridization reveals extensive diversity of K⁺ channel mRNA in isolated ferret cardiac myocytes. *Circ Res* **78**:1083–1089.

TABLE 21
K_v6.2 channels

Channel name	K _v 6.2 ¹
Description	Modifier/silencer
Other names	None
Molecular information	Human: 466aa, NM_012283, chr. 18q22–18q23, ¹ <i>KCNQ2</i> , GeneID: 26251, PMID: 10551266 ¹ Mouse: AC145610 (genomic), chr. 18 Rat: 436aa, XM_225718 (predicted), chr. 18
Associated subunits	Coassembles with K _v 2 family channels via the N termini ¹
Functional assays	Electrophysiology
Current	None
Conductance	Not functional on its own
Ion Selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Myocardium, fetal brain, germinal center B cells ^{1,2}
Physiological functions	Modifier/silencer, coassembles with K _v 2.1, producing K ⁺ channels with unique properties
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	K _v 6.2 has no function on its own, but it has important modulatory actions on K _v 2 channels

aa, amino acids; chr., chromosome.

1. Zhu XR, Netzer R, Bohlke K, Liu Q, and Pongs O (1999). Structural and functional characterization of Kv6.2: a new γ -subunit of voltage-gated potassium channel. *Receptors Channels* **6**:337–350.

2. UniGene Cluster Hs0.247905; OMIM no. 605696.

TABLE 22
K_v6.3 channels

Channel name	K _v 6.3 ¹
Description	Modifier/silencer
Other names	K _v 10.1
Molecular information	Human: 436aa, NM_133329, chr. 2p21, <i>KCNQ3</i> , GeneID: 170850, PMID: 11852086 ¹ Mouse: 433aa, NM_153512, chr. 17 Rat: 345aa, NM_133426, chr. 6q12
Associated subunits	Coassembles with K _v 2.1 ¹
Functional assays	Electrophysiology
Current	None
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Whole brain (hippocampus, caudate nucleus, frontal lobe, hypothalamus, substantia nigra), spinal cord, pituitary, testis, small intestine, thymus, adrenal gland ¹
Physiological functions	Modifier/silencer, coassembles with K _v 2.1
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	K _v 6.3 has no function on its own, but it has important modulatory actions on K _v 2 channels

aa, amino acids; chr., chromosome.

1. Sano Y, Mochizuki S, Miyake A, Kitada C, Inamura K, Yokoi H, Nozawa K, Matsushime H, and Furuichi K (2002) Molecular cloning and characterization of Kv6.3, a novel modulatory subunit for voltage-gated K⁺ channel Kv2.1. *FEBS Lett* **512**:230–234.

TABLE 23
K_v6.4 channels

Channel name	K _v 6.4 ¹
Description	Modifier/silencer
Other names	None
Molecular information	Human: 519aa, NM_172347 (transcript variant 1), chr. 16q24.1, <i>KCNG4</i> , GeneID: 93107, PMID: 12060745 ¹ Mouse: 506aa, NM_025734, chr. 8, Rat: 506aa, XM_226524 (predicted), chr. 19
Associated subunits	Coassembles with K _v 2.1 ¹
Functional assays	Electrophysiology
Current	Not functional on its own
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Brain, liver, small intestine, colon ¹
Physiological functions	Regulation of membrane potential and action potential frequency by modulation of delayed rectifier potassium currents; modulates the activity of K _v 2.1 channels by causing marked changes in activation threshold and kinetics, C-type inactivation, and deactivation ¹
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	K _v 6.4 has no function on its own, but it has important modulatory actions on K _v 2 channels

aa, amino acids; chr., chromosome.

1. Ottschytch N, Raes A, Van Hoorick D, and Snyders DJ (2002) Obligatory heterotetramerization of three previously uncharacterized Kv channel-subunits identified in the human genome. *Proc Natl Acad Sci USA* **99**:7986–7991.

TABLE 24
K_v7.1 channels

Channel name	K _v 7.1
Description	Voltage-gated potassium channel, delayed rectifier
Other names	KVLQT1, ¹ slow delayed rectifier
Molecular information	Human: 676aa, NM_000218 (transcript variant 1), chr. 11p15.5, <i>KCNQ1</i> , GeneID: 3784, PMID: 8528244 ¹ Mouse: 668aa, NM_008434, chr. 7 Rat: 669aa, NM_032073, chr. 1q41
Associated subunits	KCNE1 (minK/IsK), KCNE3 [minK-related peptide 2 (MiRP2)]
Functional assays	Voltage-clamp
Current	I _{Ks} (with KCNE1), ^{2,3} I _{K,CAMP} (with KCNE3) ¹⁶
Conductance	1.8pS (KCNQ1 alone), 5pS (with KCNE1)
Ion selectivity	K ⁺
Activation	KCNQ1 alone: V _a = 12 mV, τ _a = 30, and 800 ms at +40 mV KCNQ1 + KCNE1: V _a = +8 mV, τ _a = 0.7, 1.5, and 8 s at +40 mV
Inactivation	KCNQ1 alone: V _h = +18 mV, τ _h = 130 ms at 20 mV
Activators	R-L3 (= L364373, 1 μM for KCNQ1 alone; R-L3 does not activate the KCNQ1/KCNE1 complex; the S enantiomer blocks KCNQ1) ⁴ ; mefenamic acid, niflumic acid, and 4,4'-diisothiocyanostilbene-2,2'-disulfonic acid (10–100 μM) ^{5,6}
Gating inhibitors	None
Blockers	Chromanol 293B (1 μM), ⁷ L735821 (80 nM), ⁸ mefloquine (0.88 μM), ⁹ azimilide (3 μM), ^{9,10} HMR-1556 (120 nM), XE991 (0.78 μM KCNQ1 alone; 11.1 μM KCNQ1/KCNE1), ¹¹ linopirdine (8.9 μM KCNQ1 alone)
Radioligands	None
Channel distribution	Heart, kidney, rectum, ear, germ, pancreas, lung, cochlea, placenta
Physiological functions	Repolarization of cardiac action potentials (KCNQ1 and minK/ISK/KCNE1 coassemble to form the cardiac I _{Ks} channel); potassium recycling at basolateral membrane of intestinal crypt cells (with KCNE3) and inner ear
Mutations and pathophysiology	Loss of function mutations in the <i>KCNQ1</i> gene can cause either RWS (autosomal dominant) or JLNS (autosomal recessive); RWS is characterized by congenital long QT syndrome and electrocardiographically distinguished by a prolonged QT interval and polymorphic ventricular arrhythmias (torsade de pointes), which may result in recurrent syncope, seizure, or sudden death; JLNS patients have deafness, congenital and functional heart disease, a prolonged QT interval on an electrocardiogram, and sudden death cardioauditory syndrome; <i>KCNQ1</i> is disrupted by chromosomal rearrangements in patients with Beckwith-Wiedemann syndrome, ¹³ as well as by a balanced chromosomal translocation in an embryonal rhabdoid tumor; gain-of-function mutations in <i>KCNQ1</i> cause atrial fibrillation and short QT syndrome
Pharmacological significance	Blockers developed as class III antiarrhythmic agents to target ventricular arrhythmias ^{14,15} ; activators could be useful for the treatment of some long QT syndromes ⁶

aa, amino acids; chr., chromosome; RWS, Romano-Ward syndrome; JLNS, Jervell and Lange-Nielsen syndrome; L735821, 3-(2,4-dichlorophenyl)-N-(6-methyl-5-oxo-2-phenyl-3,6-diazabicyclo[5.4.0]undeca-2,7,9,11-tetraen-4-yl)-prop-2-enamide; XE991, 10,10-bis(pyridin-4-ylmethyl)anthracen-9-one; HMR-1556, N-(6-cyano-3-hydroxy-2,2-dimethyl-chroman-4-yl)-N-methyl-ethanesulfonamide.

1. Wang Q, Curran ME, Splawski I, Burn TC, Millholland JM, Van Raay TJ, Shen J, Timothy KW, Vincent GM, de Jager T, et al. (1996) Positional cloning of a novel potassium channel gene: KVLQT1 mutations cause cardiac arrhythmias. *Nat Genet* **12**:17–23.

2. Sanguinetti MC, Curran ME, Zou A, Shen J, Spector PS, Atkinson DL, and Keating MT (1996) Coassembly of K_v LQT1 and minK (IsK) proteins to form cardiac I_{Ks} potassium channel. *Nature (Lond)* **384**:80–83.

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4. Salata JJ, Jurkiewicz NK, Wang J, Evans BE, Orme HT, and Sanguinetti MC (1998) A novel benzodiazepine that activates cardiac slow delayed rectifier K⁺ currents. *Mol Pharmacol* **54**:220–230.

5. Busch AE, Herzer T, Wagner CA, Schmidt F, Raber G, Waldegger S, and Lang F (1994) Positive regulation by chloride channel blockers of IsK channels expressed in *Xenopus* oocytes. *Mol Pharmacol* **46**:750–753.

6. Abitbol I, Peretz A, Lerche C, Busch AE, and Attali B (1999) Stilbenes and fenamates rescue the loss of I_{Ks} channel function induced by an LQT5 mutation and other IsK mutants. *EMBO J* **18**:4137–4148.

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8. Tinel N, Lauritzen I, Chouabe C, Lazdunski M, and Borsotto M (1998) The KCNQ2 potassium channel: splice variants, functional and developmental expression: brain localization and comparison with KCNQ3. *FEBS Lett* **438**:171–176.

9. Kang J, Chen XL, Wang L, and Rampe D (2001) Interactions of the antimalarial drug mefloquine with the human cardiac potassium channels KvLQT1/minK and HERG. *J Pharmacol Exp Ther* **299**:290–296.

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12. Keating MT and Sanguinetti MC (2001) Molecular and cellular mechanisms of cardiac arrhythmias. *Cell* **104**:569–580.

13. Lee MP, Hu RJ, Johnson LA, and Feinberg AP (1997) Human KVLQT1 gene shows tissue-specific imprinting and encompasses Beckwith-Wiedemann syndrome chromosomal rearrangements. *Nat Genetics* **15**:181–185.

14. Coghlan MJ, Carroll WA, and Gopalakrishnan M (2001) Recent developments in the biology and medicinal chemistry of potassium channel modulators: update from a decade of progress. *J Med Chem* **44**:1627–1653.

15. Shieh CC, Coghlan M, Sullivan JP, and Gopalakrishnan M (2000) Potassium channels: molecular defects, diseases, and therapeutic opportunities. *Pharmacol Rev* **52**:557–594.

16. Schroeder BC, Waldegger S, Fehr S, Bleich M, Warth R, Greger R, and Jentsch TJ (2000) A constitutively open potassium channel formed by KCNQ1 and KCNE3. *Nature (Lond)* **403**:196–199.

TABLE 25
K_v7.2 channels

Channel name	K _v 7.2
Description	Voltage-gated potassium channel, delayed rectifier
Other names	KQT2
Molecular information	Human: 872aa, NM_172107 (transcript variant 1), chr. 20q13.3, <i>KCNQ2</i> , GeneID: 3785, PMID: 9836639 ¹ Mouse: 870aa, NM_010611 (transcript variant 1), chr. 2 Rat: 852aa, NM_133322, chr. 3q43
Associated subunits	KCNQ3, KCNE2
Functional assays	Voltage-clamp
Current	M current
Conductance	5.8pS ¹³
Ion selectivity	K ⁺
Activation	V _a = 26 mV, τ _a = 157 ms at +30 mV
Inactivation	V _h = 18 mV, τ _h = 130 ms at 20 mV
Activators	Retigabine (10 μM), ² BMS204352 (1 μM) ³
Gating inhibitors	None
Blockers	Tetraethylammonium (KCNQ2 alone: 0.16 mM; KCNQ2/KCNQ3: 0.5 mM), ¹ XE991 (0.7 μM), ^{1,4} linopiridine (4.8 μM), ^{1,3} L735821 (1.5 μM) ⁵
Radioligands	None
Channel distribution	Infant brain, adult brain, fetal brain, sympathetic ganglia, lung, testis, fetal heart, adult heart, breast, eye, germ cell, placenta, small intestine, neuroblastoma ¹⁰
Physiological functions	Determines subthreshold excitability of neurons; KCNQ2 and KCNQ3 coassemble to form the M current in the brain ¹ (see "Comments"); KCNQ2 and KCNQ3 proteins are colocalized in a somatodendritic pattern on pyramidal and polymorphic neurons in the human cortex and hippocampus ¹¹ ; KCNQ2 is also expressed in the absence of KCNQ3 in some presynaptic terminals ¹¹
Mutations and pathophysiology	Benign familial neonatal convulsions (<i>EBN1</i>) with myokymia ^{6,7} ; in KCNQ2 knockout mice, homozygotes (KCNQ2 ^{-/-}) die within a few hours after birth owing to pulmonary atelectasis that is not due to the status of epileptic seizures, although their development is morphologically normal; heterozygous mice have decreased expression of KCNQ2 and show hypersensitivity to pentylenetetrazole, an inducer of seizure ¹²
Pharmacological significance	Retigabine is an anticonvulsant ² (the M current is a new target for antiepileptic therapy ^{8,9}); blockers enhance learning and memory in animal models ⁹
Comments	The M current is a slowly activating and deactivating potassium conductance that plays a critical role in determining the subthreshold excitability of neurons as well as the responsiveness to synaptic inputs; the M current was first described in peripheral sympathetic neurons, and differential expression of this conductance produces subtypes of sympathetic neurons with distinct firing patterns; the M current is also expressed in many neurons in the central nervous system

aa, amino acids; chr., chromosome; BMS204352, 3-(5-chloro-2-methoxy-phenyl)-3-fluoro-6-(trifluoromethyl)-1*H*-indol-2-one; XE991, 10,10-bis(pyridin-4-ylmethyl)anthracen-9-one; L735821, 3-(2,4-dichlorophenyl)-*N*-(6-methyl-5-oxo-2-phenyl-3,6-diazabicyclo[5.4.0]undeca-2,7,9,11-tetraen-4-yl)-prop-2-enamide.

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3. Schroder RL, Jespersen T, Christophersen P, Strobaek D, Jensen BS, Olesen SP (2001) KCNQ4 channel activation by BMS-204352 and retigabine. *Neuropharmacology* **40**:888–898.

4. Robbins J (2001) KCNQ potassium channels: physiology, pathophysiology, and pharmacology. *Pharmacol Ther* **90**:1–19.

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9. Coghlan MJ, Carroll WA, and Gopalakrishnan M (2001) Recent developments in the biology and medicinal chemistry of potassium channel modulators: update from a decade of progress. *J Med Chem* **44**:1627–1653.

10. Smith JS, Iannotti C, Dargis P, Christian EP, and Aiyar J (2001) Differential expression of KCNQ2 splice variants: implications to M current function during neuronal development. *J Neurosci* **21**:1096–1103.

11. Cooper EC, Aldape KD, Abosch A, Barbaro NM, Berger MS, Peacock WS, Jan YN, and Jan LY (2000) Colocalization and coassembly of two human brain M-type potassium channel subunits that are mutated in epilepsy. *Proc Natl Acad Sci USA* **97**:4914–4919.

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TABLE 26
K_v7.3 channels

Channel name	K _v 7.3
Description	Voltage-gated potassium channel, delayed rectifier
Other names	None
Molecular information	Human: 872aa NM_004519, chr. 8q24, <i>KCNQ3</i> , GeneID: 3786, PMID: 9836639 ¹ Mouse: 873aa, NM_152923, chr. 15 Rat: 873aa, NM_031597, chr. 7q33
Associated subunits	KCNQ2, KCNQ5
Functional assays	Voltage-clamp
Current	M current ¹
Conductance	7.3pS
Ion selectivity	K ⁺
Activation	V _a = 39 mV, τ _a = 60 ms at +30 mV
Inactivation	Not established
Activators	Retigabine (<i>KCNQ3</i> alone: 0.6 μM; <i>KCNQ3/KCNQ5</i> : 1.4 μM) ² ; XE991, ³ BMS204352 (1 μM) ⁴
Gating inhibitors	None
Blockers	Tetraethylammonium (>30 mM), ⁵ linopiridine (<i>KCNQ3/KCNQ5</i> : 7.7 μM) ²
Radioligands	None
Channel distribution	Brain, testis, retina, colon, eye, head, neck
Physiological functions	Determines subthreshold excitability of neurons; <i>KCNQ2</i> and <i>KCNQ3</i> coassemble to form the M current in the brain ¹ (see "Comments"); <i>KCNQ2</i> and <i>KCNQ3</i> proteins are colocalized in a somatodendritic pattern on pyramidal and polymorphic neurons in the human cortex and hippocampus ^{7,8}
Mutations and pathophysiology	Benign familial neonatal convulsions (<i>EBN2</i>) (e.g., G263V mutation in the pore) ⁹
Pharmacological significance	Anticonvulsants (activators), cognition enhancers (blockers) ⁶
Comments	The M current is a slowly activating and deactivating potassium conductance that plays a critical role in determining the subthreshold excitability of neurons as well as the responsiveness to synaptic inputs; the M current was first described in peripheral sympathetic neurons, and differential expression of this conductance produces subtypes of sympathetic neurons with distinct firing patterns; the M current is also expressed in many neurons in the central nervous system

aa, amino acids; chr., chromosome; XE991 10,10-bis(pyridin-4-ylmethyl)anthracen-9-one; BMS204352, 3-(5-chloro-2-methoxy-phenyl)-3-fluoro-6-(trifluoromethyl)-1*H*-indol-2-one.

1. Wang HS, Pan Z, Shi W, Brown BS, Wymore RS, Cohen IS, Dixon JE, and McKinnon D (1998) *KCNQ2* and *KCNQ3* potassium channel subunits: molecular correlates of the M-channel. *Science (Wash DC)* **282**:1890–1893.

2. Wickenden AD, Zou A, Wagoner PK, and Jegla T (2001) Characterization of *KCNQ5/Q3* potassium channels expressed in mammalian cells. *Br. J. Pharmacol* **132**:381–384.

3. Wang HS, Brown BS, McKinnon D, and Cohen IS (2000) Molecular basis for differential sensitivity of *KCNQ*, and *I_{Ks}* channels to the cognitive enhancer XE991. *Mol Pharmacol* **57**:1218–1223.

4. Schroder RL, Jespersen T, Christophersen P, Strobaek D, Jensen BS, and Olesen SP (2001) *KCNQ4* channel activation by BMS-204352 and retigabine. *Neuropharmacology* **40**:888–898.

5. Hadley JK, Noda M, Selyanko AA, Wood IC, Abogadie FC, and Brown DA (2000) Differential tetraethylammonium sensitivity of *KCNQ1–4* potassium channels. *Br J Pharmacol* **129**:413–415.

6. Coghlan MJ, Carroll WA, and Gopalakrishnan M (2001) Recent developments in the biology and medicinal chemistry of potassium channel modulators: update from a decade of progress. *J Med Chem* **44**:1627–1653.

7. Smith JS, Iannotti C, Dargis P, Christian EP, and Aiyar J (2001) Differential expression of *KCNQ2* splice variants: implications to M current function during neuronal development. *J Neurosci* **21**:1096–1103.

8. Cooper EC, Aldape KD, Abosch A, Barbaro NM, Berger MS, Peacock WS, Jan YN, and Jan LY (2000) Colocalization and coassembly of two human brain M-type potassium channel subunits that are mutated in epilepsy. *Proc Natl Acad Sci USA* **97**:4914–4919.

9. Charlier C, Singh NA, Ryan SG, Lewis TB, Reus BE, Leach RJ, and Leppert M (1998) A pore mutation in a novel KQT-like potassium channel gene in an idiopathic epilepsy family. *Nat Genet* **18**:53–55.

TABLE 27
K_v7.4 channels

Channel name	K _v 7.4
Description	Voltage-gated potassium channel, delayed rectifier
Other names	None
Molecular information	Human: 695aa, NM_004700 (transcript variant 1), chr. 1p34, <i>KCNQ4</i> , ¹ GeneID: 9132, PMID: 10025409 ¹ Mouse: 724aa, XM_143960 (predicted), chr. 4 Rat: AF249748 (partial coding sequence)
Associated subunits	KCNQ3 ²
Functional assays	Voltage-clamp
Current	IK _n
Conductance	Not established
Ion selectivity	K ⁺
Activation	V _a = 10 mV
Inactivation	Not established
Activators	Retigabine (1 μM) ³ ; BMS204352 (1 μM) ³
Gating inhibitors	None
Blockers	Tetraethylammonium (3 mM), ⁴ linopirdine (14 μM), ⁵ XE991 (5 μM), ⁵ bepridil (9.4 μM) ⁵
Radioligands	None
Channel distribution	Cochlea (outer hair cells), placenta, vestibular organs (type 1 hair cells), brainstem auditory nuclei
Physiological functions	Mediates potassium efflux from outer hair cells ^{1,6}
Mutations and pathophysiology	Mutations in <i>KCNQ4</i> cause autosomal dominant nonsyndromic deafness type 2 (DFNA2) ^{1,6}
Pharmacological significance	Anticonvulsants (activators)

aa, amino acids; chr., chromosome; XE991, 10,10-bis(pyridin-4-ylmethyl)anthracen-9-one; BMS204352, 3-(5-chloro-2-methoxy-phenyl)-3-fluoro-6-(trifluoromethyl)-1H-indol-2-one.

1. Kubisch C, Schroeder BC, Friedrich T, Lutjohann B, El-Amraoui A, Marlin S, Petit C, and Jentsch TJ (1999) *KCNQ4*, a novel potassium channel expressed in sensory outer hair cells, is mutated in dominant deafness. *Cell* **96**:437–446.

2. Schroeder BC, Waldegger S, Fehr S, Bleich M, Warth R, Greger R, and Jentsch TJ (2000) A constitutively open potassium channel formed by *KCNQ1* and *KCNE3*. *Nature (Lond)* **403**:196–199.

3. Schroder RL, Jespersen T, Christophersen P, Strobaek D, Jensen BS, and Olesen SP (2001) *KCNQ4* channel activation by BMS-204352 and retigabine. *Neuropharmacology* **40**:888–898.

4. Hadley JK, Noda M, Selyanko AA, Wood IC, Abogadie FC, and Brown DA (2000) Differential tetraethylammonium sensitivity of *KCNQ1–4* potassium channels. *Br J Pharmacol* **129**:413–415.

5. Sogaard R, Ljungstrom T, Pedersen KA, Olesen SP, and Jensen BS (2001) *KCNQ4* channels expressed in mammalian cells: functional characteristics and pharmacology. *Am J Physiol* **280**:C859–C866.

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TABLE 28
K_v7.5 channels

Channel name	K _v 7.5
Description	Voltage-gated potassium channel, delayed rectifier
Other names	None
Molecular information	Human: 932aa, NM_019842, chr. 6q14, <i>KCNQ</i> , ^{1,5} GeneID: 56479, PMID: 10787416 ¹ Mouse: 933aa, NM_023872, chr. 1 Rat: 953aa, XM_237012 (predicted), chr. 9
Associated subunits	KCNQ3
Functional assays	Voltage-clamp
Current	M current ¹
Conductance	Not established
Ion selectivity	K ⁺
Activation	V _a = 30 mV
Inactivation	Not established
Activator	Retigabine (<i>KCNQ5/KCNQ3</i> : 1.4 μM), ² BMS204352 (2.4 μM) ³
Gating inhibitors	None
Blockers	Tetraethylammonium (>30 mM), ¹ linopirdine (16 μM), ¹ linopirdine <i>KCNQ5/KCNQ3</i> (7.7 μM), ² XE991 ³
Radioligands	None
Channel distribution	Brain, sympathetic ganglia (splice variant I), ⁴ skeletal muscle (splice variant III) ⁴
Physiological functions	Determines subthreshold excitability of neurons
Mutations and pathophysiology	A number of allelic variants have been identified
Pharmacological significance	Anticonvulsants (activators)

aa, amino acids; chr., chromosome; XE991, 10,10-bis(pyridin-4-ylmethyl)anthracen-9-one; BMS204352, 3-(5-chloro-2-methoxy-phenyl)-3-fluoro-6-(trifluoromethyl)-1H-indol-2-one.

1. Lerche C, Scherer CR, Seeböhm G, Derst C, Wei AD, Busch AE, and Steinmeyer K (2000) Molecular cloning and functional expression of *KCNQ5*, a potassium channel subunit that may contribute to neuronal M-current diversity. *J Biol Chem* **275**:22395–22400.

2. Wickenden AD, Zou A, Wagoner PK, and Jegla T (2001) Characterization of *KCNQ5/Q3* potassium channels expressed in mammalian cells. *Br J Pharmacol* **132**:381–384.

3. Dupuis DS, Schroder RL, Jespersen T, Christensen JK, Christophersen P, Jensen BS, and Olesen SP (2002) Activation of *KCNQ5* channels stably expressed in HEK293 cells by BMS-204352. *Eur J Pharmacol* **437**:129–137.

4. Schroeder BC, Hechenberger M, Weinreich F, Kubisch C, and Jentsch TJ (2000) *KCNQ5*, a novel potassium channel broadly expressed in brain, mediates M-type currents. *J Biol Chem* **275**:24089–24095.

TABLE 29
K_v8.1 channels

Channel name	K _v 8.1 ¹⁻³
Description	Modifier/silencer
Other names	K _v 2.3, HNKA
Molecular information	Human: 500aa, NM_014379, chr. 8q22.3-24.1, <i>KCNV1</i> , GeneID: 27012, PMID: 670833 ¹ Mouse: 503aa, NM_026200, chr. 15 Rat: 503aa, NM_021697, chr. 7q31
Associated subunits	Coassembles with K _v 2 family channels
Functional assays	Voltage-clamp
Current	None established
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Infant brain, adult brain (layers II, IV, and VI of the cerebral cortex, hippocampus, CA1–CA4 pyramidal cell layer, granule cells of the dentate gyrus, granule cell layer, Purkinje cell layer of the cerebellum), kidney
Physiological functions	Regulation of membrane potential and action potential frequency by modulation of delayed rectifier potassium current; modulates the activity of K _v 2.1 and K _v 2.2 channels by changing kinetics and levels of expression and by shifting the half-inactivation potential to more polarized values
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	K _v 8.1 has no function on its own, but it has important modulatory actions on K _v 2 channels

aa, amino acids; chr., chromosome.

1. Hugnot JP, Salinas M, Lesage F, Guillemare E, de Weille J, Heurteaux C, Mattei MG, and Lazdunski M (1996) Kv8.1, a new neuronal potassium channel subunit with specific inhibitory properties towards Shab and Shaw channels. *EMBO J* **15**:3322–3331.

2. Salinas M, de Weille J, Guillemare E, Lazdunski M, and Hugnot JP (1997) Modes of regulation of *Shab* K⁺ channel activity by the Kv8.1 subunit. *J Biol Chem* **272**:8774–8780.

3. Chiara MD, Monje F, Castellano A, and Lopez-Barneo J (1999) A small domain in the N terminus of the regulatory α -subunit Kv2.3 modulates Kv2.1 potassium channel gating. *J Neurosci* **19**:6865–6873.

TABLE 30
K_v8.2 channels

Channel name	K _v 8.2
Description	Modifier/silencer
Other names	Kv11.1 ¹
Molecular information	Human: 545aa, NM_133497, chr. 9p24.2, <i>KCNV2</i> , GeneID: 169522, PMID: 12060745 ¹ Mouse: 562aa, NM_183179, chr. 19 Rat: 561 aa, XM_220024 (predicted), chr. 1
Associated subunits	Coassembles with K _v 2 family channels
Functional assays	Voltage-clamp
Current	None established
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Lung, liver, kidney, pancreas, spleen, thymus, prostate, testis, ovary, colon ¹
Physiological functions	Regulation of membrane potential and action potential frequency by modulation of delayed rectifier potassium currents; modulates the activity of K _v 2.1 channels by causing small changes in activation threshold and kinetics and in C-type inactivation ¹
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	K _v 8.2 has no function on its own, but it has important modulatory actions on K _v 2 channels

aa, amino acids; chr., chromosome.

1. Ottschytch N, Raes A, Van Hoorick D, and Snyders DJ (2002) Obligatory heterotetramerization of three previously uncharacterized Kv channel-subunits identified in the human genome. *Proc Natl Acad Sci USA* **99**:7986–7991.

TABLE 31
K_v9.1 channels

Channel name	K _v 9.1 ¹⁻⁴
Description	Modifier/silencer
Other names	None
Molecular information	Human: 526 aa, NM_002251, chr. 20q12, <i>KCNS1</i> , GeneID: 3787, PMID: 10484328 ³ Mouse: 497 aa, NM_008435, chr. 2 Rat: 497 aa, NM_053954, chr. 3q42
Associated subunits	Coassembles with K _v 2 family channels
Functional assays	Voltage-clamp
Current	None established
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Infant brain, adult brain (frontal cortex), lens epithelium, melanocytes (in mouse brain, the distribution of K _v 9.1 is similar to K _v 9.2, with highest expression levels in the main olfactory bulb, cerebral cortex, hippocampal formation, habenula, basolateral amygdaloid nuclei, and cerebellum; K _v 9.1 and K _v 9.2 are colocalized with K _v 2.1 and/or K _v 2.2 α subunits in several regions)
Physiological functions	Regulation of membrane potential and action potential frequency by modulation of delayed rectifier potassium current; modulates the activity of K _v 2.1 and K _v 2.2 α subunits by changing kinetics and levels of expression and by shifting the half-inactivation potential to more polarised values; K _v 9.1 enhances the single-channel conductance of K _v 2.1
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	The human K _v 9.1 gene is composed of a minimum of 5 exons, with at least 2 alternatively spliced exons in the 5'-untranslated region ³

aa, amino acids; chr., chromosome.

1. Salinas M, Duprat F, Heurteaux C, Hugnot JP, and Lazdunski M (1997) New modulatory α subunits for mammalian *Shab* K⁺ channels. *J Biol Chem* **272**:24371–24379.
2. Stocker M and Kerschensteiner D (1998) Cloning and tissue distribution of two new potassium channel α -subunits from rat brain. *Biochem Biophys Res Commun* **248**:927–934.
3. Shepard AR and Rae JL (1999) Electrically silent potassium channel subunits from human lens epithelium. *Am J Physiol* **277**:C412–C424.
4. Richardson FC and Kaczmarek LK (2000) Modification of delayed rectifier potassium currents by the K_v9.1 potassium channel subunit. *Hear Res* **147**:21–30.

TABLE 32
K_v9.2 channels

Channel name	K _v 9.2 ^{1,2}
Description	Modifier/silencer
Other names	None
Molecular information	Human: 477aa, NM_020697, chr. 8q22, ³ <i>KCNS2</i> , GeneID: 3788, PMID: 9305895 ¹ Mouse: 477aa, NM_181317, chr. 15 Rat: 477 aa, NM_023966, chr. 7q22
Associated subunits	Coassembles with K _v 2 family channels
Functional assays	Voltage-clamp
Current	None established
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	Not functional on its own
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Infant and adult brain, retina, spinal cord (in mouse brain, the distribution of K _v 9.2 is similar to K _v 9.1, with highest expression levels in the main olfactory bulb, cerebral cortex, hippocampal formation, habenula, basolateral amygdaloid nuclei, and cerebellum; K _v 9.1 and K _v 9.2 are colocalized with K _v 2.1 and/or K _v 2.2 α subunits in several regions; also found in the retina, spinal cord, and pulmonary artery)
Physiological functions	Regulation of membrane potential and action potential frequency by modulation of delayed rectifier potassium current; modulates the activity of K _v 2.1 and K _v 2.2 α subunits by changing kinetics and levels of expression and by shifting the half-inactivation potential to more polarized values; K _v 9.1 enhances the single-channel conductance of K _v 2.1
Mutations and pathophysiology	Not established
Pharmacological significance	Not established

aa, amino acids; chr., chromosome.

1. Salinas M, Duprat F, Heurteaux C, Hugnot JP, and Lazdunski M (1997) New modulatory α subunits for mammalian *Shab* K⁺ channels. *J Biol Chem* **272**:24371–24379.
2. Davies AR and Kozlowski RZ (2001) Kv channel subunit expression in rat pulmonary arteries. *Lung* **179**:147–161.
3. Banfi S, Borsani G, Rossi E, Bernard L, Guffanti A, Rubboli F, Marchitello A, Giglio S, Coluccia E, Zollo M, et al. (1996) Identification and mapping of human cDNAs homologous to *Drosophila* mutant genes through EST database searching. *Nat Genet* **13**:167–174.

TABLE 33
K_v9.3 channels

Channel name	K _v 9.3 ¹⁻³
Description	Modifier/silencer
Other names	None
Molecular information	Human: 491aa, NM_023966, NM_002252, chr. 2p24, <i>KCNS3</i> (see 'Comments'), GeneID: 3790, PMID: 9362476 ¹ Mouse: 491aa, NM_173417, chr. 12 Rat: 491aa, NM_031778, chr. 6q14
Associated subunits	Coassembles with K _v 2 family channels
Functional assays	Voltage-clamp
Current	K _v 9.3/K _v 2.1 and ATP-dependent delayed rectifier channel in oxygen-sensitive pulmonary myocytes
Conductance	Not functional on its own
Ion selectivity	Not functional on its own
Activation	Not functional on its own
Inactivation	K _v 9.3/K _v 2.1 heteromers inactivate in a fast and complete fashion from intermediate closed states but in a slow and incomplete manner from open states ⁴
Activators	None
Gating inhibitors	None
Blockers	Hypoxia blocks K _v 9.3/K _v 2.1 channels ⁵
Radioligands	None
Channel distribution	Brain, breast, colon, eye, lens, heart, kidney, muscle, lung, testis, skin, stomach, uterus ⁶ ; also found in lens epithelium ³
Physiological functions	Regulation of membrane potential in pulmonary artery myocytes
Mutations and pathophysiology	Not established
Pharmacological significance	Pulmonary artery hypertension
Comments	The human K _v 9.3 gene is intronless across the coding region 3'-UTR and all of the analysed 5'-UTR

aa, amino acids; chr., chromosome; UTR, untranslated region.

1. Patel AJ, Lazdunski M, and Honore E (1997) Kv2.1/Kv9.3, a novel ATP-dependent delayed-rectifier K⁺ channel in oxygen-sensitive pulmonary artery myocytes. *EMBO J* **16**:6615–6625.

2. Stocker M and Kerschensteiner D (1998) Cloning and tissue distribution of two new potassium channel α -subunits from rat brain. *Biochem Biophys Res Commun* **248**:927–934.

3. Shepard AR and Raem JL (1999) Electrically silent potassium channel subunits from human lens epithelium. *Am J Physiol* **277**, C412–C424.

4. Kerschensteiner D and Stocker M (1999) Heteromeric assembly of Kv2.1 with Kv9.3: effect on the state dependence of inactivation. *Biophys J* **77**:248–257.

5. Hulme JT, Coppock EA, Felipe A, Martens JR, and Tamkun MM (1999) Oxygen sensitivity of cloned voltage-gated K⁺ channels expressed in the pulmonary vasculature. *Circ Res* **85**:489–497.

6. UniGeneCluster Hs0.47584; OMIM no. 603888.

TABLE 34
K_v10.1 channels

Channel name	K _v 10.1
Description	Voltage-gated potassium channel, delayed rectifier
Other names	eag1a, eag1b, KCNH1a, KCNH1b, <i>ether-à-go-go</i> ¹⁻⁴
Molecular information	Human: 989aa, NM_172362, chr. 1q32-41, <i>KCNH1</i> (see "Comments"), GeneID: 3756, PMID: 8159766 ² Mouse: 989aa, NM_010600, chr. 1 Rat: 962aa, NM_031742, chr. 13q27
Associated subunits	Hyperkinetic (Hk), ⁵ CaM, ⁶ Slob, ⁷ epsin, ⁸ KCR1 (K channel regulator) ⁹
Functional assays	Voltage-clamp
Current	Delayed rectifier
Conductance	Not established
Ion selectivity	K ⁺ and Ca, ²⁺ ¹⁰ variable Cs ⁺
Activation	Extracellular Mg ²⁺ and other divalent cations slow activation in a dose- and voltage-dependent manner, based on their enthalpy of hydration ¹¹ ; low external pH also slows activation
Inactivation	Not established
Activators	Hyperpolarization slows down the kinetics of activation; depolarization accelerates the kinetics of activation ³
Gating inhibitors	None
Blockers	Quinidine (1.4 μM), ¹² calcium/calmodulin (480 nM) ^{6,13}
Radioligands	None
Channel distribution	Brain (amygdala, caudate nucleus, cerebral cortex, cerebellum, putamen, hippocampus, frontal lobe, occipital lobe, temporal lobe, subthalamic nucleus; not in substantia nigra, thalamus, or medulla oblongata), myoblasts, skeletal muscle (ESTs, but not detected by Northern), melanoma cells, ectopic expression in cancer cell lines and many tumor cells from different tissues, spiral ligament in rat ¹⁴⁻¹⁶
Physiological functions	Role in controlling the cell cycle and/or cell proliferation ^{17,18} ; eag-1 is thought to encode the noninactivating delayed rectifier potassium channel K _{NI} that is activated at the onset of human myoblast differentiation ⁴
Mutations and pathophysiology	K _v 10.1 has been associated with human cervical carcinoma ²¹
Pharmacological significance	K _v 10.1 blockers might have use in cancer therapy
Comments	This channel has a GFG (rather than the common GYG) potassium channel signature sequence, a PAS domain in the distal part of the cytosolic N terminus, a cNBD domain in the proximal portion of the C terminus, a C-terminal assembly domain (CAD), a CaM-binding domain, a bNLS domain in the C terminus, and a C-terminal domain required for assembly ¹⁹ ; the TCC domain at the C-terminal end of K _v 10 and K _v 11 confers specificity for multimer formation, allowing K _v 10.1/K _v 10.2 heteromerization and K _v 11.1 homomerization but not K _v 10.x/K _v 11.1 heteromerization ²² ; this C-terminal TCC domain has been identified in many other channels, and mutations of the TCC have been found to be linked to genetic channelopathies; conductance properties have been shown to change with the cell cycle ²⁰

aa, amino acids; chr., chromosome; CaM, calmodulin; TCC, tetramerizing coiled-coiled; EST, expressed sequence tag.

- Warmke J, Drysdale R, and Ganetzky B (1991) A distinct potassium channel polypeptide encoded by the *Drosophila* eag locus. *Science (Wash DC)* **252**:1560-1562.
- Warmke JW and Ganetzky B (1994) A family of potassium channel genes related to eag in *Drosophila* and mammals. *Proc Natl Acad Sci USA* **91**:3438-3442.
- Ludwig J, Terlau H, Wunder F, Bruggemann A, Pardo LA, Marquardt A, Stuhmer W, and Pongs O (1994) Functional expression of a rat homologue of the voltage gated ether à go-go potassium channel reveals differences in selectivity and activation kinetics between the *Drosophila* channel and its mammalian counterpart. *EMBO J* **13**:4451-4458.
- Ochiodoro T, Bernheim L, Liu JH, Bijlenga P, Sinnreich M, Bader CR, and Fischer-Lougheed J (1998) Cloning of a human *ether-à-go-go* potassium channel expressed in myoblasts at the onset of fusion. *FEBS Lett* **434**:177-182.
- Wilson GF, Wang Z, Chouinard SW, Griffith LC, and Ganetzky B (1998) Interaction of the K channel β subunit, Hyperkinetic, with eag family members. *J Biol Chem* **273**:6389-6394.
- Schonherr R, Lober K, and Heinemann SH (2000) Inhibition of human ether à go-go potassium channels by Ca²⁺/calmodulin. *EMBO J* **19**:3263-3271.
- Schopperle WM, Holmqvist MH, Zhou Y, Wang J, Wang Z, Griffith LC, Keselman I, Kusinitz F, Dagan D, and Levitan IB (1998) Slob, a novel protein that interacts with the Slowpoke calcium-dependent potassium channel. *Neuron* **20**:565-573.
- Piros ET, Shen L, and Huang XY (1999) Purification of an EH domain-binding protein from rat brain that modulates the gating of the rat *ether-à-go-go* channel. *J Biol Chem* **274**:33677-33683.
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- Bruggemann A, Pardo LA, Stuhmer W, and Pongs O (1993) *Ether-à-go-go* encodes a voltage-gated channel permeable to K⁺ and Ca²⁺ and modulated by cAMP. *Nature (Lond)* **365**:445-448.
- Terlau H, Ludwig J, Steffan R, Pongs O, Stuhmer W, and Heinemann SH (1996) Extracellular Mg²⁺ regulates activation of rat eag potassium channel. *Pflueg Arch Eur J Physiol* **432**:301-312.
- Schonherr R, Gessner G, Lober K, and Heinemann SH (2002) Functional distinction of human EAG1 and EAG2 potassium channels. *FEBS Lett* **514**:204-208.
- Stansfeld CE, Roper J, Ludwig J, Weseloh RM, Marsh SJ, Brown DA, and Pongs O (1996) Elevation of intracellular calcium by muscarinic receptor activation induces a block of voltage-activated rat *ether-à-go-go* channels in a stably transfected cell line. *Proc Natl Acad Sci USA* **93**:9910-9914.
- Lecain E, Sauvaget E, Crisanti P, Van Den Abbeele T, and Huy PT (1999) Potassium channel ether à go-go mRNA expression in the spiral ligament of the rat. *Hear Res* **133**:133-138.
- Meyer R, Schonherr R, Gavrilova-Ruch O, Wohlrab W, and Heinemann SH (1999) Identification of ether à go-go and calcium-activated potassium channels in human melanoma cells. *J Membr Biol* **171**:107-115.
- Saganich MJ, Machado E, and Rudy B (2001) Differential expression of genes encoding subthreshold-operating voltage-gated K⁺ channels in brain. *J Neurosci* **21**:4609-4624.
- Pardo LA, del Camino D, Sanchez A, Alves F, Bruggemann A, Beckh S, and Stuhmer W (1999) Oncogenic potential of EAG K⁺ channels. *EMBO J* **18**:5540-5547.
- Camacho J, Sanchez A, Stuhmer W, and Pardo LA (2000) Cytoskeletal interactions determine the electrophysiological properties of human EAG potassium channels. *Pflueg Arch Eur J Physiol* **441**:167-174.
- Ludwig J, Owen D, and Pongs O (1997) Carboxy-terminal domain mediates assembly of the voltage-gated rat *ether-à-go-go* potassium channel. *EMBO J* **16**:6337-6345.
- Pardo LA, Bruggemann A, Camacho J, and Stuhmer W (1998) Cell-cycle related changes in the conducting properties of r-eag K⁺ channels. *J Cell Biol* **143**:767-775.
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- Jenke M, Sanchez A, Monje F, Stuhmer W, Weseloh RM, and Pardo LA (2003) C-terminal domains implicated in the functional surface expression of potassium channels. *EMBO J* **22**:395-403.

TABLE 35
K_v10.2 channels

Channel name	K _v 10.2
Description	Outward-rectifying, noninactivating voltage-dependent K ⁺ currents ^{3–5}
Other names	eag2 ^{1–5}
Molecular information	Human: 987aa, NM_139318 (transcript variant 1), chr. 14q23.1, <i>KCNH5</i> (see “Comments”), GeneID: 27133, PMID: 9738473 ² Mouse: 988aa, NM_172805, chr. 12 Rat: 988aa, NM_133610, chr. 6q24
Associated subunits	Hyperkinetic (Hk), ⁶ CaM, Slob, KCR1 (potassium channel regulator)
Functional assays	Voltage-clamp
Current	Outward-rectifying
Conductance	Not established
Ion selectivity	K ⁺
Activation	Activates at –100 mV (rat) ³
Inactivation	Noninactivating
Activators	None
Gating inhibitors	None
Blockers	Quinidine (152 μM), ⁵ intracellular calcium (nanomolar) ⁴
Radioligands	None
Channel distribution	Brain (layer IV of the cerebral cortex; thalamus, inferior colliculus, olfactory bulb, and certain brainstem nuclei) ^{3,4}
Physiological functions	Not established
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	This channel has a GFG (rather than the common GYG) potassium channel signature sequence, a PAS domain in the distal part of the cytosolic N terminus, a cNBD domain in the proximal portion of the C terminus, a C-terminal assembly domain (CAD), a CaM-binding domain, a bNLS domain in the C terminus, and a C-terminal domain is required for assembly ⁷ ; the TCC domain at the C-terminal end of K _v 10 and K _v 11 confers specificity for multimer formation, allowing K _v 10.1/K _v 10.2 heteromerization and K _v 11 homomerization but not K _v 10.x/K _v 11.x heteromerization ⁸ ; this C-terminal TCC domain has been identified in many other channels, and mutations of the TCC have been found to be linked to genetic channelopathies

aa, amino acids; chr., chromosome; CaM, calmodulin; TCC, tetramerizing coiled-coiled.

1. Shi W, Wang HS, Pan Z, Wymore RS, Cohen IS, McKinnon D, and Dixon JE (1998) Cloning of a mammalian elk potassium channel gene and EAG mRNA distribution in rat sympathetic ganglia. *J Physiol* **511**:675–682.
2. Occhiodoro T, Bernheim L, Liu JH, Bijlenga P, Sinnreich M, Bader CR, and Fischer-Lougheed J (1998) Cloning of a human *ether-à-go-go* potassium channel expressed in myoblasts at the onset of fusion. *FEBS Lett* **434**:177–182.
3. Saganich MJ, Vega-Saenz de Miera E, Nadal MS, Baker H, Coetzee WA, and Rudy B (1999) Cloning of components of a novel subthreshold-activating K⁺ channel with a unique pattern of expression in the cerebral cortex. *J Neurosci* **19**:10789–10802.
4. Ludwig J, Weseloh R, Karschin C, Liu Q, Netzer R, Engeland B, Stansfeld C, and Pongs O (2000) Cloning and functional expression of rat eag2, a new member of the *ether-à-go-go* family of potassium channels and comparison of its distribution with that of eag1. *Mol Cell Neurosci* **16**:59–70.
5. Schonherr R, Gessner G, Lober K, and Heinemann SH (2002) Functional distinction of human EAG1 and EAG2 potassium channels. *FEBS Lett* **514**:204–208.
6. Wilson GF, Wang Z, Chouinard SW, Griffith LC, and Ganetzky B (1998) Interaction of the K channel β subunit, Hyperkinetic, with eag family members. *J Biol Chem* **273**:6389–6394.
7. Ludwig J, Owen D, and Pongs O (1997) Carboxy-terminal domain mediates assembly of the voltage-gated rat *ether-à-go-go* potassium channel. *EMBO J* **16**:6337–6345.
8. Jenke M, Sanchez A, Monje F, Stuhmer W, Weseloh RM, and Pardo LA (2003) C-terminal domains implicated in the functional surface expression of potassium channels. *EMBO J* **22**:395–403.

TABLE 36
K_v11.1 channels

Channel name	K _v 11.1
Description	Voltage-gated potassium channel with inwardly rectifying properties
Other names	Human <i>ether-à-go-go</i> -related gene, HERG, erg1, Hergb ¹⁻⁸
Molecular information	Human: 1159aa, NM_000238 (transcript variant 1), chr. 7q35-36, ¹ <i>KCNH2</i> , GeneID: 3757, PMID: 8159766 ¹ Mouse: 1162aa, NM_013569, chr. 5 Rat: 1163aa, NM_053949, chr. 4q11
Associated subunits	minK, ^{9,25} possibly MiRP1 (KCNE2) ¹⁰
Functional assays	Voltage-clamp
Current	Cardiac I _{Kr} current ^{3,26}
Conductance	2pS (in physiological [K] _o), 10pS (100 mM [K] _o) ¹¹
Ion selectivity	K ⁺
Activation	Activation at currents more positive than -50 mV ^{3,26}
Inactivation	Exhibits C-type inactivation ⁴ ; inward rectification arises from a rapid and voltage-dependent inactivation process that reduces conductance at positive voltages ^{3,26,27}
Activators	None
Gating inhibitors	None
Blockers	Astemizole (1 nM), ¹³ BeKM-1 (3 nM), ¹⁴ ergtoxin (12 nM), ¹⁵ sertindole (3 nM), dofetilide (15–35 nM), ¹⁶ cisapride (6–40 nM), pimozone (18 nM), terfenadine (56 nM), halofantrine (200 nM), BRL32872 (240 nM), E-4031 (7.7 nM), CT haloperidol (1 μM), imipramine (3 μM), cocaine (5 μM), ketoconazole
Radioligands	None
Channel distribution	Heart, leiomyosarcoma, hippocampus, neuroblastoma, blood cells, brain, kidney, liver, lung, ovary, pancreas, testis, prostate, small intestine, tonsil, uterus, microglia
Physiological functions	HERG proteins form cardiac I _{Kr} channels ^{3,26} ; in the heart, HERG channels produce a resurgent current during repolarization ²⁰ due to the recovery from C-type inactivation ⁴ and a slow deactivation due to an interaction with an N-terminal domain (AA2–16) and the internal mouth of the pore ^{1,22} ; HERG contains a tetramerization domain called NAB and a structurally defined PAS domain in distinct regions of the N terminus ¹⁷ ; HERG forms a complex with MiRP1, ¹⁰ but it is as yet unclear whether MiRP1 forms a stable part of the channel itself or is otherwise involved in regulation of HERG expression or stability ²³
Mutations and pathophysiology	Mutations of this gene cause the autosomal dominant long QT syndrome 2 due to gating defects ²⁸ and trafficking abnormalities ^{29–33} and a prolonged QT interval on the electrocardiogram; syncope, sudden cardiac death, ventricular fibrillation, and torsades de pointes are also implicated in acquired long QT syndrome; mutations in MiRP1 are the cause of long QT syndrome 6 and are also found in many tumors ^{18,19}
Pharmacological significance	Proarrhythmic potential (QT prolongation) of histamine H ₁ receptor antagonists, antipsychotics, and tricyclic antidepressants that leads to torsades de pointes in some individuals (acquired long QT syndrome)
Comments	A shorter isoform encoded by an alternative transcript (1b) of K _v 11.1 ^{5,7} or a truncated isoform ⁶ can coassemble with and modulate the behavior of full-length HERG and Merg1, the mouse ortholog; the TCC domain at the C-terminal end of K _v 10 and K _v 11 confers specificity for multimer formation, allowing K _v 10.1/K _v 10.2 heteromerization and K _v 11 homomerization, but not K _v 10.x/K _v 11.x heteromerization ²⁴ ; this C-terminal TCC domain has been identified in many other channels, and mutations of the TCC are found to be linked to genetic channelopathies; C terminus interacts with Golgi matrix protein GM130 ³⁴

aa, amino acids; chr., chromosome; MiRP1, MinK-related peptide 1; TCC, tetramerizing coiled-coiled; E-4031, *N*-[4-[[1-[2-(6-methyl-2-pyridinyl)ethyl]-4-piperidinyl]carbonyl]phenyl]methanesulfonamide dihydrochloride.

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TABLE 37
K_v11.2 channels

Channelname	K _v 11.2
Description	Voltage-gated potassium channel
Other names	erg2 ^{1,2}
Molecular information	Human: 994aa, NM_030779 (transcript variant 1) chr. 17q23.3, <i>KCNH6</i> , GeneID: 81033, PMID: 10414305 ⁶ Rat: 950aa, NM_053937, chr. 10q32.1
Associated subunits	See “Comments”
Functional assays	Voltage-clamp
Current	Not established
Conductance	Not established
Ion selectivity	Not established
Activation	Not established
Inactivation	Not established
Activators	None
Gating inhibitors	None
Blockers	Sipatrigine
Radioligands	None
Channel distribution	Brain, ² uterus, leiomyosarcoma, hippocampus, neuroblastoma, lactotrophs, ³ GH3/B6 cells, rat pituitary ⁴
Physiological functions	Not established
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	K _v 11.1, K _v 11.2, and K _v 11.3 can form heteromultimers ⁵

aa, amino acids; chr., chromosome.

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TABLE 38
K_v11.3 channels

Channel name	K _v 11.3
Description	Voltage-gated potassium channel
Other names	erg3 ¹⁻³
Molecular information	Human: 1196aa, NM_033272 (transcript variant 1), chr. 2q24.2, <i>KCNH7</i> , GeneID: 90134, PMID: 10414305 ⁹ Mouse: 1195aa, NM_133207, chr. 2 Rat: 1195aa, NM_131912, chr. 3q21
Associated subunits	See "Comments"
Functional assays	Voltage-clamp
Current	Not established
Conductance	Not established
Ion selectivity	K ²⁺
Activation	Activated at -50 mV ² (see "Comments")
Inactivation	Not established
Activators	None
Gating inhibitors	None
Blockers	Sertindole (43 nM) ² and pimozone (103 nM) ²
Radioligands	None
Channel distribution	Brain, sympathetic ganglia, CA pyramidal neurons, ⁴ lactotrophs, ⁵ GH3/B6 cells, rat pituitary ⁶
Physiological functions	Not established
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	Thyrotropin-releasing hormone reduces K _v 11.3 currents and shifts the voltage dependence of activation by 6 mV ⁷ ; K _v 11.1, K _v 11.2, and K _v 11.3 can form heteromultimers ⁸

aa, amino acids; chr., chromosome.

- Shi W, Wymore RS, Wang HS, Pan Z, Cohen IS, McKinnon D, and Dixon JE (1997) Identification of two nervous system-specific members of the erg potassium channel gene family. *J Neurosci* **17**:9423-9432.
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TABLE 39
K_v12.1 channels

Channel name	K _v 12.1
Description	Slowly activating and deactivating voltage-gated potassium channel ¹
Other names	elk1, ¹ elk3 ²
Molecular information	Human: 1107aa, NM_144633, chr. 3p24.3, <i>KCNH8</i> , GeneID: 131096, PMID: 12890647 ³ Mouse: 1102aa, NM_001031811, chr. 17 Rat: 1102aa, NM_145095, chr. 9q11 (see "Comments")
Associated subunits	Not established
Functional assays	Voltage-clamp
Current	None identified
Conductance	Not established
Ion selectivity	K ⁺
Activation	Not established
Inactivation	Not established
Activators	None
Gating inhibitors	None
Blockers	Ba ²⁺ ¹
Radioligands	None
Channel distribution	Sympathetic ganglia, testis, brain, colon, lung, uterus, pre-B cell leukemia (ESTs) ^{1,2}
Physiological functions	Not established
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	There is a light oxygen voltage (LOV) and cyclic nucleotide binding (CNB) domain in the N and C terminus, respectively.

aa, amino acids; chr., chromosome.

- Shi W, Wang HS, Pan Z, Wymore RS, Cohen IS, McKinnon D, and Dixon JE (1998) Cloning of a mammalian elk potassium channel gene and EAG mRNA distribution in rat sympathetic ganglia. *J Physiol* **511**:675-682.
- Engelard B, Neu A, Ludwig J, Roeper J, and Pongs O (1998) Cloning and functional expression of rat *ether-à-go-go*-like K⁺ channel genes. *J Physiol* **513**:647-654.
- Zou A, Lin Z, Humble M, Creech CD, Wagoner PK, Krafte D, Jegla TJ, and Wickenden AD (2003) Distribution and functional properties of human *KCNH8* (Elk1) potassium channels. *Am J Physiol Cell Physiol* **285**:C1356-C1366.

TABLE 40
K_v12.2 channels

Channel name	K _v 12.2
Description	Voltage-gated potassium channel
Other names	BEC1, ¹ Elk2 ²
Molecular information	Human: 1083aa, NM_012284, chr. 12q13, ¹ <i>KCNH3</i> , GeneID: 23416, PMID: 10455180 ¹ Mouse: 1095aa, NM_010601, chr. 15 Rat: 1087aa, NM_017108, 7q36
Associated subunits	None determined
Functional assays	Voltage-clamp
Current	Not established
Conductance	Not established
Ion selectivity	K ⁺
Activation	Not established
Inactivation	F _{ast} ^{1,2}
Activators	None
Gating inhibitors	None
Blockers	None
Radioligands	None
Channel distribution	Infant brain, lung (small cell carcinoma), eye (retinoblastoma), sciatic nerve, cortex, amygdala, hippocampus (mainly in CA1 and CA3 pyramidal cell body layers and in the granule cell layers of the dentate gyrus); in the striatal regions, including the putamen and caudate nucleus, lymphocytes, leukemias, and NG108-15 cell line ¹⁻⁵
Physiological functions	Not established
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	There is a light oxygen voltage (LOV) and cyclic nucleotide binding (CNB) domain in the N and C terminus, respectively.

aa, amino acids; chr., chromosome.

- Miyake A, Mochizuki S, Yokoi H, Kohda M, and Furuichi K (1999) New *ether-à-go-go* K⁺ channel family members localized in human telencephalon. *J Biol Chem* **274**:25018–25025.
- Engeland B, Neu A, Ludwig J, Roeper J, and Pongs O (1998) Cloning and functional expression of rat *ether-à-go-go*-like K⁺ channel genes. *J Physiol* **513**:647–654.
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- Saganich MJ, Machado E, and Rudy B (2001) Differential expression of genes encoding subthreshold-operating voltage-gated K⁺ channels in brain. *J Neurosci* **21**:4609–4624.
- Smith GA, Tsui HW, Newell EW, Jiang X, Zhu XP, Tsui FW, and Schlichter LC (2002) Functional up-regulation of HERG K⁺ channels in neoplastic hematopoietic cells. *J Biol Chem* **277**:18528–18534.

TABLE 41
K_v12.3 channels

Channel name	K _v 12.3
Description	Slowly activating voltage-gated potassium channel
Other names	BEC2, ¹ elk1 ²
Molecular information	Human: 1017aa, NM_012285, <i>KCNH4</i> , chr. 17q21.2, GeneID: 23415, PMID: 10455180 ¹ Rat: 1017aa, NM_053630, chr. 10q32.1 (see “Comments”)
Associated subunits	None
Functional assays	Voltage-clamp
Current	Not established
Conductance	Not established
Ion Selectivity	K ⁺
Activation	Threshold for activation is 90 mV ²
Inactivation	Not established
Activators	None
Gating inhibitors	None
Blockers	Ba ²⁺ ²
Radioligands	None
Channel distribution	Brain (telencephalon), ^{1,3} neuroblastoma, esophagus, oligodendroglioma, lung, primary B-cell neoplasia, cerebellum, pituitary gland ⁴
Physiological functions	Not established
Mutations and pathophysiology	Not established
Pharmacological significance	Not established
Comments	There are light oxygen voltage (LOV) and cyclic nucleotide binding (CNB) domains in the N and C terminus, respectively.

aa, amino acids; chr., chromosome.

- Miyake A, Mochizuki S, Yokoi H, Kohda M, and Furuichi K (1999) New *ether-à-go-go* K⁺ channel family members localized in human telencephalon. *J Biol Chem* **274**:25018–25025.
- Engeland B, Neu A, Ludwig J, Roeper J, and Pongs O (1998) Cloning and functional expression of rat *ether-à-go-go*-like K⁺ channel genes. *J Physiol* **513**:647–654.
- Saganich MJ, Machado E, and Rudy B (2001) Differential expression of genes encoding sub threshold-operating voltage-gated K⁺ channels in brain. *J Neurosci* **21**:4609–4624.
- Wulfsen I, Hauber HP, Schiemann D, Bauer CK, and Schwarz JR (2000) Expression of mRNA for voltage-dependent and inward-rectifying K channels in GH3/B6 cells and rat pituitary. *J Neuroendocrinol* **12**:263–272.