

**Supplement**

**Contributions of natural products to ion channel pharmacology**

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Supplementary Table 1

Channel	Toxin	Species	IC <sub>50</sub> / K <sub>d</sub>	Reference	
<b>Voltage-gated potassium channels (Kv)</b>					
Kv1.1	α-dendrotoxin	<i>Dendroaspis angusticeps</i>	20 nM	Grissmer et al 1994	
	dendrotoxin-K	<i>Dendroaspis polylepis</i>	30pM, 2 nM	Robertson and Owen 1993	
	α-KTx 2.5 (Hongotoxin)	<i>Centruroides limbatus</i>	31 pM	Koschak et al 1998	
	α-KTx3.13 (MeuKTX)	<i>Mesobuthus eupeus</i>	203 pM	Gao et al 2010	
	α-KTx 2.2 (margatoxin)	<i>Centruroides margaritatus</i>	4-10 nM	Beeton et al 2005; Bartok et al 2014	
	α-KTx 3.6 (kaliotoxin)	<i>Mesobuthus martensii</i>	41 nM	Grissmer et al 1994	
	α-KTx 3.13	<i>Mesobuthus eupeus</i>	203 pM	Gao et al 2010	
	α-KTx3.7 (OsK1)	<i>Orthochirus scrobiculosus</i>	600 pM	Mouhat et al 2005	
	BgK1	<i>Bunodosma granulifera</i>	7 nM	Alessandri-Haber et al 1999	
	ShK	<i>Stichodactyla helianthus</i>	16-28 pM	Kalman et al 1998, Beeton et al. 2005	
	Kv1.2	α-dendrotoxin	<i>Dendroaspis angusticeps</i>	17 nM	Grissmer et al 1994
α-KTx 2.2 (margatoxin)		<i>Centruroides margaritatus</i>	6-520 pM	Beeton et al. 2005; Bartok et al., 2014	
α-KTx 2.5 (Hongotoxin)		<i>Centruroides limbatus</i>	10 pM	Koschak et al 1998	
α-KTx-6.2 (Maurotoxin)		<i>Scorpio maurus palmatus</i>	100-800 pM	Kharrat et al 1996; Visan et al 2004; Chen et al 2012	
α-KTx-6.21		<i>Urodacus yaschenko</i>	160pM	Luna-Ramirez et al. 2014	
α-KTx-1.1 (Charybdotoxin)		<i>Leiurus quinquestriatus hebraeus</i>	14 nM	Grissmer et al 1994	
α-KTx2.1 (Noxiustoxin)		<i>Centruroides noxius</i>	2 nM	Grissmer et al 1994	
α-KTx3.7 (OsK1)		<i>Orthochirus scrobiculosus</i>	5.4 nM	Mouhat et al 2005	
α-KTx3.13 (MeuKTX)		<i>Mesobuthus eupeus</i>	8.9 nM	Gao et al 2010	
α-KTx 13.2 (OsK2)		<i>Orthochirus scrobiculosus</i>	97 nM	Dudina et al 2001	
α-KTx 10.1		<i>Centruroides noxius</i>	27nM	Jouirou et al. 2004	
α-KTx 3.6		<i>Mesobuthus martensii</i>	15nM	Wang et al. 2015	
BgK1		<i>Bunodosma granulifera</i>	15 nM	Alessandri-Haber et al 1999	
ShK		<i>Stichodactyla helianthus</i>	9.10 nM	Kalman et al 1998, Beeton et al 2005	
BcSTx1		<i>Bunodosoma caissarum</i>	30 pM	Orts et al. 2013	
κM-R111J		<i>Conus radiatus</i>	33 nM	Chen et al 2010	
κM-R111K		<i>Conus radiatus</i>	352 nM	Chen et al 2010	
Kv1.3		BmKTX-R11-T28-H33 (ADWX-1)	Designed peptide	2 pM	Han et al 2008
		α-KTx 23.1 (Vm24)	<i>Vaejovis mexicanus smithi</i>	3 pM	Varga et al. 2012
		OsK1-K16-D20	Designed peptide	3 pM	Mouhat et al 2006
		α-KTx3.7 (OsK1)	<i>Orthochirus scrobiculosus</i>	14 pM	Mouhat et al 2005
	HsTx1	<i>Heterometrus spinnifer</i>	12 pM	Lebrun et al 1997	
	HsTx1[R14A]	Designed peptide	11 pM	Rashid et al 2014	
	ShK	<i>Stichodactyla helianthus</i>	11 pM	Kalman et al 1998	
	α-KTx 7.1 (Pi2)	<i>Pandinus imperator</i>	50 pM	Peter et al 1998	
	ShK-186 (Dalazatide)	Designed peptide	69 pM	Beeton et al 2006	
	α-KTx 2.5 (Hongotoxin)	<i>Centruroides limbatus</i>	86 pM	Koschak et al 1998	
	α-KTx2.2 (Margatoxin)	<i>Centruroides margaritatus</i>	11-120 pM	Beeton et al. 2005; Bartok et al. 2014	
	ImKTx88	<i>Isometrus maculatus</i>	91 pM	Han et al 2011	
	α-KTx3.13 (MeuKTX)	<i>Mesobuthus eupeus</i>	171 pM	Gao et al 2010	
	α-KTx3.2 (Agitoxin-2)	<i>Leiurus quinquestriatus</i>	201 pM	Garcia et al 1994	
	α-KTx2.9 (Ce2)	<i>Centruroides elegans Thorell</i>	250 pM	Olamendi-Portugal et al 2005	
	α-KTx2.1 (Noxiustoxin)	<i>Centruroides noxius</i>	310 pM	Grissmer et al 1994	
	α-KTx3.2 (Kaliotoxin)	<i>Androctonus mauretanicus</i>	410 pM	Grissmer et al 1994; Aiyar et al 1995	
	α-KTx15.10 (Ctri9577)	<i>Chaerilus tricostatus</i>	490 pM	Xie et al 2012	
	α-KTx 7.2 (Pi3)	<i>Pandinus imperator</i>	500 pM	Peter et al 1998	
	α-KTx12.1 (Ts6; Butantoxin)	<i>Tityus serrulatus</i>	550 pM	Cerni et al 2014	
	Syn-Vm24-CDR3L	Designed protein	590 pM	Wang RE et al 2016	
	α-KTx2.8 (Ce1)	<i>Centruroides elegans Thorell</i>	700 pM	Olamendi-Portugal et al 2005	
	α-KTx-1.1 (Charybdotoxin)	<i>Leiurus quinquestriatus</i>	710 pM	Sands et al., 1989; Deutsch et al 1991; Grissmer et al 1994	
	α-KTx 6.12 (Anurotoxin)	<i>Anuroctonus phaiodactylus</i>	730 pM	Bagdáány et al. 2005	
	α-KTx11.5 (J123)	<i>Buthus martensii Karsch</i>	790 pM	Shijin et al 2008	
	α-KTx3.12 (Aam-KTX)	<i>Androctonus amoreuxi</i>	1 nM	Abbas et al. 2008	
	α-KTx2.11 (Ce4)	<i>Centruroides elegans Thorell</i>	980 pM	Olamendi-Portugal et al 2005	
	Moka-1 (Mokatoxin)	Designed peptide	1 nM	Takacz et al 2009	
	PAP-1	Derivative of psoralen from <i>Ruta graveolens</i>	2 nM	Schmitz et al 2005	
	Psora-4	Derivative of psoralen from <i>Ruta graveolens</i>	3 nM	Vennekamp et al 2004	
	QdK2	<i>Odonthobuthus doriae</i>	7.2 nM	Abdel-Mottaleb et al 2008	
	Correolide	<i>Spachea corraeae</i>	11 nM	Felix et al 1999; Koo et al 1999	
	PI1	<i>Pandinus imperator</i>	9.7 nM	Peter et al 1998	
	BgK1	<i>Bunodosma granulifera</i>	10 nM	Alessandri-Haber et al 1999	
	Plectasin	<i>Pseudoplectania nigrella</i>	2.8 uM	Xiang et al. 2015	
	Candelalides A-C	<i>Sesquicillium candelabrum</i>	1-3 uM	Singh et al 2001	
	Nalanthalide	<i>Nalanthamala</i>	3.9 uM	Abe et al 2006	
	SsTx (Spooky toxin)	<i>Scolopendra subspinipes mutilans</i>	5.26 uM	Du et al 2019	
	Luteolin	<i>Broccoli, pepper, thyme, celery</i>	65 uM	Beeton et al. 2005	
	Kv1.5	Psora-4	Derivative of psoralen from <i>Ruta graveolens</i>	7.7 nM	Vennekamp et al 2004
		Myricetin	Flavonoid from plants	-5 uM	Ou et al, 2015
	Kv1.6	ShK	<i>Stichodactyla helianthus</i>	200 pM	Kalman et al 1998
		α-KTx 2.5 (Hongotoxin)	<i>Centruroides limbatus</i>	11 pM	Koschak et al 1998
		α-KTx 3.2 (Agitoxin-2)	<i>Leiurus quinquestriatus hebraeus</i>	37pM	Garcia et al 1994
		α-KTx-1.1 (Charybdotoxin)	<i>Leiurus quinquestriatus hebraeus</i>	9 nM	Garcia et al 1994
		BcSTx1	<i>Bunodosoma caissarum</i>	1.3 nM	Orts et al. 2013
		BcSTx2	<i>Bunodosoma caissarum</i>	7.7 nM	Orts et al. 2013
α-dendrotoxin		<i>Dendroaspis angusticeps</i>	9 nM	Swanson et al. 1990	
ShK		<i>Stichodactyla helianthus</i>	165-200 pM	Kalman et al., 1998; Beeton et al. 2005	
Kv1.7	Conkunitzin-S	<i>Conus striatus</i>	439 nM	Finol-Urdaneta et al 2012	
Kv2.1	HaTx1 (Hanatoxin)	<i>Grammostola spatulata</i>	42 nM	Swartz and MacKinnon 1995	
	Jingzhaotoxin-III	<i>Chilobrachys jingzhao</i>	300 nM	Tao et al. 2013	
	Jingzhaotoxin-XI	<i>Chilobrachys jingzhao</i>	740 nM	Tao et al. 2016	
	ScTx1	<i>Stromatopelma calceata</i>	12.7 nM	Escoubas et al. 2002	
Kv2.2	ScTx1	<i>Stromatopelma calceata</i>	21.4 nM	Escoubas et al. 2002	
Kv3.1	BDS-1	<i>Anemonia sulcata</i>	220 nM	Yeung SY et al 2005	
	BDS-II	<i>Anemonia sulcata</i>	750 nM	Yeung SY et al 2005	
Kv3.2	ShK	<i>Stichodactyla helianthus</i>	5 -6nM	Beeton et al. 2005; Yan et al. 2005	
Kv3.4	BDS-1	<i>Anemonia sulcata</i>	47 nM	Diocot et al. 1998	
	BDS-II	<i>Anemonia sulcata</i>	56 nM	Diocot et al. 1998	

Kv4.1	HmTX1	<i>Heteroscodra maculata</i>	280 nM	Escoubas et al. 2002	
	JZTX-XII	<i>Chilobrachys jingzhao</i>	363nM	Yuan et al. 2007	
	HpTX2	<i>Heteropoda venatoria</i>	7.1 μM	DeSimone et al 2011	
Kv4.2	ScTx1	<i>Stromatopelma calceata</i>	1.2 nM	Escoubas et al. 2002	
	PaTx1	<i>Phrixotrichus auratus</i>	5nM	Diochot et al. 1999	
	PaTx2	<i>Phrixotrichus auratus</i>	34nM	Diochot et al. 1999	
	HpTx3	<i>Heteropoda venatoria</i>	67nM	Sanguinetti et al. 1997	
	JZTX-V	<i>Chilobrachys jingzhao</i>	604.2nM	Zeng et al. 2007	
Kv4.3	TsTXK-beta (Ts8)	<i>Tityus serrulatus</i>	652 nM	Pucca et al 2016	
	HpTX2	<i>Heteropoda venatoria</i>	2.3 μM	DeSimone et al 2011	
	PaTx1	<i>Phrixotrichus auratus</i>	28 nM	Diochot et al. 1999	
	PaTx2	<i>Phrixotrichus auratus</i>	71 nM	Diochot et al. 1999	
	SNX-482	<i>Hysteroocrates gigas</i>	3nM	Kimm and Bean 2014	
Kv7.4	SsTx (Spooky toxin)	<i>Scolopendra subspinipes mutilans</i>	2.5 μM	Luo et al 2018	
Kv11.1	BeKm-1	<i>Buthus eupeus</i>	3.3 nM	Zhang M et al 2003	
	BmKKx2	<i>Mesobuthus martensii</i>	6.7 nM	Hu et al., 2014	
	APETx1	<i>Anthopleura elegantissima</i>	87 nM	Zhang M et al 2007	
<b>Calcium- and sodium-activated potassium channels (K<sub>Ca</sub>, K<sub>Na</sub>)</b>					
K <sub>Ca</sub> 1.1	Iberitoxin	<i>Buthus Tamulus</i>	2-3 nM	Candia et al 1992; Meera et al 2000	
	α-KTx3.2 (Kaliotoxin)	<i>Androctonus mauretanicus</i>	20 nM	Crest et al. 1992	
	Natrin	<i>Naja atra</i>	34 nM	Wang et al 2005	
	α-KTx-1.1 (Charybdotoxin)	<i>Leiurus quinquestriatus hebraeus</i>	50 nM	Miller et al 1985; Anderson et al 1988	
	α-KTx 1.5 (BmTx1)	<i>Buthus martensi Karsch</i>	600 pM	Romi-Lebrun et al, 1997	
	α-KTx 1.6 (BmTx2)	<i>Buthus martensi Karsch</i>	300 pM	Romi-Lebrun et al, 1997	
	α-KTx 1.11 (Slotoxin)	<i>Centruroides noxius</i>	1.5 nM	Garcia-Valdes et al, 2001	
	α-KTx 3.5 (Kaliotoxin2)	<i>Androctonus australis</i>	135 nM	Crest et al, 1992	
	α-KTx 12.1	<i>Tityus serrulatus</i>	50 nM	Novello et al, 1999	
	α-KTx (BmP09)	<i>Buthus martensi Karsch</i>	27 nM	Yao et al, 2005	
	Paxilline	<i>Penicillium paxilli</i>	10 nM	Knaus et al 1994; Sanchez and McManus 1996	
	K <sub>Ca</sub> 2.1	Scyllatoxin	<i>Leiurus quinquestriatus hebraeus</i>	325 nM	Auguste et al 1990
		Tamapin	<i>Mesobuthus tamulus</i>	32 nM	Pedarzani et al, 2002
Apamin		<i>Apis mellifera</i>	8 nM	Hugues et al, 1982	
K <sub>Ca</sub> 2.2	Apamin	<i>Apis mellifera</i>	400 pM	Hugues et al, 1982	
	Tamapin	<i>Mesobuthus tamulus</i>	24 pM	Pedarzani et al, 2002	
	Scyllatoxin	<i>Leiurus quinquestriatus hebraeus</i>	200 pM	Auguste et al 1990; Shakkottai et al 2001	
	Lei-Dab7	<i>Synthetic derivative of scyllatoxin</i>	3-6 nM	Shakkottai et al 2001	
	PO5	<i>Androctonus mauretanicus mauretanicus</i>	22 nM	Shakkottai et al 2001	
	TsK	<i>Tityus serrulatus</i>	80 nM	Shakkottai et al 2001	
	Pi1-NH2	<i>Pandinus imperator</i>	100 nM	Shakkottai et al 2001	
K <sub>Ca</sub> 2.3	Scyllatoxin	<i>Leiurus quinquestriatus hebraeus</i>	1-2 nM	Shakkottai et al 2001	
	Tamapin	<i>Mesobuthus tamulus</i>	1.7 nM	Pedarzani et al, 2002	
	PO5	<i>Androctonus mauretanicus mauretanicus</i>	25 nM	Shakkottai et al 2001	
	TsK	<i>Tityus serrulatus</i>	197 nM	Shakkottai et al 2001	
	Pi1-OH	<i>Pandinus imperator</i>	300 nM	Shakkottai et al 2001	
	Pi1-NH <sub>2</sub>	<i>Pandinus imperator</i>	250 nM	Shakkottai et al 2001	
K <sub>Ca</sub> 3.1	α-KTx-6.2 (Maurotxin)	<i>Scorpio maurus palmatus</i>	1-2 nM	Castle et al, 2003	
	α-KTx3.7 (OsK1)	<i>Orthochirus scrobiculosus</i>	225 nM	Mouhat et al 2005	
	α-KTx-1.1 (Charybdotoxin)	<i>Leiurus quinquestriatus hebraeus</i>	3-5 nM	Ghanshani et al, 2000; Rauer et al, 2000	
	ShK	<i>Stichodactyla helianthus</i>	28-30 nM	Rauer et al, 2000; Beeton et al. 2005	
	BgK1	<i>Bunodosma granulifera</i>	172 nM	Cotton et al, 1997	
<b>Inward rectifier potassium channels (K<sub>IR</sub>)</b>					
K <sub>IR</sub> 1.1	Delta-dendrotoxin	<i>Dendroapsis angusticeps</i>	150 nM	Imredy, Chen, and MacKinnon 1998	
	Tertiapin (TPN <sub>O</sub> )	<i>Apis mellifera</i>	1-2 nM	Jin and Lu 1998; Ramu et al 2008	
	α-KTx1.2 (Lq2)	<i>Leiurus quinquestriatus</i>	410nM	Lu and MacKinnon 1997	
K <sub>IR</sub> 3.1	Tertiapin	<i>Apis mellifera</i>	8 nM	Jin and Lu 1998	
K <sub>IR</sub> 6.2	SpTx-1	<i>Scolopendra polymorpha</i>	15 nM	Ramu et al 2018	
	SsdTx1-3	<i>Scolopendra subspinipes dehaani</i>		Ramu et al 2019	
	SsTx	<i>Scolopendra subspinipes mutilans</i>		Ramu et al 2019	
<b>Two pore potassium channels (K<sub>2P</sub>)</b>					
K <sub>2P</sub> 3.1	Anandamide	<i>Endocannabinoid from porcine brain</i>	700 nM	Maingret et al 2001	
<b>Voltage-gated Sodium channels (Nav)</b>					
Nav1.1	Tetrodotoxin	<i>Takifugu rupripes</i>	4.1 nM	Tsukamoto et al 2017	
	Chiriquitoxin	<i>Atelopus chiriquirensis</i>	26 nM	Tsukamoto et al 2017	
	ATX-II	<i>Anemonia sulcata</i>	6 nM	Chahine et al 1996; Oliveira et al 2004	
	BcII	<i>Bunodosma caissarum</i>	300 nM	Oliverira et al 2004	
	AFT-II	<i>Anthopleura fuscoviridis</i>	390 nM	Oliverira et al 2004	
	μO <sub>5</sub> -conotoxin GVIIJ	<i>Conus geographicus</i>	11 nM	Gajewiak et al 2014	
	Cangitoxin-II; CGTX-II	<i>Bunodosoma cangicum</i>	165 nM	Zaharenko et al, 2012	
	μ-Conotoxin BullIA	<i>Conus bullatus</i>	350 nM	Wilson et al, 2011	
	MeuNaTxα-12	<i>Mesobuthus eupeus</i>	910 nM	Zhu et al, 2012	
	MeuNaTxα-13	<i>Mesobuthus eupeus</i>	2.5 μM	Zhu et al, 2012	
	SmIIIA	<i>Conus stercusmuscarum</i>	3.8 μM	Gilchrist et al 2014	
Nav1.2	Phrixotoxin 3	<i>Phrixotrichus auratus</i>	600 pM	Bosmans et al 2006	

	Lqh-2	<i>Leiurus quinquestriatus hebraeus</i>	1, 8 nM	Chen et al 2002
	LqTx	<i>Leiurus quinquestriatus quinquestriatus</i>	1.7 nM	Rogers JC et al 1996
	Tetrodotoxin	<i>Takifugu rupripes</i>	7.8 nM	Tsukamoto et al 2017
	Chiriquitoxin	<i>Atelopus chiquensis</i>	27 nM	Tsukamoto et al 2017
	PnTx1	<i>Phoneutria nigriventer</i>	34 nM	Silva et al 2012
	ProTx-III	<i>Thrixopelma pruriens</i>	300 nM	Cardoso et al, 2015
	Hainantoxin-IV	<i>Ornithoconus hainana</i>	36 nM	Liu et al 2003
	ATX-II	<i>Anemonia sulcata</i>	41 nM	Oliveira et al 2004
	Huwentoxin IV	<i>Ornithoconus huwena</i>	150 nM	Minassian et al 2013, Xiao et al 2008
	JZTx-14	<i>Chilobrachys jingzhao</i>	194 nM	Zhang J et al 2018
	GrTx1	<i>Grammostola rosea</i>	230 nM	Redaelli et al, 2010
	GVIIJ <sub>SSG</sub>	<i>Conus geographus</i>	11 nM	Gajewiak et al, 2014
	μ-conotoxin TIIIA	<i>Conus tulipa</i>	45 nM	Wilson et al, 2011
	μ-conotoxin SIIIA	<i>Conus striatus</i>	50 nM	Wilson et al, 2011
	μ-conotoxin KIIIA	<i>Conus kinoshitai</i>	3 nM	Wilson et al, 2011
	μ-conotoxin MIIIA	<i>Conus magus</i>	450 nM	Wilson et al, 2011
	μ-conotoxin BuIIIA	<i>Conus bullatus</i>	12 nM	Wilson et al, 2011
	SmIIIA	<i>Conus stercusmuscarum</i>	1.3 μM	Gilchrist et al 2014
Nav1.3	Tetrodotoxin	<i>Takifugu rupripes</i>	2 nM	Tsukamoto et al 2017
	Chiriquitoxin	<i>Atelopus chiquensis</i>	14 nM	Tsukamoto et al 2017
	Huwentoxin IV	<i>Ornithoconus huwena</i>	338 nM	Xiao et al 2008
	AFT-II	<i>Anthopleura fuscoviridis</i>	460 nM	Oliveira et al, 2004
	ATX-II	<i>Anemonia sulcata</i>	759 nM	Oliveira et al, 2004
	Bc-III	<i>Bunodosoma caissarum</i>	1.5 μM	Oliveira et al, 2004
	ProTx-III	<i>Thrixopelma pruriens</i>	900 nM	Cardoso et al, 2015
	Hainantoxin-IV	<i>Ornithoconus hainana</i>	375 nM	Liu et al, 2003
	GrTx1	<i>Grammostola rosea spider</i>	770 nM	Redaelli et al, 2010
	GVIIJ <sub>SSG</sub>	<i>Conus geographus</i>	15 nM	Gajewiak et al, 2014
	μ-conotoxin BuIIIA	<i>Conus bullatus</i>	350 nM	Wilson et al, 2011
	JZTx-14	<i>Chilobrachys jingzhao</i>	426 nM	Zhang J et al 2018
	SmIIIA	<i>Conus stercusmuscarum</i>	35 μM	Gilchrist et al 2014
Nav1.4	Tetrodotoxin	<i>Takifugu rupripes</i>	4.5 nM	Tsukamoto et al 2017
	Chiriquitoxin	<i>Atelopus chiquensis</i>	50 nM	Tsukamoto et al 2017
	Saxitoxin	<i>Marine dinoflagellates, freshwater cyanobacteria</i>	2.8 nM	Walker JR et al 2012
	SmIIIA	<i>Conus stercusmuscarum</i>	220 nM	Gilchrist et al 2014
	μO-Conotoxins MrVIA	<i>Conus marmoreus</i>	250 nM	Leipold et al 2007
	AFT-II	<i>Anthopleura fuscoviridis</i>	31 nM	Oliveira et al, 2004
	ATX-II	<i>Anemonia sulcata</i>	109 nM	Oliveira et al, 2004
	Bc-III	<i>Bunodosoma caissarum</i>	821 nM	Oliveira et al, 2004
	MrVIB (μO-Conotoxin)	<i>Conus marmoreus</i>	222 nM	Zorn et al, 2006
	MfVIA (μO-Conotoxin)	<i>Conus magnificus</i>	81 nM	Vetter et al, 2012
	GrTx1	<i>Grammostola rosea</i>	1.3 μM	Redaelli et al, 2010
	GVIIJ <sub>SSG</sub>	<i>Conus geographus</i>	47 nM	Gajewiak et al, 2014
	μ-conotoxin TIIIA	<i>Conus tulipa</i>	5 nM	Wilson et al, 2011
	μ-conotoxin SIIIA	<i>Conus striatus</i>	130 nM	Wilson et al, 2011
	μ-conotoxin MIIIA	<i>Conus magus</i>	330 nM	Wilson et al, 2011
	μ-conotoxin BuIIIA	<i>Conus bullatus</i>	12 nM	Wilson et al, 2011
	JZTx-14	<i>Chilobrachys jingzhao</i>	290 nM	Zhang J et al 2018
	Huwentoxin IV	<i>Ornithoconus huwena</i>	400 nM	Xiao et al 2008
Nav1.5	Tetrodotoxin	<i>Takifugu rupripes</i>	2 μM	Tsukamoto et al 2017
	Chiriquitoxin	<i>Atelopus chiquensis</i>	1.9 μM	Tsukamoto et al 2017
	ProTx-II	<i>Thrixopelma pruriens</i>	79 nM	Middleton et al, 2002
	ATX-II	<i>Anemonia sulcata</i>	49 nM	Oliveira et al, 2004
	AFT-II	<i>Anthopleura fuscoviridis</i>	62.5 nM	Oliveira et al, 2004
	Bc-III	<i>Bunodosoma caissarum</i>	307 nM	Oliveira et al, 2004
	CGTX-II	<i>Bunodosoma cangicum</i>	50 nM	Zaharenko et al, 2012
	JZTx-14	<i>Chilobrachys jingzhao</i>	478 nM	Zhang J et al 2018
Nav1.6	Tetrodotoxin	<i>Takifugu rupripes</i>	3.8 nM	Tsukamoto et al 2017
	Chiriquitoxin	<i>Atelopus chiquensis</i>	43 nM	Tsukamoto et al 2017
	ATX-II	<i>Anemonia sulcata</i>	180 nM	Oliveira et al, 2004
	AFT-II	<i>Anthopleura fuscoviridis</i>	300 nM	Oliveira et al, 2004
	Bc-III	<i>Bunodosoma caissarum</i>	900 nM	Oliveira et al, 2004
	ProTx-II	<i>Thrixopelma pruriens</i>	47 nM	Maertens et al, 2006
	CGTX-II	<i>Bunodosoma cangicum</i>	50 nM	Zaharenko et al, 2012
	ProTx-III	<i>Thrixopelma pruriens</i>	290 nM	Cardoso et al, 2015
	GrTx1	<i>Grammostola rosea</i>	630 nM	Redaelli et al, 2010
	JZTx-14	<i>Chilobrachys jingzhao</i>	158 nM	Zhang J et al 2018
Nav1.7	ProTx II	<i>Thrixopelma pruriens</i>	300-400 pM	Schmalhofer et al, 2008
	Tetrodotoxin	<i>Takifugu rupripes</i>	5.5 nM	Tsukamoto et al 2017
	Huwentoxin IV	<i>Ornithoconus huwena</i>	26 nM	Xiao et al 2008
	JZTx-14	<i>Chilobrachys jingzhao</i>	189 nM	Zhang J et al 2018

	ProTx-I	<i>Thrixopelma pruriens</i>	51 nM	Middleton et al, 2002
	ProTx-III	<i>Thrixopelma pruriens</i>	2.1 nM	Cardoso et al, 2015
	Lqh-2	<i>Leiurus quinquestriatus hebraeus</i>	32 nM	Chen et al, 2002
	Lqh-3	<i>Leiurus quinquestriatus hebraeus</i>	13 nM	Chen et al, 2002
	GpTx-1	<i>Grammostola porteri</i>	10 nM	Murray et al, 2015
	μ-SLPTX-Ssm6a	<i>Scolopendra subspinipes mutilans</i>	25 nM	Yang et al, 2013
	Hainantoxin-IV	<i>Ornithoconus hainana</i>	21 nM	Liu et al, 2003
	μ-TRTx-Pn3a	<i>Pamphobeteus nigricolor</i>	900 pM	Deuis et al, 2017
	GrTx1	<i>Grammostola rosea</i>	370 nM	Redaelli et al, 2010
	GVIIJ <sub>SSG</sub>	<i>Conus geographus</i>	41 nM	Gajewiak et al, 2014
	Chiriquitoxin	<i>Atelopus chinquensis</i>	471 nM	Tsukamoto et al 2017
	Saxitoxin	<i>Marine dinoflagellates, fresh water cyanobacteria</i>	702 nM	Walker JR et al 2012
Nav1.8	Tetrodotoxin	<i>Takifugu rupripes</i>	1.3 μM	Tsukamoto et al 2017
	ProTx-I	<i>Thrixopelma pruriens</i>	27 nM	Middleton et al, 2002
	MrVIB (μO-Conotoxin)	<i>Conus marmoreus</i>	102 nM	Ekberg et al, 2006
	MfVIA (μO-Conotoxin)	<i>Conus magnificus</i>	529 nM	Vetter et al, 2012
	HSTX-I	<i>Haemadipsa sylvestris</i>	2.4 μM	Wang G et al, 2018
	JZTx-14	<i>Chilobrachys jingzhao</i>	824 nM	Zhang J et al 2018
Nav1.9	Tetrodotoxin	<i>Takifugu rupripes</i>	59.6 μM	Tsukamoto et al 2017
	HSTX-I	<i>Haemadipsa sylvestris</i>	3.3 μM	Wang G et al, 2018
<b>Voltage-gated calcium channels (Cav)</b>				
Cav1.1- Cav1.4	Calcicludine	<i>Dendroaspis augusticeps</i>	90 nM	Schweitz H et al., 1994; Schroeder, Lewis, Adams 2013
	Calciseptine	<i>Dendroaspis poluepis polyepis</i>	15 nM	de Weille et al, 1991
	Phα1β (PnTx3-6)	<i>Phoneutria nigriventer</i>	122 nM	Vieira et al 2005
	DW13.3	<i>Filistata hibernalis</i>	27 nM	Schroeder, Lewis, Adams 2013
Cav2.1 (P/Q)	ω-Agatoxin IVA	<i>Agelenopsis aperta</i>	2 nM	Adams ME et al 1990; Adams ME 2004
	ω-Agatoxin IVB	<i>Agelenopsis aperta</i>	15 nM	Adams ME 2004
	ω-conotoxin GVIA	<i>Conus geographicus</i>	1 μM	Lewis RS et al 2000
	ω-Conotoxin MVIIA (Prialt)	<i>Conus magus</i>	156 nM	Favreau et al 2001
	ω-Conotoxin MVIIIC	<i>Conus magus</i>	600 pM	Lewis RS et al 2000
	ω-Conotoxin CVIA	<i>Conus catus</i>	850 nM	Lewis RS et al 2000; Ramirez et al 2017
	ω-Conotoxin CnVIA	<i>Conus consors</i>	179 nM	Favreau et al 2001; Ramirez et al 2017
	Phα1β (PnTx3-6)	<i>Phoneutria nigriventer</i>	263 nM	Vieira LB et al 2005
	ω-Phonetoxin IIA	<i>Phoneutria nigriventer</i>	7-8 nM	Cassola AC et al 1998; Dos Santos et al 2002
	ω-grammotoxin SIA	<i>Grammostola rosea</i>	50nM	Lampe et al, 1993; McDonough et al, 1997
	DW13.3	<i>Filistata hibernalis</i>	4.3 nM	Schroeder, Lewis, Adams 2013
Cav2.2 (N)	ω-conotoxin GVIA	<i>Conus geographicus</i>	2 pM	Favreau et al 2001
	ω-conotoxin GVIIA	<i>Conus geographicus</i>	22.9 nM	Miljanich et al US Patent 5,424,218 A, 4 November 1993; Miljanich G 2004; Ramirez et al 2017
	ω-Conotoxin MVIIA (Prialt)	<i>Conus magus</i>	1-11 nM	Lewis R et al 2000; Miljanich 2004; Ramirez et al 2017
	ω-Conotoxin MVIIIB	<i>Conus magus</i>	101 pM	Ramirez et al 2017
	ω-Conotoxin MVIIIC	<i>Conus magus</i>	7 nM	Lewis RJ et al 2000
	ω-Conotoxin SVIB	<i>Conus striatus</i>	1.09 nM	Ramirez et al 2017
	ω-Conotoxin SO3	<i>Conus striatus</i>	160 nM	Wang F et al 2016; Ramirez et al 2017
	ω-Conotoxin CVIA	<i>Conus catus</i>	560 pM	Lewis R et al 2000; Ramirez et al 2017
	ω-conotoxin CVID	<i>Conus catus</i>	2-3 nM	Lewis R et al 2000
	ω-conotoxin FVIA	<i>Conus fulmen</i>	11.5 nM	Lee S et al 2010; Ramirez et al 2017
	ω-conotoxin RVIA	<i>Conus radiatus</i>	229 nM	Ramirez et al 2017
	ω-Conotoxin CnVIA	<i>Conus consors</i>	2-4 pM	Favreau et al 2001; Ramirez et al 2017
	ω-Conotoxin TVIA	<i>Conus tulipa</i>	228 pM	Ramirez et al 2017
	ω-Phonetoxin IIA	<i>Phoneutria nigriventer</i>	0.2 nM	Dos Santos et al 2002
	DW13.3	<i>Filistata hibernalis</i>	14.4 nM	Schroeder, Lewis, Adams 2013
	ω-agatoxin IIA	<i>Agelenopsis aperta</i>	10 nM	Bindokas et al, 1989; Adams ME et al, 1990
	ω-agatoxin IIIA	<i>Agelenopsis aperta</i>	1.4 nM	Ertel et al, 1994; Olivera et al, 1994
	ω-agatoxin IIIB	<i>Agelenopsis aperta</i>	140 nM	Ertel et al, 1994; Yan L and Adams ME 2000
	ω-agatoxin IIID	<i>Agelenopsis aperta</i>	35 nM	Ertel et al, 1994
	Phα1β (PnTx3-6)	<i>Phoneutria nigriventer</i>	136 nM	Vieira LB et al 2005
Ca <sub>v</sub> 2.3 (R)	SNX-482	<i>Hysteroocrates gigas</i>	15-30 nM	Newcomb R et al, 1998
	DW13.3	<i>Filistata hibernalis</i>	96.4 nM	Schroeder, Lewis, Adams 2013
	Phα1β (PnTx3-6)	<i>Phoneutria nigriventer</i>	607 nM	Vieira LB et al 2005
Ca <sub>v</sub> 3.1 (T)	ProTxI	<i>Thrixopelma pruriens</i>	200 nM	Ohkubo T et al, 2010; Bladen C et al 2014
	Kurtoxin	<i>Parabuthus transvaalicus</i>	15-50nM	Chuang RS et al, 1998; Sidach and Mintz, 2002
Ca <sub>v</sub> 3.2	ProTxII	<i>Thrixopelma pruriens</i>	1-10 uM	Bladen C et al 2014
	Kurtoxin	<i>Parabuthus transvaalicus</i>	25-50nM	Chuang RS et al, 1998; Sidach and Mintz, 2002

## Supplementary Table 2

Channel	Disease or Therapeutic area	References
<b>Voltage-gated potassium channels (K<sub>v</sub>)</b>		
K <sub>v</sub> 1.1	Episodic ataxia type 1 and myokymia; Acquired neuromyotonia	Adelman et al 1995; Browne et al 1994; Chen et al 2007; Zuberi et al. 1989; Irani et al 2010; Kleopa et al 2006.
K <sub>v</sub> 1.2	Episodic ataxia and pharmacoresponsive epilepsy Epileptic encephalopathy; Ataxia and myoclonic epilepsy	Corbett et al 2016; Syrbe et al 2015; Pena and Coimbra 2015.
K <sub>v</sub> 1.3	Therapeutic target for autoimmune diseases Polymorphism associated with autoimmune pancreatic diabetes	Cahalan and Chandy, 2009; Chi et al., 2012, Tschrirter et al 2006; Ota et al 2011
K <sub>v</sub> 1.5	Atrial fibrillation	Olson et al 2006
K <sub>v</sub> 1.6	Acquired neuromyotonia	Antozzi et al 2005
K <sub>v</sub> 1.7	Glucose-dependent Insulin secretagogue for diabetes mellitus	Finol-Urdaneta RK et al 2012
K <sub>v</sub> 2.1	Non-syndromic intellectual disability; Epileptic encephalopathy; Infantile epilepsy	Latypova et al 2017; Thiffault et al 2015; Torkamani et al 2014; Saitu et al 2015
K <sub>v</sub> 2.2	Non-familial Brugada syndrome	Juang et al 2014
K <sub>v</sub> 3.1	Myoclonus epilepsy and ataxia; Intellectual disability	Muona et al 2015; Oliver et al 2017; Poirier et al 2017
K <sub>v</sub> 3.3	Spinocerebellar ataxia 13	Waters et al 2006
K <sub>v</sub> 4.2	Temporal lobe epilepsy	Singh B et al 2006
K <sub>v</sub> 4.3	Early onset cerebellar ataxia, intellectual disability, oral apraxia and epilepsy; Lone atrial fibrillation	Smets K et al 2015; Olesen et al 2013
K <sub>v</sub> 7.1	Long QT syndrome and epilepsy; Jervell and Lange-Nielsen syndrome; Romano-Ward syndrome; Atrial fibrillation; short QT syndrome; Atrioventricular block	Chouabe et al 1997; Neyroud et al 1997; Wang Q et al 1996; Chen YH et al 2003; Hong K et al 2005a; Yang Y et al 2007
K <sub>v</sub> 7.2	Vitamin B6-responsive epilepsy; Drug-resistant pediatric epilepsies; Early-onset epileptic encephalopathy; Benign familial neonatal epilepsy; Myokymia and neonatal epilepsy	Klotz KA et al 2017; Micelli et al 2013; Micelli et al 2015; Orhan et al 2014; Biervert et al 1998; Singh NA et al 1998; Singh NA et al 2003; Dedek K et al 2001
K <sub>v</sub> 7.3	Benign familial neonatal epilepsy	Micelli et al 2015;
K <sub>v</sub> 7.4	Nonsyndromic dominant deafness	Kubisch et al 1999
K <sub>v</sub> 8.2	Epilepsy susceptibility	Jorge et al 2011
K <sub>v</sub> 10.1	Zimmermann-Laband syndrome; Temple-Baraitser syndrome	Simons et al 2015; Fukai et al 2016
K <sub>v</sub> 11.1	Long QT syndrome, syncope, epilepsy; Drug-induced long QT syndrome; Atrial fibrillation and short QT syndrome	Curran et al 1995; Cubeddu et al 2016 ; Hong K et al 2005b
<b>Calcium- and sodium-activated potassium channels (K<sub>Ca</sub>, K<sub>Na</sub>)</b>		
K <sub>Ca</sub> 1.1	Generalized epilepsy and paroxysmal dyskinesia Channel openers may have applications in stroke, epilepsy, bladder over-reactivity, asthma, hypertension, gastric hypermotility and psychoses	Du W et al. 2005; Zhang ZB et al 2015 Gribkoff VK et al 2001
K <sub>Ca</sub> 2.1	Potential target for treatment of ataxia, epilepsy, memory disorders, pain and possibly schizophrenia and Parkinson's disease	Lam J et al 2013
K <sub>Ca</sub> 2.2	K <sub>Ca</sub> 2 activators have potential for treatment of alcohol dependence, stroke, and cerebellar ataxia, and as anti-convulsants K <sub>Ca</sub> 2.x inhibitors as memory enhancers for Alzheimer's disease	Hopf YT et al 2011, Allen D et al 2011; Wulff et al 2007, Alvina K et al 2010 Wulff et al 2007
K <sub>Ca</sub> 2.3	Associated with lone atrial fibrillation. Negative K <sub>Ca</sub> 2 channel gating modulators have been proposed for the treatment of atrial fibrillation. De novo mutation associated with autosomal dominant idiopathic non-cirrhotic portal hypertension. Gain-of-Function Mutations cause Zimmermann-Laband Syndrome	Ellinor PT et al, 2010 Koot BG et al 2016 Bauer CK et al 2019
K <sub>Ca</sub> 3.1	Dehydrated hereditary stomatocytosis 2 Phase-3 clinical trials for ICA-17043 (senicapoc) were stopped in 2007 apparently due to lack of efficacy in reducing the incidence of sickling crisis K <sub>Ca</sub> 3.1 inhibitors proposed for treatment of inflammatory bowel disease, vascular restenosis, stroke, Alzheimer's disease, multiple sclerosis, renal fibrosis, lung fibrosis, cardiac fibrosis	Andolfo let al 2015 Ataga KI et al. 2011 Feske S, Wulff, Skolnik 2015
K <sub>Na</sub> 1.1	Early infantile epileptic encephalopathy type 14 Ohtahara syndrome Epilepsy, nocturnal frontal lobe, 5	Barcia G et al 2012 Martin HC et al 2014 Heron SE et al 2012; Vanderver A et al 2014
<b>Inward rectifier potassium channels (K<sub>IR</sub>)</b>		
K <sub>IR</sub> 1.1	Bartter syndrome type 2	Simon DB et al 1996
K <sub>IR</sub> 2.1	Anderson Tawil syndrome (Long QT syndrome type 7) Familial Atrial fibrillation type 9 Short QT syndrome type 3	Plaster NM et al 2001 Xia M et al 2005 Priori SG et al 2005
K <sub>IR</sub> 3.4	Familial hyperaldosteronism type 3 Congenital long QT syndrome	Scholl UI et al 2009 ; Mulatero et al 2013 Kokunai Y et al 2014
K <sub>IR</sub> 4.1	Neurosensory nonsyndromic recessive deafness 4 EAST/SeSAME syndrome Hypokalemic periodic paralysis and prominent U waves Type 13 long QT syndrome	Yang T et al, 2009 Scholl UI et al 2009; Bockenhauer D et al 2009 Kokunai Y et al 2014 Wang F et al 2013
K <sub>IR</sub> 6.1	Brugada Syndrome 1 Cantu syndrome (Hypertrichotic osteochondrodysplasia)	Barajas-Martínez H et al 2012 Brownstein CA et al 2013; Cooper PE et al 2014
K <sub>IR</sub> 6.2	Permanent neonatal diabetes mellitus Transient neonatal diabetes mellitus type 3 Familial hyper-insulinemic hypoglycemia type 2	Gloyn et al 2004 Colombo C et al 2005 Nestorowicz A et al 1997
K <sub>IR</sub> 7.1	Leber congenital amaurosis 16 Snowflake vitreoretinal degeneration	Sergouniotis PI et al 2011 Hejtmancik JF et al 2008
<b>Two pore potassium channels (K<sub>2P</sub>)</b>		
K <sub>2P</sub> 17.1	Severe progressive cardiac conduction disorder	Friedrich C et al. 2014
K <sub>2P</sub> 18.1	Migraine, with or without aura, susceptibility to, 13	Lafrenière RG et al 2010
<b>Voltage-gated sodium channels (Nav)</b>		
Nav1.1	Dravet syndrome Generalized epilepsy with febrile seizures-plus, type 2 Migraine, familial hemiplegic, 3 Myoclonic-astatic epilepsy	Wallace RH et al. 2003 Escayg A et al 2000; Wallace RH et al. 2003 Dichgans M et al 2005 Ebach K et al 2005

Nav1.2	Dravet syndrome	Shi X et al 2009
	Early infantile epileptic encephalopathy, type 11	Kamiya, K et al 2004
	Ohtahara syndrome	Touma, M., et al 2013
	Benign familial infantile epilepsy, 3	Heron SE et al 2002
Nav1.3	Cryptogenic pediatric partial epilepsy	Estacion M et al 2010
Nav1.4	Hyperkalemic Periodic Paralysis	Ptacek L et al 1991
	Hypokalemic periodic paralysis, type 2	Cannon SC 2002
	Congenital myasthenic syndrome, type 16	Tsujino A et al 2003
	Potassium aggravated myotonia	Cannon SC 2002
	Normokalemic periodic paralysis	Vicart S et al 2004
	Paramyotonia Congenita of Von Eulenburg	Ptácek LJ et al 1992
Nav1.5	Familial atrial fibrillation, type 10	Laitinen-Forsblom, P. J et al 2006
	Atrial standstill	Makita, N et al 2005;
	Brugada syndrome 1	Chen Q et al 1998
	Dilated cardiomyopathy 1E	McNair WP et al. 2004
	Long QT syndrome 3	Wang Q et al 1995
Nav1.6	Early infantile epileptic encephalopathy, 13	Veeramah KR et al 2012
Nav1.7	Acromesomelic dysplasia and painful neuropathy	Hoeijmakers JG et al 2012
	Dravet syndrome	Singh, N. A et al 2009
	Primary erythromelalgia	Dib-Hajj SD et al 2010
	Generalized epilepsy with febrile seizures-plus, type 7	Singh, N. A et al 2009
	Hereditary sensory and autonomic neuropathy, type 2	Yuan J et al 2013
	Channelopathy-associated congenital insensitivity to pain	Cox JJ et al 2006
	Paroxysmal Extreme Pain Disorder	Fertleman CR et al 2006
Nav1.8	Episodic pain familial 2	Faber CG et al 2012
Nav1.9	Episodic pain familial 3	Huang J et al 2014
	Hereditary sensory and autonomic neuropathy, type VII	Leipold E et al 2013
	Sodium channelopathy-related small fiber neuropathy	Han C et al 2015
<b>Voltage-gated calcium channels (Cav)</b>		
Cav1.1	Hypokalemic periodic paralysis, type 1	Ptácek LJ et al 1994
	Malignant hyperthermia, 5	Monnier N et al 1997
	Normokalemic periodic paralysis	Fan C et al 2013
Cav1.2	Brugada syndrome 3	Antzelevitch C et al 2007
	Early repolarization syndrome	Burashnikov E et al 2010
	Idiopathic ventricular fibrillation	Fukuyama M et al 2013
	Non syndromic autosomal dominant long QT-syndrome	Boczek NJ et al 2013
	Timothy syndrome	Splawski I et al 2004
Cav1.3	Aldosterone-producing adenoma	Scholl UI et al 2013; Azizan EA et al 2013
	Autism	O'Roak BJ et al 2012
	Congenital hyperaldosteronism	Scholl UI et al 2013
	Primary aldosteronism, seizures, and neurologic abnormalities	Scholl UI et al 2013
	Sinoatrial node dysfunction and deafness	Baig SM, et al 2011
Cav1.4	Aland Island eye disease	Jalkanen R et al 2007
	Cone-rod dystrophy, X-linked, 3	Jalkanen R et al 2006
	Night blindness, congenital stationary, type 2	Strom TM et al 1998; Bech-Hansen NT et al 1998
Cav2.1	Alternating hemiplegia of childhood 1	de Vries B et al 2008
	Benign paroxysmal torticollis of infancy	Giffin NJ et al 2004
	Episodic ataxia, type 2	Ophoff RA et al 1996
	Migraine, familial hemiplegic, 1	Ophoff RA et al 1996
	Spinocerebellar ataxia 6	Ishikawa K et al 1999
Cav3.3	Absence epilepsy	Klassen T et al 2011

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