

Table S1. Ion channel genes involved in this study

Gene symbol	Gene title	Channel type
<i>ANO1</i>	anoctamin 1, Calcium activated chloride channel	Calcium activated chloride channel
<i>ANO2</i>	anoctamin 2	Calcium activated chloride channel
<i>CACNA1A</i>	calcium channel, voltage-dependent, P/Q type, alpha 1A subunit	Voltage-gated calcium channels
<i>CACNA1B</i>	calcium channel, voltage-dependent, N type, alpha 1B subunit	Voltage-gated calcium channels
<i>CACNA1C</i>	calcium channel, voltage-dependent, L type, alpha 1C subunit	Voltage-gated calcium channels
<i>CACNA1D</i>	calcium channel, voltage-dependent, L type, alpha 1D subunit	Voltage-gated calcium channels
<i>CACNA1E</i>	calcium channel, voltage-dependent, R type, alpha 1E subunit	Voltage-gated calcium channels
<i>CACNA1F</i>	calcium channel, voltage-dependent, L type, alpha 1F subunit	Voltage-gated calcium channels
<i>CACNA1G</i>	calcium channel, voltage-dependent, T type, alpha 1G subunit	Voltage-gated calcium channels
<i>CACNA1H</i>	calcium channel, voltage-dependent, T type, alpha 1H subunit	Voltage-gated calcium channels
<i>CACNA1I</i>	calcium channel, voltage-dependent, T type, alpha 1I subunit	Voltage-gated calcium channels
<i>CACNA1S</i>	calcium channel, voltage-dependent, L type, alpha 1S subunit	Voltage-gated calcium channels
<i>CACNA2D1</i>	calcium channel, voltage-dependent, alpha 2/delta subunit 1	Voltage-gated calcium channels
<i>CACNA2D2</i>	calcium channel, voltage-dependent, alpha 2/delta subunit 2	Voltage-gated calcium channels
<i>CACNA2D3</i>	calcium channel, voltage-dependent, alpha 2/delta subunit 3	Voltage-gated calcium channels
<i>CACNA2D4</i>	calcium channel, voltage-dependent, alpha 2/delta subunit 4	Voltage-gated calcium channels
<i>CACNB1</i>	calcium channel, voltage-dependent, beta 1 subunit	Voltage-gated calcium channels
<i>CACNB2</i>	calcium channel, voltage-dependent, beta 2 subunit	Voltage-gated calcium channels
<i>CACNB3</i>	calcium channel, voltage-dependent, beta 3 subunit	Voltage-gated calcium channels
<i>CACNB4</i>	calcium channel, voltage-dependent, beta 4 subunit	Voltage-gated calcium channels
<i>CACNG1</i>	calcium channel, voltage-dependent, gamma subunit 1	Voltage-gated calcium channels
<i>CACNG2</i>	calcium channel, voltage-dependent, gamma subunit 2	Voltage-gated calcium channels
<i>CACNG3</i>	calcium channel, voltage-dependent, gamma subunit 3	Voltage-gated calcium channels
<i>CACNG4</i>	calcium channel, voltage-dependent, gamma subunit 4	Voltage-gated calcium channels
<i>CACNG5</i>	calcium channel, voltage-dependent, gamma subunit 5	Voltage-gated calcium channels
<i>CACNG6</i>	calcium channel, voltage-dependent, gamma subunit 6	Voltage-gated calcium channels
<i>CACNG7</i>	calcium channel, voltage-dependent, gamma subunit 7	Voltage-gated calcium channels
<i>CACNG8</i>	calcium channel, voltage-dependent, gamma subunit 8	Voltage-gated calcium channels
<i>CATSPER1</i>	cation channel, sperm associated 1	CatSper and Two-Pore channels
<i>CATSPER2</i>	cation channel, sperm associated 2	CatSper and Two-Pore channels
<i>CATSPER3</i>	cation channel, sperm associated 3	CatSper and Two-Pore channels
<i>CATSPER4</i>	cation channel, sperm associated 4	CatSper and Two-Pore channels
<i>CATSPERB</i>	catsper channel auxiliary subunit beta	CatSper and Two-Pore channels
<i>CATSPERD</i>	catsper channel auxiliary subunit delta	CatSper and Two-Pore channels
<i>CATSPERG</i>	catsper channel auxiliary subunit gamma	CatSper and Two-Pore channels
<i>CHRNA1</i>	cholinergic receptor, nicotinic, alpha 1 (muscle)	Nicotinic acetylcholine receptors
<i>CHRNA10</i>	cholinergic receptor, nicotinic, alpha 10 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNA2</i>	cholinergic receptor, nicotinic, alpha 2 (neuronal)	Nicotinic acetylcholine receptors

<i>CHRNA3</i>	cholinergic receptor, nicotinic, alpha 3 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNA4</i>	cholinergic receptor, nicotinic, alpha 4 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNA5</i>	cholinergic receptor, nicotinic, alpha 5 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNA6</i>	cholinergic receptor, nicotinic, alpha 6 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNA7</i>	cholinergic receptor, nicotinic, alpha 7 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNA9</i>	cholinergic receptor, nicotinic, alpha 9 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNB1</i>	cholinergic receptor, nicotinic, beta 1 (muscle)	Nicotinic acetylcholine receptors
<i>CHRNB2</i>	cholinergic receptor, nicotinic, beta 2 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNB3</i>	cholinergic receptor, nicotinic, beta 3 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRNB4</i>	cholinergic receptor, nicotinic, beta 4 (neuronal)	Nicotinic acetylcholine receptors
<i>CHRND</i>	cholinergic receptor, nicotinic, delta (muscle)	Nicotinic acetylcholine receptors
<i>CHRNE</i>	cholinergic receptor, nicotinic, epsilon (muscle)	Nicotinic acetylcholine receptors
<i>CHRNG</i>	cholinergic receptor, nicotinic, gamma (muscle)	Nicotinic acetylcholine receptors
<i>CLCA1</i>	chloride channel accessory 1	Calcium activated chloride channel
<i>CLCA2</i>	chloride channel accessory 2	Calcium activated chloride channel
<i>CLCA3</i>	chloride channel accessory 3	Calcium activated chloride channel
<i>CLCC1</i>	chloride channel CLIC-like 1	Mid-1-related chloride channel
<i>CLCN1</i>	chloride channel, voltage-sensitive 1	Voltage-sensitive chloride channel
<i>CLCN2</i>	chloride channel, voltage-sensitive 2	Voltage-sensitive chloride channel
<i>CLCN3</i>	chloride channel, voltage-sensitive 3	Voltage-sensitive chloride channel
<i>CLCN4</i>	chloride channel, voltage-sensitive 4	Voltage-sensitive chloride channel
<i>CLCN5</i>	chloride channel, voltage-sensitive 5	Voltage-sensitive chloride channel
<i>CLCN6</i>	chloride channel, voltage-sensitive 6	Voltage-sensitive chloride channel
<i>CLCN7</i>	chloride channel, voltage-sensitive 7	Voltage-sensitive chloride channel
<i>CLCNKA</i>	chloride channel, voltage-sensitive Ka	Voltage-sensitive chloride channel
<i>CLCNKB</i>	chloride channel, voltage-sensitive Kb	Voltage-sensitive chloride channel
<i>CLIC1</i>	chloride intracellular channel 1	Chloride intracellular channel
<i>CLIC2</i>	chloride intracellular channel 2	Chloride intracellular channel
<i>CLIC3</i>	chloride intracellular channel 3	Chloride intracellular channel
<i>CLIC4</i>	chloride intracellular channel 4	Chloride intracellular channel
<i>CLIC5</i>	chloride intracellular channel 5	Chloride intracellular channel
<i>CLIC6</i>	chloride intracellular channel 6	Chloride intracellular channel
<i>CNGA1</i>	cyclic nucleotide gated channel alpha 1	Cyclic nucleotide-regulated channels
<i>CNGA2</i>	cyclic nucleotide gated channel alpha 2	Cyclic nucleotide-regulated channels
<i>CNGA3</i>	cyclic nucleotide gated channel alpha 3	Cyclic nucleotide-regulated channels
<i>CNGA4</i>	cyclic nucleotide gated channel alpha 4	Cyclic nucleotide-regulated channels
<i>CNGB1</i>	cyclic nucleotide gated channel beta 1	Cyclic nucleotide-regulated channels
<i>CNGB3</i>	cyclic nucleotide gated channel beta 3	Cyclic nucleotide-regulated channels
<i>GABARAP</i>	GABA(A) receptor-associated protein	GABA <sub>A</sub> receptors
<i>GABRA1</i>	gamma-aminobutyric acid (GABA) A receptor, alpha 1	GABA <sub>A</sub> receptors
<i>GABRA2</i>	gamma-aminobutyric acid (GABA) A receptor, alpha 2	GABA <sub>A</sub> receptors
<i>GABRA3</i>	gamma-aminobutyric acid (GABA) A receptor, alpha 3	GABA <sub>A</sub> receptors
<i>GABRA4</i>	gamma-aminobutyric acid (GABA) A receptor, alpha 4	GABA <sub>A</sub> receptors
<i>GABRA5</i>	gamma-aminobutyric acid (GABA) A receptor, alpha 5	GABA <sub>A</sub> receptors

<i>GABRA6</i>	gamma-aminobutyric acid (GABA) A receptor, alpha 6	GABA <sub>A</sub> receptors
<i>GABRB1</i>	gamma-aminobutyric acid (GABA) A receptor, beta 1	GABA <sub>A</sub> receptors
<i>GABRB2</i>	gamma-aminobutyric acid (GABA) A receptor, beta 2	GABA <sub>A</sub> receptors
<i>GABRB3</i>	gamma-aminobutyric acid (GABA) A receptor, beta 3	GABA <sub>A</sub> receptors
<i>GABRD</i>	gamma-aminobutyric acid (GABA) A receptor, delta	GABA <sub>A</sub> receptors
<i>GABRE</i>	gamma-aminobutyric acid (GABA) A receptor, epsilon	GABA <sub>A</sub> receptors
<i>GABRG1</i>	gamma-aminobutyric acid (GABA) A receptor, gamma 1	GABA <sub>A</sub> receptors
<i>GABRG2</i>	gamma-aminobutyric acid (GABA) A receptor, gamma 2	GABA <sub>A</sub> receptors
<i>GABRG3</i>	gamma-aminobutyric acid (GABA) A receptor, gamma 3	GABA <sub>A</sub> receptors
<i>GABRP</i>	gamma-aminobutyric acid (GABA) A receptor, pi	GABA <sub>A</sub> receptors
<i>GABRQ</i>	gamma-aminobutyric acid (GABA) A receptor, theta	GABA <sub>A</sub> receptors
<i>GABRR1</i>	gamma-aminobutyric acid (GABA) A receptor, rho 1	GABA <sub>A</sub> receptors
<i>GABRR2</i>	gamma-aminobutyric acid (GABA) A receptor, rho 2	GABA <sub>A</sub> receptors
<i>GABRR3</i>	gamma-aminobutyric acid (GABA) A receptor, rho 3	GABA <sub>A</sub> receptors
<i>GLRA1</i>	glycine receptor, alpha 1	Glycine receptors
<i>GLRA2</i>	glycine receptor, alpha 2	Glycine receptors
<i>GLRA3</i>	glycine receptor, alpha 3	Glycine receptors
<i>GLRA4</i>	glycine receptor, alpha 4	Glycine receptors
<i>GLRB</i>	glycine receptor, beta	Glycine receptors
<i>GRIA1</i>	glutamate receptor, ionotropic, AMPA 1	Ionotropic glutamate receptors
<i>GRIA2</i>	glutamate receptor, ionotropic, AMPA 2	Ionotropic glutamate receptors
<i>GRIA3</i>	glutamate receptor, ionotropic, AMPA 3	Ionotropic glutamate receptors
<i>GRIA4</i>	glutamate receptor, ionotropic, AMPA 4	Ionotropic glutamate receptors
<i>GRID1</i>	glutamate receptor, ionotropic, delta 1	Ionotropic glutamate receptors
<i>GRID2</i>	glutamate receptor, ionotropic, delta 2	Ionotropic glutamate receptors
<i>GRIK1</i>	glutamate receptor, ionotropic, kainate 1	Ionotropic glutamate receptors
<i>GRIK2</i>	glutamate receptor, ionotropic, kainate 2	Ionotropic glutamate receptors
<i>GRIK3</i>	glutamate receptor, ionotropic, kainate 3	Ionotropic glutamate receptors
<i>GRIK4</i>	glutamate receptor, ionotropic, kainate 4	Ionotropic glutamate receptors
<i>GRIK5</i>	glutamate receptor, ionotropic, kainate 5	Ionotropic glutamate receptors
<i>GRIN1</i>	glutamate receptor, ionotropic, N-methyl D-aspartate 1	Ionotropic glutamate receptors
<i>GRIN2A</i>	glutamate receptor, ionotropic, N-methyl D-aspartate 2A	Ionotropic glutamate receptors
<i>GRIN2B</i>	glutamate receptor, ionotropic, N-methyl D-aspartate 2B	Ionotropic glutamate receptors
<i>GRIN2C</i>	glutamate receptor, ionotropic, N-methyl D-aspartate 2C	Ionotropic glutamate receptors
<i>GRIN2D</i>	glutamate receptor, ionotropic, N-methyl D-aspartate 2D	Ionotropic glutamate receptors
<i>GRIN3A</i>	glutamate receptor, ionotropic, N-methyl-D-aspartate 3A	Ionotropic glutamate receptors
<i>GRIN3B</i>	glutamate receptor, ionotropic, N-methyl-D-aspartate 3B	Ionotropic glutamate receptors
<i>HCN1</i>	hyperpolarization activated cyclic nucleotide-gated potassium channel 1	Cyclic nucleotide-regulated channels
<i>HCN2</i>	hyperpolarization activated cyclic nucleotide-gated potassium channel 2	Cyclic nucleotide-regulated channels
<i>HCN3</i>	hyperpolarization activated cyclic nucleotide-gated potassium channel 3	Cyclic nucleotide-regulated channels
<i>HCN4</i>	hyperpolarization activated cyclic nucleotide-gated potassium channel 4	Cyclic nucleotide-regulated channels
<i>HTR3A</i>	5-hydroxytryptamine (serotonin) receptor 3A, ionotropic	5-HT <sub>3</sub> receptors
<i>HTR3B</i>	5-hydroxytryptamine (serotonin) receptor 3B, ionotropic	5-HT <sub>3</sub> receptors
<i>HTR3C</i>	5-hydroxytryptamine (serotonin) receptor 3C, ionotropic	5-HT <sub>3</sub> receptors
<i>HTR3D</i>	5-hydroxytryptamine (serotonin) receptor 3D, ionotropic	5-HT <sub>3</sub> receptors

<i>HTR3E</i>	5-hydroxytryptamine (serotonin) receptor 3E, ionotropic	5-HT <sub>3</sub> receptors
<i>HVCN1</i>	hydrogen voltage-gated channel 1	Voltage-gated proton channel
<i>KCNA1</i>	potassium voltage-gated channel, shaker-related subfamily, member 1 (episodic ataxia with myokymia)	Voltage-gated potassium channels
<i>KCNA10</i>	potassium voltage-gated channel, shaker-related subfamily, member 10	Voltage-gated potassium channels
<i>KCNA2</i>	potassium voltage-gated channel, shaker-related subfamily, member 2	Voltage-gated potassium channels
<i>KCNA3</i>	potassium voltage-gated channel, shaker-related subfamily, member 3	Voltage-gated potassium channels
<i>KCNA4</i>	potassium voltage-gated channel, shaker-related subfamily, member 4	Voltage-gated potassium channels
<i>KCNA5</i>	potassium voltage-gated channel, shaker-related subfamily, member 5	Voltage-gated potassium channels
<i>KCNA6</i>	potassium voltage-gated channel, shaker-related subfamily, member 6	Voltage-gated potassium channels
<i>KCNA7</i>	potassium voltage-gated channel, shaker-related subfamily, member 7	Voltage-gated potassium channels
<i>KCNAB1</i>	potassium voltage-gated channel, shaker-related subfamily, beta member 1	Voltage-gated potassium channels
<i>KCNAB2</i>	potassium voltage-gated channel, shaker-related subfamily, beta member 2	Voltage-gated potassium channels
<i>KCNAB3</i>	potassium voltage-gated channel, shaker-related subfamily, beta member 3	Voltage-gated potassium channels
<i>KCNB1</i>	potassium voltage-gated channel, Shab-related subfamily, member 1	Voltage-gated potassium channels
<i>KCNB2</i>	potassium voltage-gated channel, Shab-related subfamily, member 2	Voltage-gated potassium channels
<i>KCNC1</i>	potassium voltage-gated channel, Shaw-related subfamily, member 1	Voltage-gated potassium channels
<i>KCNC2</i>	potassium voltage-gated channel, Shaw-related subfamily, member 2	Voltage-gated potassium channels
<i>KCNC3</i>	potassium voltage-gated channel, Shaw-related subfamily, member 3	Voltage-gated potassium channels
<i>KCNC4</i>	potassium voltage-gated channel, Shaw-related subfamily, member 4	Voltage-gated potassium channels
<i>KCND1</i>	potassium voltage-gated channel, Shal-related subfamily, member 1	Voltage-gated potassium channels
<i>KCND2</i>	potassium voltage-gated channel, Shal-related subfamily, member 2	Voltage-gated potassium channels
<i>KCND3</i>	potassium voltage-gated channel, Shal-related subfamily, member 3	Voltage-gated potassium channels
<i>KCNE1</i>	potassium voltage-gated channel, Isk-related family, member 1	Voltage-gated potassium channels
<i>KCNE1L</i>	KCNE1-like	Voltage-gated potassium channels
<i>KCNE2</i>	potassium voltage-gated channel, Isk-related family, member 2	Voltage-gated potassium channels
<i>KCNE3</i>	potassium voltage-gated channel, Isk-related family, member 3	Voltage-gated potassium channels
<i>KCNE4</i>	potassium voltage-gated channel, Isk-related family, member 4	Voltage-gated potassium channels
<i>KCNF1</i>	potassium voltage-gated channel, subfamily F, member 1	Voltage-gated potassium channels
<i>KCNG1</i>	potassium voltage-gated channel, subfamily G, member 1	Voltage-gated potassium channels
<i>KCNG2</i>	potassium voltage-gated channel, subfamily G, member 2	Voltage-gated potassium channels

<i>KCNG3</i>	potassium voltage-gated channel, subfamily G, member 3	Voltage-gated potassium channels
<i>KCNG4</i>	potassium voltage-gated channel, subfamily G, member 4	Voltage-gated potassium channels
<i>KCNH1</i>	potassium voltage-gated channel, subfamily H (eag-related), member 1	Voltage-gated potassium channels
<i>KCNH2</i>	potassium voltage-gated channel, subfamily H (eag-related), member 2	Voltage-gated potassium channels
<i>KCNH3</i>	potassium voltage-gated channel, subfamily H (eag-related), member 3	Voltage-gated potassium channels
<i>KCNH4</i>	potassium voltage-gated channel, subfamily H (eag-related), member 4	Voltage-gated potassium channels
<i>KCNH5</i>	potassium voltage-gated channel, subfamily H (eag-related), member 5	Voltage-gated potassium channels
<i>KCNH6</i>	potassium voltage-gated channel, subfamily H (eag-related), member 6	Voltage-gated potassium channels
<i>KCNH7</i>	potassium voltage-gated channel, subfamily H (eag-related), member 7	Voltage-gated potassium channels
<i>KCNH8</i>	potassium voltage-gated channel, subfamily H (eag-related), member 8	Voltage-gated potassium channels
<i>KCNJ1</i>	potassium inwardly-rectifying channel, subfamily J, member 1	Inwardly rectifying potassium channels
<i>KCNJ10</i>	potassium inwardly-rectifying channel, subfamily J, member 10	Inwardly rectifying potassium channels
<i>KCNJ11</i>	potassium inwardly-rectifying channel, subfamily J, member 11	Inwardly rectifying potassium channels
<i>KCNJ12</i>	potassium inwardly-rectifying channel, subfamily J, member 12	Inwardly rectifying potassium channels
<i>KCNJ13</i>	potassium inwardly-rectifying channel, subfamily J, member 13	Inwardly rectifying potassium channels
<i>KCNJ14</i>	potassium inwardly-rectifying channel, subfamily J, member 14	Inwardly rectifying potassium channels
<i>KCNJ15</i>	potassium inwardly-rectifying channel, subfamily J, member 15	Inwardly rectifying potassium channels
<i>KCNJ16</i>	potassium inwardly-rectifying channel, subfamily J, member 16	Inwardly rectifying potassium channels
<i>KCNJ18</i>	potassium inwardly-rectifying channel, subfamily J, member 18	Inwardly rectifying potassium channels
<i>KCNJ2</i>	potassium inwardly-rectifying channel, subfamily J, member 2	Inwardly rectifying potassium channels
<i>KCNJ3</i>	potassium inwardly-rectifying channel, subfamily J, member 3	Inwardly rectifying potassium channels
<i>KCNJ4</i>	potassium inwardly-rectifying channel, subfamily J, member 4	Inwardly rectifying potassium channels
<i>KCNJ5</i>	potassium inwardly-rectifying channel, subfamily J, member 5	Inwardly rectifying potassium channels
<i>KCNJ6</i>	potassium inwardly-rectifying channel, subfamily J, member 6	Inwardly rectifying potassium channels
<i>KCNJ8</i>	potassium inwardly-rectifying channel, subfamily J, member 8	Inwardly rectifying potassium channels
<i>KCNJ9</i>	potassium inwardly-rectifying channel, subfamily J, member 9	Inwardly rectifying potassium channels
<i>KCNK1</i>	potassium channel, subfamily K, member 1	Two-P potassium channels
<i>KCNK10</i>	potassium channel, subfamily K, member 10	Two-P potassium channels
<i>KCNK12</i>	potassium channel, subfamily K, member 12	Two-P potassium channels
<i>KCNK13</i>	potassium channel, subfamily K, member 13	Two-P potassium channels

<i>KCNK15</i>	potassium channel, subfamily K, member 15	Two-P potassium channels
<i>KCNK16</i>	potassium channel, subfamily K, member 16	Two-P potassium channels
<i>KCNK17</i>	potassium channel, subfamily K, member 17	Two-P potassium channels
<i>KCNK18</i>	potassium channel, subfamily K, member 18	Two-P potassium channels
<i>KCNK2</i>	potassium channel, subfamily K, member 2	Two-P potassium channels
<i>KCNK3</i>	potassium channel, subfamily K, member 3	Two-P potassium channels
<i>KCNK4</i>	potassium channel, subfamily K, member 4	Two-P potassium channels
<i>KCNK5</i>	potassium channel, subfamily K, member 5	Two-P potassium channels
<i>KCNK6</i>	potassium channel, subfamily K, member 6	Two-P potassium channels
<i>KCNK7</i>	potassium channel, subfamily K, member 7	Two-P potassium channels
<i>KCNK9</i>	potassium channel, subfamily K, member 9	Two-P potassium channels
<i>KCNMA1</i>	potassium large conductance calcium-activated channel, subfamily M, alpha member 1	Calcium-activated potassium channels
<i>KCNMB1</i>	potassium large conductance calcium-activated channel, subfamily M, beta member 1	Calcium-activated potassium channels
<i>KCNMB2</i>	potassium large conductance calcium-activated channel, subfamily M, beta member 2	Calcium-activated potassium channels
<i>KCNMB3</i>	potassium large conductance calcium-activated channel, subfamily M beta member 3	Calcium-activated potassium channels
<i>KCNMB4</i>	potassium large conductance calcium-activated channel, subfamily M, beta member 4	Calcium-activated potassium channels
<i>KCNN1</i>	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 1	Calcium-activated potassium channels
<i>KCNN2</i>	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 2	Calcium-activated potassium channels
<i>KCNN3</i>	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 3	Calcium-activated potassium channels
<i>KCNN4</i>	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	Calcium-activated potassium channels
<i>KCNQ1</i>	potassium voltage-gated channel, KQT-like subfamily, member 1	Voltage-gated potassium channels
<i>KCNQ2</i>	potassium voltage-gated channel, KQT-like subfamily, member 2	Voltage-gated potassium channels
<i>KCNQ3</i>	potassium voltage-gated channel, KQT-like subfamily, member 3	Voltage-gated potassium channels
<i>KCNQ4</i>	potassium voltage-gated channel, KQT-like subfamily, member 4	Voltage-gated potassium channels
<i>KCNQ5</i>	potassium voltage-gated channel, KQT-like subfamily, member 5	Voltage-gated potassium channels
<i>KCNS1</i>	potassium voltage-gated channel, delayed-rectifier, subfamily S, member 1	Voltage-gated potassium channels
<i>KCNS2</i>	potassium voltage-gated channel, delayed-rectifier, subfamily S, member 2	Voltage-gated potassium channels
<i>KCNS3</i>	potassium voltage-gated channel, delayed-rectifier, subfamily S, member 3	Voltage-gated potassium channels
<i>KCNT1</i>	potassium channel, subfamily T, member 1	Calcium-activated potassium channels
<i>KCNT2</i>	potassium channel, subfamily T, member 2	Calcium-activated potassium channels
<i>KCNU1</i>	potassium channel, subfamily U, member 1	Calcium-activated potassium channels
<i>KCNV1</i>	potassium channel, subfamily V, member 1	Voltage-gated potassium channels
<i>KCNV2</i>	potassium channel, subfamily V, member 2	Voltage-gated potassium channels

<i>MCOLN1</i>	mucolipin 1	Transient receptor potential channels
<i>MCOLN2</i>	mucolipin 2	Transient receptor potential channels
<i>MCOLN3</i>	mucolipin 3	Transient receptor potential channels
<i>NALCN</i>	sodium leak channel, non-selective	Voltage-independent cation channel
<i>P2RX1</i>	purinergic receptor P2X, ligand-gated ion channel, 1	P2X receptors
<i>P2RX2</i>	purinergic receptor P2X, ligand-gated ion channel, 2	P2X receptors
<i>P2RX3</i>	purinergic receptor P2X, ligand-gated ion channel, 3	P2X receptors
<i>P2RX4</i>	purinergic receptor P2X, ligand-gated ion channel, 4	P2X receptors
<i>P2RX5</i>	purinergic receptor P2X, ligand-gated ion channel, 5	P2X receptors
<i>P2RX6</i>	purinergic receptor P2X, ligand-gated ion channel, 6	P2X receptors
<i>P2RX7</i>	purinergic receptor P2X, ligand-gated ion channel, 7	P2X receptors
<i>PKD1</i>	polycystic kidney disease 1 (autosomal dominant)	Transient receptor potential channels
<i>PKD2</i>	polycystic kidney disease 2 (autosomal dominant)	Transient receptor potential channels
<i>PKD2L1</i>	polycystic kidney disease 2-like 1	Transient receptor potential channels
<i>PKD2L2</i>	polycystic kidney disease 2-like 2	Transient receptor potential channels
<i>SCN10A</i>	sodium channel, voltage-gated, type X, alpha subunit	Voltage-gated sodium channels
<i>SCN11A</i>	sodium channel, voltage-gated, type XI, alpha subunit	Voltage-gated sodium channels
<i>SCN1A</i>	sodium channel, voltage-gated, type I, alpha subunit	Voltage-gated sodium channels
<i>SCN1B</i>	sodium channel, voltage-gated, type I, beta subunit	Voltage-gated sodium channels
<i>SCN2A</i>	sodium channel, voltage-gated, type II, alpha subunit	Voltage-gated sodium channels
<i>SCN2B</i>	sodium channel, voltage-gated, type II, beta subunit	Voltage-gated sodium channels
<i>SCN3A</i>	sodium channel, voltage-gated, type III, alpha subunit	Voltage-gated sodium channels
<i>SCN3B</i>	sodium channel, voltage-gated, type III, beta subunit	Voltage-gated sodium channels
<i>SCN4A</i>	sodium channel, voltage-gated, type IV, alpha subunit	Voltage-gated sodium channels
<i>SCN4B</i>	sodium channel, voltage-gated, type IV, beta subunit	Voltage-gated sodium channels
<i>SCN5A</i>	sodium channel, voltage-gated, type V, alpha subunit	Voltage-gated sodium channels
<i>SCN7A</i>	sodium channel, voltage-gated, type VII, alpha subunit	Voltage-gated sodium channels
<i>SCN8A</i>	sodium channel, voltage gated, type VIII, alpha subunit	Voltage-gated sodium channels
<i>SCN9A</i>	sodium channel, voltage-gated, type IX, alpha subunit	Voltage-gated sodium channels
<i>SCNN1A</i>	sodium channel, non-voltage-gated 1 alpha subunit	Nonvoltage-gated sodium channels
<i>SCNN1B</i>	sodium channel, non-voltage-gated 1, beta subunit	Nonvoltage-gated sodium channels
<i>SCNN1D</i>	sodium channel, non-voltage-gated 1, delta subunit	Nonvoltage-gated sodium channels
<i>SCNN1G</i>	sodium channel, non-voltage-gated 1, gamma subunit	Nonvoltage-gated sodium channels
<i>TPCN1</i>	two pore segment channel 1	CatSper and two-pore channels
<i>TPCN2</i>	two pore segment channel 2	CatSper and two-pore channels
<i>TRPA1</i>	transient receptor potential cation channel, subfamily A, member 1	Transient receptor potential channels
<i>TRPC1</i>	transient receptor potential cation channel, subfamily C, member 1	Transient receptor potential channels
<i>TRPC3</i>	transient receptor potential cation channel, subfamily C, member 3	Transient receptor potential channels
<i>TRPC4</i>	transient receptor potential cation channel, subfamily C, member 4	Transient receptor potential channels

<i>TRPC5</i>	transient receptor potential cation channel, subfamily C, member 5	Transient receptor potential channels
<i>TRPC6</i>	transient receptor potential cation channel, subfamily C, member 6	Transient receptor potential channels
<i>TRPC7</i>	transient receptor potential cation channel, subfamily C, member 7	Transient receptor potential channels
<i>TRPM1</i>	transient receptor potential cation channel, subfamily M, member 1	Transient receptor potential channels
<i>TRPM2</i>	transient receptor potential cation channel, subfamily M, member 2	Transient receptor potential channels
<i>TRPM3</i>	transient receptor potential cation channel, subfamily M, member 3	Transient receptor potential channels
<i>TRPM4</i>	transient receptor potential cation channel, subfamily M, member 4	Transient receptor potential channels
<i>TRPM5</i>	transient receptor potential cation channel, subfamily M, member 5	Transient receptor potential channels
<i>TRPM6</i>	transient receptor potential cation channel, subfamily M, member 6	Transient receptor potential channels
<i>TRPM7</i>	transient receptor potential cation channel, subfamily M, member 7	Transient receptor potential channels
<i>TRPM8</i>	transient receptor potential cation channel, subfamily M, member 8	Transient receptor potential channels
<i>TRPV1</i>	transient receptor potential cation channel, subfamily V, member 1	Transient receptor potential channels
<i>TRPV2</i>	transient receptor potential cation channel, subfamily V, member 2	Transient receptor potential channels
<i>TRPV3</i>	transient receptor potential cation channel, subfamily V, member 3	Transient receptor potential channels
<i>TRPV4</i>	transient receptor potential cation channel, subfamily V, member 4	Transient receptor potential channels
<i>TRPV5</i>	transient receptor potential cation channel, subfamily V, member 5	Transient receptor potential channels
<i>TRPV6</i>	transient receptor potential cation channel, subfamily V, member 6	Transient receptor potential channels
<i>VDAC1</i>	voltage-dependent anion channel 1	voltage-dependent anion channel
<i>VDAC2</i>	voltage-dependent anion channel 2	voltage-dependent anion channel
<i>VDAC3</i>	voltage-dependent anion channel 3	voltage-dependent anion channel
<i>ZACN</i>	zinc activated ligand-gated ion channel	ZAC



Table S2. Comparison in gene expression level between p53 mutant and wildtype tumors in validation cohorts

Gene symbol	FRA	
	Fold change <sup>a</sup>	Adjusted <i>P</i> -value <sup>b</sup>
<i>ANO1</i>	0.69	5.93E-03
<i>CACNA1D</i>	0.58	2.13E-04
<i>CACNA2D1</i>	0.99	2.44E-01
<i>CACNA2D2</i>	0.50	2.13E-04
<i>CLCA2</i>	2.00	4.04E-01
<i>CLIC5</i>	1.02	8.28E-01
<i>CLIC6</i>	0.68	1.87E-02
<i>GLRB</i>	0.64	6.92E-04
<i>KCND3</i>	0.74	5.59E-05
<i>KCNE3</i>	1.04	2.35E-01
<i>KCNE4</i>	0.42	6.92E-04
<i>KCNJ3</i>	0.49	1.43E-02
<i>KCNK1</i>	1.11	2.35E-01
<i>KCNK6</i>	0.71	1.80E-03
<i>KCNMA1</i>	0.83	1.08E-02
<i>KCNN4</i>	1.53	7.61E-04
<i>MCOLN2</i>	1.28	4.19E-02
<i>P2RX4</i>	0.78	5.06E-03
<i>SCN7A</i>	0.84	3.13E-03
<i>SCNN1A</i>	0.84	4.49E-03
<i>TPCN1</i>	0.96	2.03E-01
<i>TRPC1</i>	0.92	2.35E-01

<sup>a</sup> Fold change is calculated by dividing the mean expression of p53 mutant tumor by the mean expression of p53 wildtype tumor.

<sup>b</sup> *P*-value is calculated by two-tailed t-test and adjusted by Benjamini & Hochberg correction.

Table S3. Comparison in gene expression level between ER positive and negative tumors

Gene symbol	FRA		USA1		USA2	
	Fold change <sup>a</sup>	Adjusted <i>P</i> -value <sup>b</sup>	Fold change <sup>a</sup>	Adjusted <i>P</i> -value <sup>b</sup>	Fold change <sup>a</sup>	Adjusted <i>P</i> -value <sup>b</sup>
<i>ANO1</i>	1.60	9.74E-08	1.86	1.05E-12	1.57	1.45E-05
<i>CACNA1A</i>	0.84	2.24E-03	0.84	1.54E-04	0.75	4.66E-04
<i>CACNA1D</i>	2.49	1.83E-21	1.80	1.25E-22	1.90	1.09E-12
<i>CACNA2D1</i>	1.13	2.26E-02	0.96	1.72E-01	0.96	5.30E-01
<i>CACNA2D2</i>	2.48	9.18E-16	2.19	5.05E-23	2.23	2.06E-14
<i>CLCA2</i>	0.19	8.86E-06	0.93	4.17E-01	0.50	1.61E-02
<i>CLIC4</i>	0.72	1.68E-04	0.60	1.64E-24	0.67	3.65E-10
<i>CLIC6</i>	7.29	8.25E-18	NA	NA	NA	NA
<i>GABRP</i>	0.12	1.04E-14	0.14	1.05E-29	0.20	4.02E-09
<i>GLRB</i>	2.11	2.50E-14	1.96	1.94E-10	2.20	3.90E-11
<i>KCNAB2</i>	0.92	1.96E-03	0.89	8.32E-04	0.95	2.80E-01
<i>KCND3</i>	1.46	3.37E-09	1.48	4.40E-13	1.70	3.65E-10
<i>KCNE3</i>	0.86	3.65E-06	NA	NA	NA	NA
<i>KCNE4</i>	3.80	8.25E-18	5.43	1.22E-28	3.34	2.58E-13
<i>KCNJ3</i>	7.88	2.50E-14	2.25	4.74E-13	1.84	4.06E-06
<i>KCNK6</i>	1.84	3.37E-14	NA	NA	NA	NA
<i>KCNMA1</i>	1.02	1.81E-01	1.27	1.17E-06	1.38	1.37E-04
<i>KCNN4</i>	0.37	3.80E-20	0.44	5.05E-23	0.34	2.06E-14
<i>KCNS3</i>	1.16	2.60E-01	1.36	7.85E-07	1.19	1.61E-02
<i>MCOLN2</i>	0.65	8.61E-09	NA	NA	NA	NA
<i>P2RX4</i>	1.51	3.12E-11	1.51	1.97E-25	1.31	2.23E-03
<i>SCN7A</i>	1.27	2.88E-06	1.04	2.70E-01	1.13	1.05E-01
<i>SCNN1A</i>	1.43	5.77E-11	1.69	4.85E-20	1.46	3.43E-08
<i>TPCN1</i>	1.13	1.37E-06	1.28	8.25E-11	1.16	2.38E-03

<sup>a</sup> Fold change is calculated by dividing the mean expression of ER positive tumor by the mean expression of ER negative tumor.

<sup>b</sup> *P*-value is calculated by two-tailed t-test and adjusted by Benjamini & Hochberg correction.

Table S4. Correlation between gene expression and histological tumor grade

Gene symbol	FRA		GER		USA1	
	$\rho^a$	Adjusted <i>P</i> -value <sup>b</sup>	$\rho^a$	Adjusted <i>P</i> -value <sup>b</sup>	$\rho^a$	Adjusted <i>P</i> -value <sup>b</sup>
<i>ANO1</i>	-0.17	9.08E-03	-0.26	7.24E-04	-0.24	5.09E-07
<i>CACNA1D</i>	-0.44	2.03E-12	-0.45	7.54E-10	-0.38	3.24E-16
<i>CACNA2D1</i>	-0.21	1.13E-03	0.02	7.75E-01	-0.06	2.88E-01
<i>CACNA2D2</i>	-0.33	1.59E-07	-0.36	2.04E-06	-0.33	6.13E-13
<i>CLIC1</i>	0.24	1.66E-04	0.09	2.27E-01	0.14	2.61E-03
<i>CLIC4</i>	0.21	1.05E-03	0.06	3.97E-01	0.25	1.16E-07
<i>CLIC5</i>	-0.14	3.41E-02	-0.17	3.16E-02	-0.10	4.21E-02
<i>CLIC6</i>	-0.34	9.74E-08	NA	NA	NA	NA
<i>GLRB</i>	-0.40	1.43E-10	-0.31	5.91E-05	-0.22	1.87E-06
<i>KCNAB2</i>	0.28	9.70E-06	0.25	1.23E-03	0.15	1.63E-03
<i>KCND3</i>	-0.42	9.95E-12	-0.22	3.40E-03	-0.28	3.97E-09
<i>KCNE3</i>	0.34	6.01E-08	NA	NA	NA	NA
<i>KCNE4</i>	-0.32	2.50E-07	-0.28	2.78E-04	-0.36	7.39E-15
<i>KCNK1</i>	0.17	7.76E-03	0.10	1.88E-01	0.12	1.65E-02
<i>KCNMA1</i>	-0.28	9.70E-06	-0.24	1.38E-03	-0.27	1.04E-08
<i>KCNN4</i>	0.37	4.86E-09	0.17	2.81E-02	0.25	1.12E-07
<i>MCOLN2</i>	0.40	1.43E-10	NA	NA	NA	NA
<i>P2RX4</i>	-0.20	1.68E-03	-0.23	2.86E-03	-0.28	4.86E-09
<i>PKD1</i>	-0.02	7.68E-01	-0.16	3.67E-02	-0.02	6.02E-01
<i>PKD2</i>	-0.01	8.34E-01	-0.23	2.36E-03	-0.03	4.83E-01
<i>SCN1B</i>	-0.29	6.46E-06	-0.07	3.67E-01	-0.03	4.83E-01
<i>SCN7A</i>	-0.51	3.77E-17	-0.02	7.75E-01	-0.04	4.34E-01
<i>SCNN1A</i>	-0.21	1.13E-03	-0.15	5.48E-02	-0.36	1.42E-14
<i>TPCN1</i>	-0.22	7.85E-04	-0.37	1.28E-06	-0.27	9.87E-09
<i>TPCN2</i>	0.10	1.09E-01	NA	NA	NA	NA
<i>TRPC1</i>	-0.13	4.86E-02	-0.26	6.99E-04	-0.13	8.13E-03
<i>TRPM4</i>	-0.22	5.94E-04	-0.09	2.62E-01	-0.15	1.89E-03
<i>VDAC1</i>	0.21	1.14E-03	0.13	1.04E-01	0.04	4.17E-01
<i>VDAC2</i>	0.37	4.86E-09	0.21	6.17E-03	0.20	2.20E-05
<i>VDAC3</i>	0.30	2.85E-06	0.12	1.41E-01	0.16	7.21E-04

<sup>a</sup>  $\rho$  is the Spearman's rank correlation coefficient.

<sup>b</sup> *P*-value is calculated by Spearman's rank correlation test and adjusted by Benjamini & Hochberg correction.

Table S5. Comparison in prognostic power between IC30 and clinicopathological factors for the USA1 cohort. Hazard ratio was calculated separately for each variable by univariate Cox proportional hazard regression of survival.

Covariate	Hazard ratio	95% Confidence interval	<i>P</i> -value
IC30 + vs. -	3.11	(2.05, 4.70)	9.06E-8
Age (per year)	1.00	(0.98, 1.02)	8.60E-1
Lymph node + vs. -	2.48	(1.67, 3.68)	6.20E-6
Tumor size $\geq$ T3 vs. $<$ T3	1.79	(1.23, 2.60)	2.35E-3
Grade 3 vs. 1,2	1.57	(1.05, 2.37)	2.95E-2
ER + vs. -	0.35	(0.24, 0.52)	1.03E-7
PR + vs. -	0.39	(0.26, 0.58)	4.91E-6

Table S6. Comparison in prognostic power between IC30 and clinicopathological factors for the FRA cohort. Hazard ratio was calculated separately for each variable by univariate Cox proportional hazard regression of survival.

Covariate	Hazard ratio	95% Confidence interval	<i>P</i> -value
IC30 + vs. -	1.99	(1.28, 3.10)	0.002
Age (per year)	1.00	(0.98, 1.02)	0.948
Grade 3 vs. 1,2	1.66	(1.07, 2.59)	0.025
ER + vs. -	0.66	(0.43, 1.02)	0.059
PR + vs. -	0.84	(0.55, 1.30)	0.435
p53 mutant vs. wild-type	1.72	(1.05, 2.82)	0.031