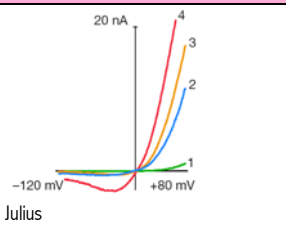
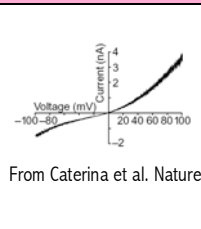
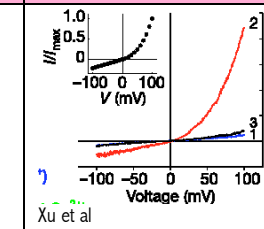
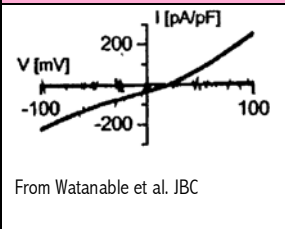
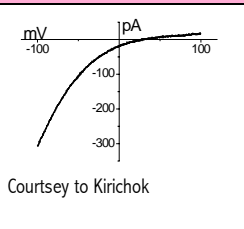
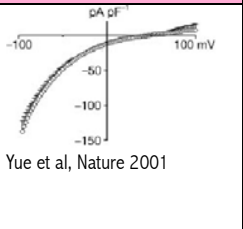


The TRPV Vanilloid Receptor Subfamily

TRP Subtype Unigene	V1 (VR1) Hs.283010 Splice variants	V2 (VRL1, OTRPC2)Hs.279746	V3 (VRL2) Hs.375034 Splice variants	V4 (OTRPC4, VR-OAC) Hs.287776 Splice variants	V5 (ECaC1, CaT2) Hs.283369	V6 (ECaC2, CaT1) Hs.302740
# Amino acids Human Rat Mouse	839 838 839	764 761 756	790 781 791	871 871 871	729 723 723	725 727 727
Accession # Human Rat Mouse	Q8NER1 Q35433 Q704Y3	Q9Y5S1 Q9WUD2 Q9WTR1	Q8NET8 AY325813 Q8K424	Q9HBA0 Q9ERZ8 Q9EPK8	Q9NQA5 Q9JIP0 P69744	Q9H1D0 Q9R186 Q91WD2
Splice variants and other accession #s	Q8NER1 Hs 839 Q704Y3 Mm 839 α AAS15575 Mm 829 β	Q9Y5S1 Hs 764 Q9WTR1 Mm 756	Q8NET8 Hs 790 a AAM80559 Hs 791 a AAM80558 Hs 765 b Q8K424 Mm 791	Q9HBA0 Hs 871 α NP_671737 Hs 811 β Q9EPK8 Mm 871 NP_071300i Mm 871	Q9NQA5 Hs 729 P69744 Mm 723	Q9H1D0 Hs 725 Q91WD2 Mm 727
OMIM gene map Human Rat Mouse	17p13.3 10q24 11 B3	17p11.2 10q22 11 B2	17p13.3 10q24 11 B4	12q24.1 12q16 5 F	7q35 4q23 6 B2	7q33-34 4q22 6 B2
Genetic model or disease mutation	Mouse TRPV1-/- Defects in nociception	Mouse TRPV2-/-	Mouse TRPV3-/- Mild temp-related pain deficit	Mouse TRPV4-/- ADH volume regulation affected, temperature preference	Mouse TRPV5-/- causes hypocalciuric hypercalcemia, diabetes?	Mouse TRPV6-/- Decreases intestinal Ca reabsorption; alopecia and dermatitis
Known Functions	Basis of "hot" pepper sensation Heat evoked nociception Inflammatory thermal hyperalgesia, Bladder distension sensing Chronic cough, bronchial sensitization Upregulated in: Inflammatory bowel disease Vulvodynia Osteoarthritis	Thermal pain (medium diameter neurons); Trigeminal neuron, pterygopalatine and submandibular ganglia, myenteric plexus & nodose ganglion neurons, spinal cord lamina I, II, hypothalamic paraventricular, suprachiasmatic, and supraoptic nuclei, retina Osmo-sensing in aortic myocytes	Warm sensing Pain-sensing	CNS osmotic sensing (circumventricular) Pressure sensing (DRG) Nociception in primary afferents sensitized by PGE2 Inflammatory thermal hyperalgesia,	Ca uptake in kidney	Ca uptake in kidney and intestine
Likely role in	Other pain pathways	Skeletal and cardiac muscle degeneration Other pain pathways (visceral sensory)	Warm temp sensing in 308 ketatinocytes Pain	Temperature sensing in skin, 308 ketatinocytes	Ca ²⁺ uptake in kidney (Vit D regulated), potential role in beta cell of pancreas	Ca ²⁺ uptake in intestine (Vit D regulated)
N or C terminal domain modules	3x N-AnkR C-TRP (IWKLQR) box C- Putative PIP ₂ binding site	3x N-AnkR C-TRP (IWKLQK) box	3x N-AnkR C-TRP (IWRLQR) box	4x N-AnkR C-TRP (IWKLQW) box	5x N-AnkR C-TRP (LWRAQV) box N-PDZ	4x N-AnkR C-TRP (LWRAQI) box N-PDZ
Reported Interacting Proteins	TRPV3, TRPV2 Calmodulin, PI3K Snapin, synaptotagmin IX β -tubulin	TRPV1 RGA protein	TRPV1	Calmodulin (C term) Src family kinases (potentiation) Aquaporin 5 Pacsin 3	TRPV6 S100A10/annexin 2, 80K-H, NHERF4, BSPRY, Rab11a	TRPV5 S100A10/annexin 2
Activation	T>43°C Capsaicin, (0.7 μ M) Resiniferatoxin; 40 nM Anandamide, ACEA satiety factor oleoylethanolamide	T>53°C 2-APB ~100mM Neuropeptide head activator Diphenylboronic anhydride	T>30°C 2-APB 30 μ M, DPA (50-100 μ M) Activation by two identical consecutive heat stimuli shifts	Decreased Osmolarity (260-200 mOsm) T>24°C Phorbol esters	Constitutive [Ca ²⁺] _i inhibits	Constitutive [Ca ²⁺] _i inhibits

	H ⁺ 2-APB ~200μM Heat-induced activation of TRPV1 is the result of a marked leftward shift of the voltage dependence of activation (9.1 mV°C ⁻¹)		V _{0.5} to the less positive potential without affecting slope factor (31.7 ± 1.3 versus 36.6 ± 1.9 mV, respectively)			
Q₁₀	~20 at negative voltages, Q ₁₀ is much smaller at positive voltages	N.D.	25	10-20	N.D.	N.D.
Direct Agonist (bind channel protein to activate)	0.7 μM Capsaicin 40 nM Resiniferatoxin Anandamide (5 μM) H ⁺ 15-(S) HETE (9 μM) Leukotriene B4 (10 μM) Olvanil (8 nM) Arvanil (0.27 nM) Piperine (38 μM) 2-APB (200 μM) allicin (100 μM) vanillotoxin (5-10 μM)	Capsaicin <i>Insensitive</i>	Capsaicin <i>Insensitive</i> Carvacrol, thymol, eugenol, vanillin, ethyl vanillin (~1 mM), menthol, cinnamaldehyde (mM)	Capsaicin <i>Insensitive</i> Endocannabinoids (anandamide), arachidonic acid, 5'6'-epoxyeicosatrienoic acids (150 nM), 4a-phorbol 12,13 didecanoate (10 nM), PMA (12 nM) bisandrographalide (1 μM)		2-aminoethyl diphenylborate
~P_{Ca}/P_{Na}	10 (5 for P _{Mg} /P _{Na}) Ca>Mg>Na=K=Cs	3 Ca>Mg>Na=K=Cs	~10	6 Ca>Mg>K>Cs~Rb>Na>Li	>100 (Ca>Mn>Ba~Sr) Na>Li>K>Cs>NMDG	>100 (Ca>Ba~Sr>Mn) Na~Li>K>Cs
Blockers and inhibitors	Capsazepine (.3 μM) Desensitization with camphor 1 μM RuR acylpolyamines (0.3 μM)	1 μM RuR, La ³⁺ , SKF96365	100 nM RuR La ³⁺	1 μM RuR, 100 μM Gd ³⁺ , 0.5 mM La ³⁺	120 nM RuR; 1 μM econazole μM Cd>>Gd>La, Mg Cu, Pb Intracellular Mg block is voltage-sensitive	9 μM RuR μM Cd>>Gd>La Mg
Single channel conductance (γ) in pS.	~80 pS (+V, 140 Na/140 Na)	N.D.	170 pS, conductance is dependent on temperature with low Q ₁₀	90 pS (+60 mV, 140Na/140K) 30-60 pS (-60 mV)	75 pS (Ca-free)	42-58 pS (Ca-free)
I-V shape	 Julius	 From Caterina et al. Nature	 Xu et al	 From Watanabe et al. JBC	 Courtesy to Kirichok	 Yue et al, Nature 2001
Tissue expression	DRG, trigeminal ganglion, kidney, pancreas, placenta Testis, uterus, spleen, stomach, small intestine, lung, liver	Brain, DRG, Trigeminal ganglia; spinal cord, lung, spleen, intestine	Brain, spinal cord, skin, testis, stomach, tongue, trachea, small intestine, placenta, hair follicles, adipose, pituitary, placenta	Brain, Trigeminal ganglia, cochlea, lung, spleen, kidney, testis, fat, heart, prostate, pancreas, placenta, salivary gland	Kidney, prostate, testis, placenta, pancreas, brain	Intestines, stomach, kidney, lung, spleen, liver, brain, placenta, prostate, pancreas, adrenal glands, skin
Comments	PKC enhances activation PKA reg desensitization Acid potentiates Heat sensitizes Not store-activated Activation of PLC releases TRPV1 from PIP ₂ inhibition Capsaicin induced neuronal death	Difficult expression. Most data from oocytes. IGF-1 appears to translocate TRPV2 to membranes in mouse. Heat sensitizes TRPV2 on repetitive stimulation	Current displays marked sensitization with repeated temperature ramps and 2APB activation. Marked hysteresis of temperature response (gradual increase with T, sharp decline with cooling)	May play a role in thermosensation (moderate heat), bone regulation, blood volume regulation, hearing	Most Ca ²⁺ -selective of TRPs-conserved asp in pore. Voltage-dependent [Mg ²⁺] _i -block Upregulated in various adenocarcinomas	Most Ca ²⁺ -selective of TRPs-conserved Asp in pore. Voltage-dependent [Mg ²⁺] _i -block Upregulated in various adenocarcinomas

David Clapham last updated February 2, 2007

<p>REFS</p>	<p>Hayes, 11050376[Caterina, 9349813 Correll, 15489011;Liapi, 16115206 Rutter, 16237318;Smith, 12077606 Numazaki, 12808128 Stein, 17074976;Voets, 15306801 Smart, 11301059[Zygmunt, 1044037; Smart, 10694225;Hwang, 10823958; Jerman, 10864900 McNamara, 15685214;Hu, 15194687-McIntyre, 11226139 Macpherson, 15916949 Siemens, 17093448;Bhave, 14523239;Trevisani, 11992116 Wahl, 11125018;Valenzano, 1272133; Kitaguchi, 16300403;Prescott, 12764195 Birder, 11606761;Caterina, 10764638; Tominaga, 9768840[Geppetti, 15051629 Yiangou, 11343743 Tympanidis, 14987622 Cho, Bl abstact; Fernihough, 16039054</p>	<p>Caterina, 10201375 Kanzaki, 10559903 Liapi, 16115206 Rutter, 16237318 Hu, 15194687 Boels, 11707512 Chung, 15722340 Muraki, 14512441 lwata, 12796481</p>	<p>Xu, 12077604 Peier, 12016205 Smith, 12077606 Chung, 15722340 Chung, 15175387 Moqrich, 15746429 Xu, 16617338 Macpherson, 16829128 Chung, 12783886 Asakawa, 16858425</p>	<p>Liedtke, 0011081638 Strotmann, 12724311 Liu, 16571723 Sidhaye, 16537379 Cuajungco, 16627472 Strotmann, 11025659 Voets, 12093812 Watanabe, 12354759 Watanabe, 11827975 Xu, 12970074 Watanabe, 12879072 Suzuki, 12692122 Smith, 16899456 Güler, 12151520 Delany, 11160995 Alessandri-Haber, 12895423 Todaka 15187078 Mizogushi Tabuchi, 15925108</p>	<p>Müller, 0010945469 Peng, 10875938 Suzuki, 0010913341 Weber, 11741335 Hoenderop, 12574114 Lambers, 15123711 Van de Graaf, 12660155 Gkika, 17005931 van de Graaf, 16565876 van de Graaf, 16380433 van de Graaf, 16354700 Nilius, 10970426 Vennekens, 10660551 Vennekens, 11417220 Yeh, 14525991 Yeh, 16121193 Nilius, 11588099 van der Eerden, 16291808 Nilius, 11352507 Hoenderop, 14679186 van Abel, 16164647 Janssen, 12019295</p>	<p>Peng, 11097838; Peng, 10428857; Hirnet, 12765696 Hoenderop, 12574114 Niemeyer, 11248124 Van de Graaf, 12660155 van de Graaf 16565876 van de Graaf, 16354700 Voets, 11687570 Yue, 11287959; Voets, 12601087; Hoenderop, 11744752; Suzuki, 001091334. Wissenbach, 11278579;Zhuang, 12480925; Peng, 11401523; Peng, 11549322; Weber, 11741335;Nilius, 12077127 Hoenderop, 12574114 Voets, 14736889 Lambers, 15123711;Gkika 17005931;Nijenhuis, 14569082; Van Cromphaut, 11687634 Barley, 11208552; Peng, 10875938; Bianco, 17129178</p>
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