Supporting Information for

Structure of the mammalian TRPM7, a magnesium channel required during embryonic development

Jingjing Duan^{1*}, Zongli Li^{2*}, Jian Li^{3,4}, Raymond E. Hulse^{1,5}, Ana Santa-Cruz^{1,5}, William C. Valinsky⁵, Sunday A. Abiria¹, Grigory Krapivinsky¹, Jin Zhang^{3#} and David E. Clapham^{1,5,6#}

Affiliations:

¹Howard Hughes Medical Institute, Department of Cardiology, Boston Children's Hospital, Enders Building 1309, 320 Longwood Avenue, Boston, MA 02115, USA.

²Howard Hughes Medical Institute, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115, USA.

 ³School of Basic Medical Sciences, Nanchang University, Nanchang, Jiangxi, 330031, China.
⁴Department of Molecular and Cellular Biochemistry, University of Kentucky, Lexington, Kentucky 40536, USA.

⁵Howard Hughes Medical Institute, Janelia Research Campus, Ashburn, VA 20147, USA. ⁶Department of Neurobiology, Harvard Medical School, 220 Longwood Avenue, Boston, MA 02115, USA.

*These authors contributed equally to this work.

[#]Corresponding authors <u>zhangxiaokong@hotmail.com</u> (J.Z.), <u>claphamd@hhmi.org</u> (D.E.C.)

Figure legends of supplementary figures

Fig. S1. Biochemical and electrophysiological properties of the truncated TRPM7 construct used for structural investigation.

(a) Size exclusion chromatography trace of the MBP-tagged truncated mouse TRPM7 protein. Void volume and peak corresponding to tetrameric channels are indicated. Protein samples of the indicated TRPM7 protein fraction were subjected to SDS-PAGE and Coomassie-blue staining. (b) Representative micrograph of the negatively-stained image of the TRPM7 protein. (c) Whole-cell I-V relationship of HEK293T TRPM6/7 double KO cells transiently transfected with EGFP (gray) or the MBP-tagged truncated mouse TRPM7 construct (mTRPM7; black). Inward current and reversal potential are shown in the inset. (d) Mean current density at ± 100 mV (top) and -100 mV (bottom) of the conditions described in A (n = 3 EGFP; n = 7 mTRPM7). (e) Representative recording of current growth over time at +100 mV (black) and -100 mV (gray) during whole-cell dialysis. (f) Plot of time-to-peak current at +100 mV (n = 7). (g) Wholecell recording of mTRPM7 transfected cells elicited from the step protocol (21 steps of 500 ms duration in increments of $\pm 10 \text{ mV}$ from $\pm 100 \text{ mV}$ to $\pm 100 \text{ mV}$. (h) Whole-cell I-V relationship of mTRPM7 transfected cells before (2 mM Ca²⁺; black), and after (110 mM Mg²⁺; violet) perfusion of the high Mg²⁺ solution. Inward current and reversal potential are shown in the inset. (i) Current density at +90 mV for the conditions described in F (n = 5). Current is presented in nA and current density in pA/pF. Averaged data are presented as mean \pm SEM.

Fig. S2. Flow chart for cryo-EM data processing.

Cryo-EM data processing of TRPM7-EDTA (**a**), TRPM7-Mg²⁺ (**b**), and TRPM7-DVF (**c**). These show representative images of the purified TRPM7 protein, 2D class averages of TRPM7 particles, side views of the 3D reconstructions from RELION 3D classification, final reconstructions from 3D auto-refinement, Fourier shell correlation (FSC) curves for the 3D reconstructions, local resolution maps (from ResMap (1)) and Euler distribution plots of particles used in the final three-dimensional reconstructions, with regions in red denoting the views containing the highest number of particles.

Fig. S3. Cryo-EM densities of selected regions of TRPM7.

Density maps showing the transmembrane helices (S1-6), TRP domain and coiled-coil domain of TRPM7-Mg²⁺ (top), TRPM7-DVF (middle), and TRPM7-EDTA (bottom). The maps were contoured at a level of 5.0σ .

Fig. S4. Comparison of the transmembrane domains of TRPM7 with other known TRP channel structures.

Side views of the channel transmembrane domain monomers for TRPM7-Mg²⁺ (pink, PDB: 6BWD), TRPV1 (cyan, PDB:3J5P), TRPA1 (green, PDB:3J9P), PKD2 (polycystin-2; blue, PDB:5T4D), and TRPML1 (orange, PDB:5WPV; left). TRPM7-Mg²⁺ and TRPV1 are directly compared at right.

Fig. S5. Comparison of TRPM7 with other known TRPM structures.

(a) Superimposed side views of TRPM7-Mg²⁺ (blue, PDB:6BWD), TRPM4 (gray, PDB:6BWI),
TRPM2 (yellow, PDB:6CO7) and TRPM8 (green, PDB:6BPQ) monomers, showing overall

similarity in these structures. Regions of the (**b**) S2-S3 helix and (**c**) pre-S1 helix are enlarged. Intracellular domains of TRPM structures including the (**d**) N and (**e**) C termini are aligned for comparison. N termini are shown with the linker-helical domain (LH), ankyrin-repeat domain (AR) and the N-terminal domain (NT). C termini are shown with the connecting helices (CH) and coiledcoil domain (CC).

Fig. S6. Sequence alignment of TRPM7 to TRPM family members.

Regions of the C terminus (a.a. 1150-1280) of mouse (**a**) and human (**b**) TRPM7 to other TRPM family members are shown with the connecting helix (a.a. 1165-1189) and the coiled-coil domain (a.a. 1194-1224) highlighted in boxes. The pore domain of TRPM7 mouse (**c**) and human (**d**) were aligned with other TRPM members. Regions corresponding to the pore helix (a.a. 1031-1043) are boxed. The selectivity filter (yellow), lower gate (yellow), and two highly conserved cysteines are (red circles) marked. Sequence alignments used Clustal Omega.

Fig. S7. Comparison of the ion conducting pathway in TRPM7 structures with other available TRPM structures.

(a) The conduction pathway of TRPM7-Mg²⁺ (blue), TRPM7-DVF (pink) and TRPM7-EDTA (orange) are compared; distances between specific side chains along the pore are listed. (b) The pore regions of TRPM7 (TRPM7-Mg²⁺, blue), TRPM4 (gray) and TRPM2 (yellow) are compared with key residues labeled. (c) Superimposed side views of (b).

Fig. S8. Density maps of the TRPM7-Mg²⁺ and TRPM7-EDTA structures at the Mg²⁺-binding site.

Density map of TRPM7-Mg²⁺ (blue) shown at three different contour levels: $\sigma=3$ (**a**), $\sigma=4$ (**c**) and $\sigma=5$ (**e**). Density map of TRPM7-EDTA (pink) shown at three different contour levels: $\sigma=3$ (**b**), $\sigma=4$ (**d**) and $\sigma=5$ (**f**).

	TRPM7-Mg ²⁺	TRPM7-DVF	TRPM7-EDTA
	(EMD-7297)	(EMD-7298)	(EMD-6975)
	(PDB 6BWD)	(PDB 6BWF)	(PDB 5ZX5)
Data collection and processing			
Magnification	40607	40607	40607
Voltage (kV)	300	300	300
Electron exposure $(e - / Å^2)$	52.8	52.8	52.8
Defocus range (µm)	1.5-3.0	1.5-3.0	1.5-3.0
Pixel size (Å)	1.23	1.23	1.23
Symmetry imposed	C4	C4	C4
Initial particle images (#)	897,613	721,767	2,068,004
Final particle images (#)	232,930	206,032	1,039,775
Map resolution (Å) FSC threshold	3.7	4.1	3.28
Refinement			
Initial model used (PDB code)	de novo	de novo	de novo
Model resolution (Å)	3.7	4.1	3.28
FSC threshold			
Model composition			
Non-hydrogen atoms	25621	23944	25444
Protein residues	3236	3108	3256
Ligands	1	0	0
r.m.s. deviations			
Bond lengths (Å)	0.01	0.01	0.01
Bond angles (°)	1.27	1.51	1.60
Validation			
MolProbity score	2.03	2.02	1.73
Ramachandran plot			
Favored (%)	97.82	95.36	96.05
Allowed (%)	2.05	4.51	3.69
Disallowed (%)	0.13	0.13	0.26

Table S1. Cryo-EM data collection, refinement and validation statistics

References:

1. Kucukelbir, A., Sigworth, F.J. & Tagare, H.D. Quantifying the local resolution of cryo-EM density maps. *Nat Methods* **11**, 63-5 (2014).











a. Connecting helix and coiled-coil domain (TRPM7 mouse aa 1150-1280)

			1150 _	
sp	0923J1	TRPM7 MOUSE	OVKAISNIVWKYORYHFIMAYHEKPVLPPPLIILSHIVSLFCCVCKRRKKDK	1153
sp	Q2TV84	TRPM1 MOUSE	EVKSISNOVWKFORYOLIMTFHDRPVLPPPMIILSHIYIIIMRLSGRCRKKREGDOEE	1183
sp	Q91YD4	TRPM2 MOUSE	EVQEHTDQIWKFQRHDLIEEYHGRPPAPPPLILLSHLQLLIKRIVLKIPAK	1101
tr	F6M2J8	TRPM3 MOUSE	EVKSISNQVWKFQRYQLIMTFHERPVLPPPLIIFSHMTMIFQHVCCRWR-KHESDQDE	1186
sp	Q7TN37	TRPM4_MOUSE	KVHGNSDLYWKAQRYSLIREFHSRPALAPPLIIISHVRLLIKWLRRCRRCR-RANLPASP	1103
sp	Q9JJH7	TRPM5_MOUSE	VVQGNADMFWKFQRYHLIVEYHGRPALAPPFILLSHLSLVLKQVFRKEAQH	1033
sp	Q8CIR4	TRPM6_MOUSE	DIKSISNKLWKYNRYRYIMTYHQKPWLPPPFILLNHLCLLLRGLCCRPAPQDQEE	1135
sp	Q8R4D5	TRPM8_MOUSE	IVQENNDQVWKFQRYFLVQEYCNRLNIPFPFVVFAYFYMVVKKCFKCCCKE	1035
			** * ** ** * * * * ********************	
			Connecting helix (a.a. 1165-1189)	
sp	Q923J1	TRPM7_MOUSE	TSDGPKLFLTEEDQKKLHDFEEQCVEMYFDEKDDKFNSGSEERIRVTFERVEQMSIQIKE	1213
sp	Q2TV84	TRPM1_MOUSE	RDRGLKLFLSDEELKKLHEFEEQCVQEHFREKEDEQQSSSDERIRVTSERVENMSMRLEE	1243
sp		TRPM2_MOUSE	RHKQLKNKLEKNEETALLSWELYLKENYLQNQQYQQKQRPEQKIQDISEKVDTMVDLLDM	1161
tr	F6MZJ8	TRPM3_MOUSE	RDYGLKLFITDDELKKVHDFEEQCIEEYFREKDDKFNSSNDERIRVTSERVENMSMRLEE	1246
sp		TRPM4_MOUSE	VFEHFRVCLSREAERKLLTWESVHKENFLLAQARDRRDDDSERLKRTSQKVDTALKQLG-	1002
sp		TRPM5_MOUSE		1105
sp		TRPM0_MOUSE		1000
sp	QOK4D3	TRPM6_MOUSE	.* . . .	1090
			Coiled coil domain $(2.2, 1104, 1224)$	
sp	0923J1	TRPM7 MOUSE	V-GDRVNYIKRSLOSLDSOIGHLODLSALTVDTLKTLTAOKASEASKVHNEITR	1266
sp	02TV84	TRPM1 MOUSE	I-NERENFMKTSLOTVDLRLSOLEELSGRMVSALENLAGIDRSDLIOARSRASSECE-	1299
sp	Q91YD4	TRPM2 MOUSE	DQVKRSGSTEQRLASLEEQVTQVTRALHWIVTTLKDSGFGSGAGALTLAPQRAFDEPD	1219
tr	F6M2J8	TRPM3 MOUSE	V-NEREHSMKASLQTVDIRLAQLEDLIGRMATALERLTGLERAESNKIRSRTSSDCTD	1303
sp	Q7TN37	TRPM4_MOUSE	QIREYDRRLRGLEREVQHCSRVLTWMAEALSHSALLPPGAPPPPSPTGSKD	1213
sp	Q9JJH7	TRPM5_MOUSE	GLREQEKRIKCLESQANYCMLLLSSMTDTLAPGGTYSSSQNCGCRSQPASARDREY	1148
sp	Q8CIR4	TRPM6_MOUSE	M-NEKVSFIKDSLLSLDSQVGHLQDLSAITVDTLKVLSAVDTLQEDEILLANRKHSTCRK	1254
sp	Q8R4D5	TRPM8_MOUSE	DLKSLLKEIANNIK	1104
			1280	
	002271	MDDW7 MOUGH		1205
sp		TRPM7_MOUSE	-ELSISANLAQULIDDVFVKPLWA-APSAVNILS-SSLFQGD	12/5
sp		TRPMI_MOUSE		1266
- 5 μ	F6M2.TQ	TRPM3 MOUSE		1350
SD	0701200	TRPM4 MOUSE		1213
sp	09.1.117	TRPM5 MOUSE	LESGLPPSDT	1158
sp	08CIR4	TRPM6 MOUSE	RPHSWTNVICAKVLSDMESCGKKKLOYYSMPPSLLRSLARSOLP-PSVORGALVEVTHSK	1313
SD	08R4D5	TRPM8 MOUSE		1104
~ [2	201120			

b. Connecting helix and coiled-coil domain (TRPM7 human aa 1150-1280)

1150 Connecting helix (a.a. 1165-1189)		
sp 0960T4 TRPM7 HUMAN	RRKKDKTSDGPKLFLTEEDQKKLHDFEEQCVEMYFNEKDDKFHSGSEERIRVTF	1201
sp Q7Z4N2 TRPM1 HUMAN	KKREGDQEERDRGLKLFLSDEELKRLHEFEEQCVQEHFREKEDEQQSSSDERIRVTS	1186
sp 094759 TRPM2 HUMAN	AKRHKQLKNKLEKNEEAALLSWEIYLKENYLQNRQFQQKQRPEQKIEDIS	1152
sp Q9HCF6 TRPM3_HUMAN	-KHESDPDERDYGLKLFITDDELKKVHDFEEQCIEEYFREKDDRFNSSNDERIRVTS	1247
sp Q8TD43 TRPM4_HUMAN	SPQPSSPALEHFRVYLSKEAERKLLTWESVHKENFLLARARDKRESDSERLKRTS	1152
sp Q9NZQ8 TRPM5_HUMAN	EHKREHLERDLPDPLDQKVVTWETVQKENFLSKMEKRRRDSEGEVLRKTA	1082
sp Q9BX84 TRPM6_HUMAN	PHDQEEGDVGLKLYLSKEDLKKLHDFEEQCVEKYFHEKMEDVNCSCEERIRVTS	1177
sp Q7Z2W7 TRPM8_HUMAN	KEKNMESSVCCFKNEDNETLAWEGVMKENYLVKINTKANDTSEEMRHRFRQLD	1086
	. :* : . : : .	
	Coiled coil domain (a.a. 1194-1224)	
sp Q96QT4 TRPM7_HUMAN	ERVEQMCIQIKEV-GDRVNYIKRSLQSLDSQIGHLQDLSALTVDTLKTLTAQKASEASKV	1260
sp Q7Z4N2 TRPM1_HUMAN	ERVENMSMRLEEI-NERETFMKTSLQTVDLRLAQLEELSNRMVNALENLAGIDRSDLIQA	1245
sp 094759 TRPM2_HUMAN	NKVDAMVDLLDLDPLKRSGSMEQRLASLEEQVAQTAQALHWIVRTLRASGFSSEAD	1208
sp Q9HCF6 TRPM3_HUMAN	ERVENMSMRLEEV-NEREHSMKASLQTVDIRLAQLEDLIGRMATALERLTGLERAESNKI	1306
sp Q8TD43 TRPM4_HUMAN	QKVDLALKQLGHIREYEQRLKVLEREVQQCSRVLGWVAEALSRSALLPPGG	1203
sp Q9NZQ8 TRPM5_HUMAN	HRVDFIAKYLGGLREQEKRIKCLESQINYCSVLVSSVADVLAQGGG	1128
sp Q9BX84 TRPM6_HUMAN	ERVTEMYFQLKEM-NEKVSFIKDSLLSLDSQVGHLQDLSALTVDTLKVLSAVDTLQEDEA	1236
sp Q7Z2W7 TRPM8_HUMAN	TKLNDLKGLLKEIANKIK	1104
	1280	
sp Q96QT4 TRPM7_HUMAN	HNEITRELSISKHLAQNLIDDGPVRPSVWKKHG-VVN	1296
sp Q7Z4N2 TRPM1_HUMAN	RSRASSECE-ATYLLRQSSINSA-DGYSLYRYHFNGEELLFEDTSLS-	1290
sp 094759 TRPM2_HUMAN	VPTLASQKAAEEPDAEPGGRKKTEEPGDSYHVNARHLLYP	1248
sp Q9HCF6 TRPM3_HUMAN	RSRTSSDCTDAAYIVRQSSFNSQ-EGNTFKLQESIDPAGEETMSP-	1350
sp Q8TD43 TRPM4_HUMAN	PPPPDLPGSKD	1214
sp Q9NZQ8 TRPM5_HUMAN	PRSSQHCGEGSQLVAADHRGGLDGWEQPGAGQPPSDTSDT	1165
sp Q9BX84 TRPM6_HUMAN	LLAK-RKHSTCKKLPHSWSNVI-CAEVLGSMEIAGEKKY-QYYSMPS	1280
sp Q7Z2W7 TRPM8_HUMAN		1104

c. Pore domain (TRPM7 mouse aa 1016-1100)

			1016 Pore belix (a a 1031-1043) 1056	_
sp	Q923J1	TRPM7_MOUSE	FYIVVIMALVLLSFGVPRKAILYPHEEPSWSLAKDIVFHPYWMIFGEVYAYEIDVCAN-	- 1058
sp	Q2TV84	TRPM1_MOUSE	LYFVVIMLVVLMSFGVARQAILHPEEKPSWKLARNIFYMPYWMIYGEVFADQIDLYAM-	- 1069
sp	Q91YD4	TRPM2_MOUSE	FFFLFLLAVWVVSFGVAKQAILIHNESRVDWIFRGVVYHSYLT <mark>IFGQ</mark> IPTYIDGVNFS-	M 990
tr	F6M2J8	TRPM3_MOUSE	MYFVIIMLVVLMSFGVARQAILFPNEEPSWKLAKNIFYMPYWM <mark>IYGE</mark> VFADQI	- 1073
sp	Q7TN37	TRPM4_MOUSE	FFFLFFLCVWLVAYGVATEGILRPQDRSLPSILRRVFYRPYLQ <mark>IFGQIPQEEMDVALMI</mark>	P 986
sp	Q9JJH7	TRPM5_MOUSE	FFFLFFLSVWLVAYGVTTQALLHPHDGRLEWIFRRVLYRPYLQ <mark>IFGQ</mark> IPLDEIDEA-	R 929
sp	Q8CIR4	TRPM6_MOUSE	FYIVIIMAIVLLSFGVARKAILSPKEPPSWRLARDIVFEPYWMMYGEVYASDIDVCSN-	- 1041
sp	Q8R4D5	TRPM8_MOUSE	FFFLFLFAVWMVAFGVARQGILRQNEQRWR <mark>WIFRSVIYEPYLA</mark> MFGQVPSDVDSTTYD-	F 926
			1066 Selectivity filter (a.a. 1045-1047)	0
sp	Q923J1	TRPM7_MOUSE	DSTLPTICGPGTWLTPFLQAVYLFVQYIIMVNLLIAFFNNVY	L 1101
sp	Q2TV84	TRPM1_MOUSE	EINPROGENLYDEEGKRLPPOIPGAWLTPALMACYLLVANILLVNLLIAVFNNTF	F 1125
sp	Q91YD4	TRPM2_MOUSE	DQCSPNGTDPYKPKCPESDWTGQAPAFPEWLTVTLLCLYLLFANILLLNLL	Q 1050
tr	F6M2J8	TRPM3_MOUSE	DPFCGQNETREDGKTIQLPFCKTGAWIVPAIMACYLLVANILLVNLLIAVFNNTF	F 1129
sp	Q7TN37	TRPM4_MOUSE	GNOSMERGSWAHPEGPVAGSOVSQYANWLVVLLLIVFLLVANILLLNLL	S 1044
sp	Q9JJH7	TRPM5_MOUSE	VNOSLHPLLLE-SSASOPNLYANWLVILLLVTFLLVTNVLLMNLLIAMFSYTF	Q 982
sp	Q8CIR4	TRPM6_MOUSE	ETSCPPGSFLTPFLQAVYLFVQYIIMVNLLIACFNNIY	L 1080
sp	Q8R4D5	TRPM8_MOUSE	SHOFFSG-NESKPLOVEL-DEHNLPRFPEWITIPLVCIYMLSTNILLVNLLVAMFGYTV	G 984

Lower gate (a.a. 1093-1097)

d. Pore domain (TRPM7 human aa 1016-1100)

	1016	Pore hel	ix (a.a. 1031-	1043)	
HUMAN	MMIGKMVANMFYIVVIMALVLLSFGVPRKAILYPHEAPS	WT <mark>LAKD</mark> I	VFHPYWMI	FGE <mark>VYA</mark>	1050
HUMAN	MMIGKMMIDMLYFVVIMLVVLMSFGVARQAILHPEEKPS	WKLARNI	FYMPYWMI	YGEVFA	1016
HUMAN	IIVKRMMKDVFFFLFLLAVWVVSFGVAKQAILIHNERRV	DWLFRGA	VYHSYLTI	FGQ <mark>IPG</mark>	984
B_HUMAN	MMIGKMMIDMMYFVIIMLVVLMSFGVARQAILFPNEEPS	WKLAKNI	FYMPYWMI	YGEVFA	1083
HUMAN	VIVSKMMKDVFFFLFFLGVWLVAYGVATEGLLRPRDSDF	P <mark>S</mark> ILRRV	FYRPYLQI	FGQ <mark>IPQ</mark>	980
5_HUMAN	IVVERMMKDVFFFLFFLSVWLVAYGVTTQALLHPHDGRL	EWIFRRV	LYRPYLQI	FGQIPL	923
5_HUMAN	TMIAKMTANMFYIVIIMAIVLLSFGVARKAILSPKEPPS	WS <mark>LARD</mark> I	VFEPYWMI	YGE <mark>VYA</mark>	1027
B_HUMAN	IMLQRMLIDVFFFLFLFAVWMVAFGVARQGILRQNEQRW	RWIFRSV	IYEPYLAM	FGOVPS	917
	1 <u>056</u> 1066	Selec	tivity filter (a	a.a. 1045-	1047)
HUMAN	YEIDVOANDSVIPQIOGPG	TWLTPFL	QAVYLFVQ	YIIMVN	1090
HUMAN	DQIDLYAMEINPPOGENLYDEEGKRLPPOIPG	AWLTPAL	MACYLLVA	NILLVN	1069
HUMAN	Y-IDGVNFNP-EHCSPNGTDPYKPKOPESDATQQRPAFP	EWLTVLL	LCLYLLFT	NILLLN	1042
 HUMAN	DQIDPPOGQNETREDGKIIQLPFOKTG	AWIVPAI	MACYLLVA	NILLVN	1131
HUMAN	EDMDVALMEH-SNOSSEPGFWAHPPGAQAGTOVSQYA	NWLVVLL	LVIFLLVA	NILLVN	1037
5_HUMAN	DEIDEARVNOSTHPLLLEDSPSOPSLYA	NWLVILL	LVTFLLVT	NVLLMN	972
5_HUMAN	GEIDVOSSQPSOPPG	SFLTPFL	QAVYLFVQ	YIIMVN	1063
B_HUMAN	D-VDGTTYDF-AHOTFTGNE-SKPLOVELDE-HNLPRFP	EWITIPL	VCIYMLST	NILLVN	973
	: 1100	::. :	* * *	:::*	
_HUMAN	LLIAFFNNVYLQVKAISNIVWKYQRYHFIMAYHEKPVLP	PPLIILS	HIVSLF	-CCICK	1147
_HUMAN	LLIAVFNNTFFEVKSISNQVWKFQRYQLIMTFHDRPVLP	PPMIIL <mark>S</mark>	HIYIIMR	LSGRCR	1129
2_HUMAN	LLIAMFNYTFQQVQEHTDQIWKFQRHDLIEEYHGRPAAP	PPFILL <mark>S</mark>	HLQLFIKR	VVLKTP	1102
B_HUMAN	LLIAVFNNTFFEVKSISNQVWKFQRYQLIMTFHERPVLP	PPLIIF <mark>S</mark>	HMTMIFQH	LCCRWR	1191
L_HUMAN	LLIAMFSYTFGKVQGNSDLYWKAQRYRLIREFHSRPALA	PPFIVI <mark>S</mark>	HLRLLLRQ	LCRRPR	1097
5_HUMAN	LLIAMFSYTFQVVQGNADMFWKFQRYNLIVEYHERPALA	PPFILLS	HLSLTLRR	VFKKEA	1032
5_HUMAN	LLIAFFNNVYLDMESISNNLWKYNRYRYIMTYHEKPWLP	PPLILLS	HVGLLLRR	LCCHRA	1123
B_HUMAN	LLVAMFGYTVGTVQENNDQVWKFQRYFLVQEYCSRLNIP	FPFIVFA	YFYMVVKK	CFKCCC	1033
	:*********************************	* : * : : :	:		
	Lower gate (a.a. 1093-1097)				

sp	Q96QT4	TRPM7_	HUMAN
sp	Q7Z4N2	TRPM1_	HUMAN
sp	094759	TRPM2	HUMAN
sp	Q9HCF6	TRPM3_	HUMAN
sp	Q8TD43	TRPM4	HUMAN
sp	Q9NZQ8	TRPM5	HUMAN
sp	Q9BX84	TRPM6_	HUMAN
sp	Q7Z2W7	TRPM8	HUMAN
sp	Q96QT4	TRPM7_	HUMAN
sp	Q7Z4N2	TRPM1_	HUMAN
sp	094759	TRPM2	HUMAN

sp|094759|TRPM2_HUMAN sp|Q9HCF6|TRPM3_HUMAN sp|Q8TD43|TRPM4_HUMAN sp|Q9NZQ8|TRPM5_HUMAN sp|Q9BX84|TRPM6_HUMAN sp|Q7Z2W7|TRPM8_HUMAN

sp	Q96QT4	TRPM7_HUMAN
sp	Q7Z4N2	TRPM1_HUMAN
sp	094759	TRPM2_HUMAN
sp	Q9HCF6	TRPM3_HUMAN
sp	Q8TD43	TRPM4_HUMAN
sp	Q9NZQ8	TRPM5_HUMAN
sp	Q9BX84	TRPM6_HUMAN
sp	Q7Z2W7	TRPM8_HUMAN







е



5.0 σ





3.0 σ

d

f

b



5.0 σ