

**Figure S9.**

MC5R-Human	1	-----MNSS-----FHLHFLDLNLNATEGNL	21
P2Y6-Human	1	-----MAAD-----LGPWNDTINGTWDGDE	20
P2Y6-Takifugu	1	-----FFTEGVISLTSLDFASSEPF TGPNTHNI IKGI	32
P2Y6-Tetraodon	1	-----MPGSAHLGPFLTESVIRTSLAFPSSEPFADLNNTNNTN-	40
P2Y6-Medaka	1	-----TEPY-----GADIFSVGNSSSVAET	20
P2Y6-Sickleback	1	LGNPLLFSRRLLAGSVHLFQTASCEWETETLISDSFPSDSFSTSAWPPET	50
P2Y6-Danio	1	-----LKMD-----SLNVSTM	11

			<b>TM1</b>	
MC5R-Human	22	SGPN-----VKNKSSPCEDMG--IAVEVFLTLGVISLLENIL		56
P2Y6-Human	21	LGYR-----CRFN----EDFKYVLLPVSYGVVVCVPGLCNAV		53
P2Y6-Takifugu	33	SNSN-----CTYK----EDFKRILLPTVYTMVCLLGLPLNTV		65
P2Y6-Tetraodon	41	-----CTYK----EDFKRILLPAVYTLVLLGLPLNAV		69
P2Y6-Medaka	21	ASPR-----CTYK----EDFKOILLPAVYSIVFLLGFPNAA		53
P2Y6-Sickleback	51	YAADGFVANVSVSGALRCTYK----EDFKRILLPAVYTLVFLGLPLNVA		96
P2Y6-Danio	12	ALPS-----CTYK----EDFKRFLLPVYSLVFIIFGLPLNFI		44

			<b>TM2</b>	
MC5R-Human	57	VIGAVKKNKLNHSPMYFFVCSLAVADMLVSMSSAWETITIIYLLNNKHLVI		106
P2Y6-Human	54	ALYIFLCRLKTWNASTTYMFHLAVSDALYAAS--LPLLVIYYVARGDHWPF		101
P2Y6-Takifugu	66	VILKIWRARPNSRSNIYMLNLAIAADFLYVMS--LPLLVIYNYGSRDYWPF		113
P2Y6-Tetraodon	70	VILKIWRTRPNLSRNNIYMLNLAIAADFLYVTS--LPLLIYNYGSRDYWPF		117
P2Y6-Medaka	54	VILKIWRTRPNLSRSNIYMLNLAIAADFLYVMS--LPLLIYNYASHDYWPF		101
P2Y6-Sickleback	97	VILKIWRTRPKLSKSNVYMLNLAIAADFLYVMS--LPLLIYNYGSHDHWPF		144
P2Y6-Danio	45	IILRVWGSRRALTRTKIYMLNLAIVADFLYVCS--LPLLIYNYASKDYWPF		92

		120c		
			<b>TM3</b>	###
MC5R-Human	107	ADAFVRHIDNVFDSMICISVVASMCSSLATAVDRYVITIFYALRYHHIMTA		156
P2Y6-Human	102	STVLCKLVRFQFYTNLYCSILFLTC----ISVHRC LGVLRPLRSL--RWGR		146
P2Y6-Takifugu	114	GEFTCKLVRFQFYSNLHGSILFLTC----ISVQRYVGVCHPLAMWHKKG		159
P2Y6-Tetraodon	118	GELTCKLVRFQFYSNLHGSILFLTC----ISVQRYVGI CHPLAMWHKRG		163
P2Y6-Medaka	102	GEFTCKLVRFQFYSNLHGSILFLTC----ISMQRYMGI CHPLAVWHKOG		147
P2Y6-Sickleback	145	GEFTCKLVRFQFYSNLHGSILFLTC----ISVQRYVGI CHPMAMWPROG		190
P2Y6-Danio	93	GDFTCRLVRFQFYSNLHGSIFFLTC----ISFQRYMGI CHPLSLWPKOG		138

			<b>TM4</b>	
MC5R-Human	157	RRSG-ATIAGIWAFC TGGGIVF ILYSES-----TYV		186
P2Y6-Human	147	ARYARRVAGAVVWLVLACQAPVLYFVTTTSARGGRVTCHDTSAPELFSRFV		196
P2Y6-Takifugu	160	RKMWRVCGGVWLLVIALCAPTFHF AATGVQRNRTVCYDLSTPAHSVDYY		209
P2Y6-Tetraodon	164	RKMWRVCGAVWLLVIALCAPTFHF AETGIQRNRTVCYDLSTPARSVDYY		213
P2Y6-Medaka	148	RKKVWLCGGVWLLVITLCAPTFYFAS TGTQRNRTVCYDLSTPORSGDYY		197
P2Y6-Sickleback	191	IRLAWCICGGVWLVVVL CAPTFHF AATGTQRNRTVCYDLSTPKSSLDYY		240
P2Y6-Danio	139	RRLAWWVCAGVWVAVALCAPTFEF AATGTQRNRTVCYDLSEPSRSTSYF		188

			<b>TM5</b>	
MC5R-Human	187	ILCLISMFFAMFLLVSLYTHMFLLRTHVKRIAALPGASSARORTSMQG		236
P2Y6-Human	197	AVSSVMLGLLFAVPFAVILVCYVLMARR--LLKPAY--GTS GGLPRAKRKS		243
P2Y6-Takifugu	210	PYGMALTCGLFLLPFLGIMVCYCRMAOI--LCRPVSYQGVSMATKEKRKA		258
P2Y6-Tetraodon	214	PYGMALTCGLFLLPFLGIMVCYCRMAOI--LCRPVSYRGVSMATGEKRDKA		262
P2Y6-Medaka	198	PYGLALTLGLFLLPFLGIMVCYCOMARI--LCRPVSHQGVPMATGEKRDR		246
P2Y6-Sickleback	241	PYGMALTCGLFLLPFLGIMVCYCRMACI--LCRPVTYRGVSMATGEKRDOA		289
P2Y6-Danio	189	PYGIALTFLGFVVPFLVIIVLYCKMARV--LWQVGEAREVSAA--EKKNKA		235

TM6

MC5R-Human	237	AVTVTMLLGVFTVCWAPFFLHLTLMLSCPO--NLYCSR---FMSHFNMYL	281
P2Y6-Human	244	VRTIAVVLAVFALCFLPFHVTRTLYSFRSL-DLSCHTLNAINMAYKVTR	292
P2Y6-Takifugu	259	VRMIIVVAVTFVCISFLPFHLTKTVYLVVRSFPGTPCETKNLFSVIYKSTR	308
P2Y6-Tetraodon	263	VKMIIVVAAVFCISFLPFHLTKTVYLVVRSIQGMPCTRNLFSDVIYKSTR	312
P2Y6-Medaka	247	VRMIIVVASVFCVSVFLPFHLTKTVYLVVRTLPHASCETRNLFSDVIYKSTR	296
P2Y6-Sickleback	290	VRMIIVVAVTFVCISFLPFHLTKTVYLVVRTLPGAPCETRNLFSDVIYKSTR	339
P2Y6-Danio	236	VRMIIVVAVTFVCISFLPFHVTKTVYLVVRSVPTAPCELNLFSDVIYKSTR	285

TM7

MC5R-Human	282	ILIMCNSVMDPLIYAFRSOE-----MRKTF	306
P2Y6-Human	293	PLASANSCLDPVLYFLAGORLVRFARDAKPPTGSPATPARRRLGLRRSD	342
P2Y6-Takifugu	309	PFASMNSFLDPILFYFTQPR-----YRQST	333
P2Y6-Tetraodon	313	PFASMNSFLDPILFYFTQPR-----YRQST	337
P2Y6-Medaka	297	PFASMNSFLDPILFYFTQPR-----YRRST	321
P2Y6-Sickleback	340	PFASMNSFLDPILFYFTQPR-----YR---	361
P2Y6-Danio	286	PFASMNSVLDPILFYFTQPO-----YRRST	310

MC5R-Human	307	KEIICCRGFRIACSFPRD-----	325
P2Y6-Human	343	RTDMORIEDVLGSSSEDSRRTESTPAGSENTKDIRL	377
P2Y6-Takifugu	334	KRFVLRVTTLKG-----	345
P2Y6-Tetraodon	338	RRFVLRV-----	344
P2Y6-Medaka	322	RRLLLRVTARGDKAPPTLKKHSTSASLYCRYEL--	354
P2Y6-Sickleback	-	-----	-
P2Y6-Danio	311	KSLLLKITSLKDKTVKV-----	327