

Figure S7.

MC5R-Human	1	-----MNSSFHLHFLDLNLNATEGNLSGPNVK-NKSSPCEDM	36
P2Y2-Human	1	-----MAADLGPWNDTINGTWGDDELGYRCRFNEDFKYVLL	36
P2Y2-Takifugu	1	-----INP--LYCKFOEDFKYILL	17
P2Y2-Tetraodon	1	-----MVALDNATVDP--LYCKFKEDFKYILL	25
P2Y2-Medaka	1	RALPSAVNLVNLASAGVSTSNMNASGLNLTENNRSRDFCRFNEDFKFILL	50
P2Y2-1-Stickleback	1	-----IFITKMATWDNNVTSQTNYSN--FYCRFEERFKYILL	35
P2Y2-2-Stickleback	1	-----WDNNVTSQTNYSN--FYCRFEERFKYILL	27
P2Y2-1-Danio	1	-----MATFNNTTIA-NASDL--YSCIFDETFKYILL	29
P2Y2-2-Danio	1	-----MAAFNNTGPT-NGSNE--TDCDLQDDFKHILL	29
P2Y2-3-Danio	1	----MICFLCLNLRQIWIRMAMNNTTVSTNDIDI--YRCTLKEDFKYILL	44
P2Y2-Callorhinchus	1	-----YNCTFNEEFKYILL	14

		TM1		TM2		
MC5R-Human	37	GI	AVEVFLTLGVISLLENILVIGAI	VKKNLHSPMYFFVCSLAVADMI	VS	86
P2Y2-Human	37	PVS	YGVVCPG---	LCLNAVALYIFLCRLKTWNASTTYMFHLAVSDALYA		83
P2Y2-Takifugu	18	PVS	YALVFVFG---	LALNGTALYVIVFRTRLWKPSTIYMFNLTMCDTLYI		64
P2Y2-Tetraodon	26	PVS	YALVFVFG---	LALNGLALYVIVFRTRKAWKPSIVYMFNLTMCDTLYI		72
P2Y2-Medaka	51	PVS	YALVFVFG---	LALNFTALFVMVFRTRKHWKPSIYMFNLTMCDTLYI		97
P2Y2-1-Stickleback	36	PVS	YSLVFVIG---	LALNATALYVMLFRTKRWKSSTIYMFNLTVCDTLYV		82
P2Y2-2-Stickleback	28	PVS	YSLVFVIG---	LALNATALYVMLFRTKRWKSSTIYMFNLTVCDTLYV		74
P2Y2-1-Danio	30	PVS	YSLVFVFG---	LGLNITAMYVILFRTKOWKPNTIYMINLNACDTLYI		76
P2Y2-2-Danio	30	PVS	YSLVFVFG---	LGLNITAMYFIFFRTKOWKPNTIYIINLSICDTLYI		76
P2Y2-3-Danio	45	PVS	YSLVFVFG---	LGLNITAMYFILFOTKHWKPNTIYMINLNACDTLYI		91
P2Y2-Callorhinchus	15	PVS	YGVIVFVVG---	LVLNCLAIWVVFVRMRPWNTTITTYMFNLAI	SDTMYV	61

				124a		
				TM3		
MC5R-Human	87	MSS	AWETITITVLLN	NKHLVIADAFVRHIDNVFDSMICISVVASMC	SLLAI	136
P2Y2-Human	84	ASL	PL--LVYYYARGDHWPF	STVLCCLVRFVLYTNLYCSILFLTC---	I	127
P2Y2-Takifugu	65	LTL	PF--LIYYYADENDWPF	SEPLCKIIRFLFYANLYGSILFLCC---	I	108
P2Y2-Tetraodon	73	LTL	PF--LIYYYADENDWPF	SEPFCKIIRFLFYANLYGSILFLCC---	I	116
P2Y2-Medaka	98	FTL	PF--LIFYYADENDWPF	TEPLCKMIRFLFYSNLYGSILFMCC---	I	141
P2Y2-1-Stickleback	83	LTL	PF--LIYYYADENDWPF	SEPLCKIIRFLFYTNLYGSIMFLCC---	I	126
P2Y2-2-Stickleback	75	LTL	PF--LIYYYADENDWPF	SEPLCKIIRFLFYTNLYGSIMFLCC---	I	118
P2Y2-1-Danio	77	LTL	PF--LIYYYADENAWPF	GELMCKLIRFLFYTNLYGSILFLSC---	I	120
P2Y2-2-Danio	77	LTL	PF--LIYYYADESDWPF	GEAMCKFIRFLFYTNLYGSILFLSC---	I	120
P2Y2-3-Danio	92	LTL	PF--LIYYYAGANAWPF	GDPMCRFIRFFYTNLYGSILFLSC---	I	135
P2Y2-Callorhinchus	62	ISL	PL--LVYYYARRNWPFGAAL	CKIVRFLFYTNLYCSILFLTC---	M	105

				181c		
		###		TM4		
MC5R-Human	137	AVD	RYVTFYALRYHHIMTARRSGAIIAGI	WAF---CTGCGIVFILI	YSES	183
P2Y2-Human	128	SVH	RCLGVLRPLRSLRWGRARYARRVAGAVWV	LVLACQAPVLYFV	TTSAR	177
P2Y2-Takifugu	109	SLH	RFIGICYPVRSLYWLSARRAKFISAAV	WGVVLCQGPVLYFS	RIRDK	158
P2Y2-Tetraodon	117	SLH	RFIGVCPVRSLYWLSARRAKFISAVAV	WVLSQSPVLYFS	RIRDK	166
P2Y2-Medaka	142	SLH	RFIGICFPVRSLSWVSTRRARLVSAV	WASVLFQCGPVLYFS	RTRST	191
P2Y2-1-Stickleback	127	SLH	RFIGVCPVRSLSWVSARRAKLVSAV	WACVLLCQAPILYFS	RTSKS	176
P2Y2-2-Stickleback	119	SLH	RFIGVCPVRSLSWVSARRAKLVSAV	WACVLLCQAPILFF	TRTSVR	168
P2Y2-1-Danio	121	SVH	RFIGVCHPVRSLSWTNARRARFISL	CIWATMLIFQAPILYFS	RMKSD	170
P2Y2-2-Danio	121	SVH	RFIGVCHPVRSLSLNTQYARIVSV	GIWVILILQAPILFF	SRTTQK	170
P2Y2-3-Danio	136	SVH	RFIGVCHPVRSLSWMNARRARWISV	GIWLIILILQTPLLYFS	RTLNL	185
P2Y2-Callorhinchus	106	SIH	RFLGVCFPMESLRWVKVRNTRIVCAV	VWVIVIMCQAPILAFV	TTEDEK	155

**TM5**

MC5R-Human	184	TYV-ILC-----LISMFF----AMLFLLVSLYIHMFLLRARTHVKRIAA	221
P2Y2-Human	178	GGR-VTCHDTSAPELFSRFVAYSSVMLGLLFAVPPFAVILVCYVLMARRLL	226
P2Y2-Takifugu	159	NSS-RTCYDITTSPELFDDFLVYSSVISVLMFALPFMVVLCNGLMVRKLL	207
P2Y2-Tetraodon	167	NSS-RICVDITTSPELFDDFLVYSSVISVLMFALPFMIVMVCNGLMVRKLL	215
P2Y2-Medaka	192	TTKQIICVDITTSPELFDDFLVYSSVISVLMFALPFMVLMVCYGLMVRKLL	241
P2Y2-1-Stickleback	177	ESV-RICVDITTSPELFDDFLVYSSVISVLMFALPFMVVMVCYGLMVRKLL	225
P2Y2-2-Stickleback	169	EGK-RICVDITTSPELFDDFLVYSSVISVLMFALPFMVVMVCYGLMVRKLL	217
P2Y2-1-Danio	171	T---MVCYDITTSPELFDDFLVYSSVVMLELLFVLPFGVVLVCNAMMVKKLR	217
P2Y2-2-Danio	171	KD--IVCHDITTSPELFDDFLVYSSVVMLELLFGLPFVVLVCNAMMVKKLR	218
P2Y2-3-Danio	186	DEV-LVCHDITTSPELFDDFLVYSSVVMLELLFVLPFGVVLVCNFLIVKKLR	234
P2Y2-Callorhinchus	156	GTN-TLCYDITTSRENFNQFVIYNMVQLVLLFCGPFVIVMVCYWFMTKELL	204

**TM6**

MC5R-Human	222	LPGASS-----ARORTSMOGAVTVTMLLGVFTVCWAPFFLHLTLMLS	263
P2Y2-Human	227	KPAYGT-----SGGLPRAKRKSVRTIAVVLAVFALCFLPFHVTRTLIYS	270
P2Y2-Takifugu	208	EFSWRS-----EGRAEGKSVKMI IIVLATFMLCFLPFHLTRSLIYS	248
P2Y2-Tetraodon	216	EVSWRS-GAKRGNLSARQSRQKSVKMI IIVLATFMLCFLPFHLTRSLIYS	264
P2Y2-Medaka	242	EPGWGP-GGE--VLTAORTKOKSVKMI IIVLAAFMLCFLPFHLTRSLIYS	288
P2Y2-1-Stickleback	226	EPGWASEGGERGGLSARRLKOKSVKMI IIVLATFMICFLPFHLTRSLIYS	275
P2Y2-2-Stickleback	218	EPGWASEGGTRGGLSARRLKOKSVEMI IIVLAMFILCFLPFH-----	259
P2Y2-1-Danio	218	EPGVGD-----GPMSQKSKOKSVKMI IIVLVAFMLCFLPFHVNRSIYYG	261
P2Y2-2-Danio	219	EPRVGG-----GSTSORSKOKSVKMI IIVLLTFILCFLPFHVNRIVHYT	262
P2Y2-3-Danio	235	EPGVGD-----APTSORSKOKSVKMI IIVLVAFMLCFLPFHVNRSVYYT	278
P2Y2-Callorhinchus	205	RPNTAH-----PENSRSRKSIKMIIVILSVFVLCFLPFHITRSIYS	247

267a

**TM7**

MC5R-Human	264	CPO-----NLYCSRFSHFNMVLI---LIMCNSVMDPLIYAFRSQEM	302
P2Y2-Human	271	FRSL-----DLSCHTLEINMAYKVTRPLASANSCLDPVLYFLAGQRL	313
P2Y2-Takifugu	249	FRYLRLQISP-QOITCNTLEAINVAYKVTRPLASANSCLDPILYFLAGQDI	297
P2Y2-Tetraodon	265	FRYLIR-----OITCGMLEAINVAYKVTRPLASANSCLDPILYFLAGQDI	308
P2Y2-Medaka	289	LRYLR-----KVSCSLESSVAYKVTRPLASANSVDPILYFLAGQGT	332
P2Y2-1-Stickleback	276	FRYLRLQVDPSQA-----SSVAYKVTRPLASTNSCVDPILYFLAGQNR	318
P2Y2-2-Stickleback	-	-----	-
P2Y2-1-Danio	262	FRYLDK----QVSCSMLEIASMAYKITRPLASANSCLDPILYFMAGQGFK	307
P2Y2-2-Danio	263	LRYM-----DRSCDQLRLSNIIYQATRPLLSINSCIDPILYFMAGQSFR	306
P2Y2-3-Danio	279	LRYLD-----QANCTVIRLSNNVYKATRPLVSNFNSCIDPILYFMAGQSFR	323
P2Y2-Callorhinchus	248	SRSIL-----HLSCTLENAVNLAYKLTRPLASANSCLDPILYVLAGO---	288

MC5R-Human	304	RKTFKEIICCRGFRIACSFPRD-----	325
P2Y2-Human	315	VRFARDAKPPGSPATPARRRLGLRRSDRTDMQRIEDVLGSSSEDSRRT	363
P2Y2-Takifugu	299	RSNLTKKSRTTTHKAGMKMCERKHROIATMLHTAVTSPFMTS-----	339
P2Y2-Tetraodon	310	RSNLTKKCR TANQKLT-----	325
P2Y2-Medaka	334	RSSFIR-----	338
P2Y2-1-Stickleback	319	SSLTKKIR-----	326
P2Y2-2-Stickleback	-	-----	-
P2Y2-1-Danio	308	SSIKRNKSPVARSGKPPSTSL-----	329
P2Y2-2-Danio	307	NNSTRSNPSSERSISTV-----	323
P2Y2-3-Danio	324	KSIKKTSSQRYDKSMSTY-----	341
P2Y2-Callorhinchus	-	-----	-

MC5R-Human	-	-----	-
P2Y2-Human	364	STPAGSENTKDIRL	377
P2Y2-Takifugu	-	-----	-
P2Y2-Tetraodon	-	-----	-
P2Y2-Medaka	-	-----	-
P2Y2-1-Stickleback	-	-----	-
P2Y2-2-Stickleback	-	-----	-
P2Y2-1-Danio	-	-----	-
P2Y2-2-Danio	-	-----	-
P2Y2-3-Danio	-	-----	-
P2Y2-Callorhinchus	-	-----	-