Supplemental Table 1. Distances between matching α -carbons in a model of a rat M3R dimer characterized by a TM5-TM5 interface. The M3R dimer model was generated as described under Materials and Methods and corresponds to the energetically most favorable M3R dimer compatible with experimental BRET data (14). C α numbers refer to amino acid positions in the rat M3R sequence.

	Distance
Cα-Cα	(Å)
252-252	15.83
253-253	19.53
254-254	14.73
255-255	9.47
256-256	15.13
257-257	16.70
258-258	10.45
259-259	8.50
260-260	13.30
261-261	13.17

	5	10	15	20	25	30	35	40	45	50	55	60	65	70
beta2AR (3SN6)	34	39	44	49	54	59	64	69	74	79	84	89	94	
Deta2/11 (00110)] E V WV V G	MGIVMS	5 L I V L A	\ I V F <mark>G N</mark>		AIAKF	ERLQT	VTNYF	ITSLA	CADLV	MGLAV	VPFGA		ТΨ
Rat M3	68	73	78	83	88	93	98	103	108	113	118	123	128	
- Hat mo] I WQ <mark>V V</mark> F	IAFLTO	3 F L A <mark>L</mark> V	' T I I <mark>G</mark> N		AFKVN	KQLKT	VNNYF	LLSLA	CADLI	IGVIS	MNLFT	TYIIMN	IRW

	75	80	85	90	95	100	105	110	115	120	125	130	135	140
beta2AR (3SN6)			114 SDVLC				134 YFA T		144 QSLLT		154		164 GLTSFI	
Rat M3		143 CDLWL	148 S I D Y V A	ISNASV	158 MNLLV	ISFDR	Y F S I T	¹⁷³ R P L T Y			™ G L	AWV I S	FVLWA	ΡΑΙ

	145	150	155	160	165	170	175	180	185	190	195	200	205	210
beta2AR (3SN6)				тс			• CDFF	= T • • N Q	AYAIAS	207 S V S F	212 YVPLV	217	222 Y S R V F Q	EA
Rat M3] LF··· ·			•••WQ Y	21: FVGKR	³ X T V P P G	⁸ SECFIC	23 27 F L S E P	T I T F G T		YMPVT		YWR IYK	ЕТ

			20 22	5 230	235	240	24	5 250	255	260	265 270	275 280
beta2AR (3SN6)	²²⁷ KRQL	232 .QKIDKS	SEGR••		۰۰۰c	267 LKEHK	272 ALKTI	GIMG	282 283	7 292 . PFFIVN		
Rat M3	EKRT	K <mark>ELAG</mark>	L ²⁶⁸	²⁷³ EAEAE N	FVHL	IKEKK	AAQTL	⁴⁹³ SAILL	⁴⁹⁸ AFIITWT	• PYN I MV I	513 VNTFCDS	

	285	290	295 30	0 305	310	315	320	325	330	335	340	345	350
beta2AR (3SN6)		NSGFN			³³⁷ FQELLC								
Rat M3	GYWLCY I	N S T <mark>V N I</mark>	PVC <mark>Y</mark> ALCN	⁵⁴⁸ K T F R T T	FKTL								

Supplemental Figure 1. Alignment of the sequences of the human β_2 -adrenergic receptor (β_2 -AR; PDB ID: 3SN6; ref. 17) and the rat M₃ muscarinic receptor (M3R). The residues that are conserved among the two receptors are highlighted in red. The bars above the sequences indicate the secondary structure found in the crystal structure of the β_2 AR (red, α -helix; blue, 1-4 turn). Figure generated with MOE (31).