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

MC1R-Gs complexes	α-MSH-MC1R-Gs-Nb35	Afamelanotide-MC1R-Gs-scFv16	Afamelanotide-MC1R-Gs-Nb35-scFv16	SHU9119-MC1R-Gs-Nb35
Data collection and processing				
Magnification	81,000	81,000	81,000	81,000
Voltage (kV)	300	300	300	300
Electron exposure (e^{-}/Å^2)	80	80	80	70
Defocus range (μm)	-0.5 to -3.0	-0.5 to -3.0	-0.5 to -3.0	-0.5 to -3.0
Pixel size (Å)	1.045	1.045	1.045	1.071
Symmetry imposed	C1	C1	C1	C1
Initial particle projections (no.)	4,151805	3,968,825	3,968,825	4,337,394
Final particle projections (no.)	454,593	312,962	460,989	502,722
Map resolution (Å)	3.0	2.9	2.7	3.1
FSC threshold	0.143	0.143	0.143	0.143
Map resolution range (Å)	2.0-5.0	2.0-5.0	2.0-5.0	2.0-5.0
Refinement				
Initial model used (PDB code)	PDB: 6W25	PDB: 6W25	PDB: 6W25	PDB: 6W25
Model resolution (Å)	3.1	3.0	2.9	3.2
FSC threshold	0.5	0.5	0.5	0.5
Model resolution range (Å)	50-3.0	50-2.9	50-2.7	50-3.1
Map sharpening *B* factor (Å^2)	-116.20	-80.97	-76.84	-122.70
Model composition				
Non-hydrogen atoms	8048	8882	9850	8032
Protein residues	1030	1138	1265	1030
Lipids	0	0	0	0
B factors (Å^2)				
Protein	111.94	48.91	89.69	129.70
RMSD				
Bond lengths (Å)	0.009	0.010	0.010	0.009
Bond angles (°)	1.066	1.100	1.043	1.093
Validation				
MolProbity score	1.40	1.50	1.46	1.22
Clashscore	3.86	4.64	3.88	1.69
Rotamer outliers (%)	0.00	0.00	0.00	0.00
Ramachandran plot				
Favored (%)	96.55	96.14	95.89	95.74
Allowed (%)	3.45	3.86	4.11	4.26
Disallowed (%)	0.00	0.00	0.00	0.00
PDB accession number	7F4D	7F4F	7F4H	7F4I
EMDB accession number	EMD-31448	EMD-31449	EMD-31452	EMD-31453