

Cryo-EM data collection, refinement and validation statistics

	CDPPB bound inactive mGlu5 (EMDB-41069) (PDB 8T6J)	Quis bound intermediate mGlu5- Nb43 (EMDB-41092) (PDB 8T7H)	Quis bound active mGlu5-Nb43 (EMDB-41099) (PDB 8T8M)	Quis+CDPPB bound active mGlu5-Nb43 (EMDB-41139) (PDB 8TAO)
Data collection and processing				
Magnification	107000	82000	82000	82000
Voltage (kV)	300	300	300	300
Electron exposure (e-/Å ²)	52.2	50	50	51.6
Defocus range (µm)	0.7-2	0.7-2	0.7-2	0.7-2
Pixel size (Å)	0.8521	1.111	1.111	1.111
Symmetry imposed	C2	C2	C2	C1
Initial particle images (no.)	3,565,734	4,317,126	4,317,126	5,033,648
Final particle images (no.)	246,232	211,019	183,295	245,439
Map resolution (Å)	3.5	3.3	3.0	2.9
FSC threshold	0.143	0.143	0.143	0.143
Map resolution range (Å)	2.8-5.6	3.0-7.0	3.0-7.0	2.5-7.2
Refinement				
Initial model used (PDB code)	6N52	6N51 and 6N52	6N51	6N51
Model resolution (Å)	3.4	3.5	3.2	3.1
FSC threshold	0.5	0.5	0.5	0.5
Model resolution range (Å)	31.6-3.4	38.5-3.5	42.6-3.2	2.9-3.1
Map sharpening <i>B</i> factor (Å ²)	-22.85	-59.41	-25.33	-51.06
Model composition				
Non-hydrogen atoms	11652	13100	13146	13422
Protein residues	1534	1794	1770	1794
Ligands	2	2	2	3
<i>B</i> factors (Å ²)				
Protein	60.67	30.43	36.58	45.08
Ligand	55.65	17.07	11.77	46.72
R.m.s. deviations				
Bond lengths (Å)	0.002	0.003	0.003	0.002
Bond angles (°)	0.579	0.597	0.534	0.509
Validation				
MolProbity score	1.69	1.73	1.64	1.48
Clashscore	6.09	7.94	6.10	4.70
Poor rotamers (%)	0.00	0.00	0.00	0.00
Ramachandran plot				
Favored (%)	94.88	95.73	95.66	96.40
Allowed (%)	5.12	4.27	4.34	3.60
Disallowed (%)	0.00	0.00	0.00	0.00