

Supplementary information, Fig. S15

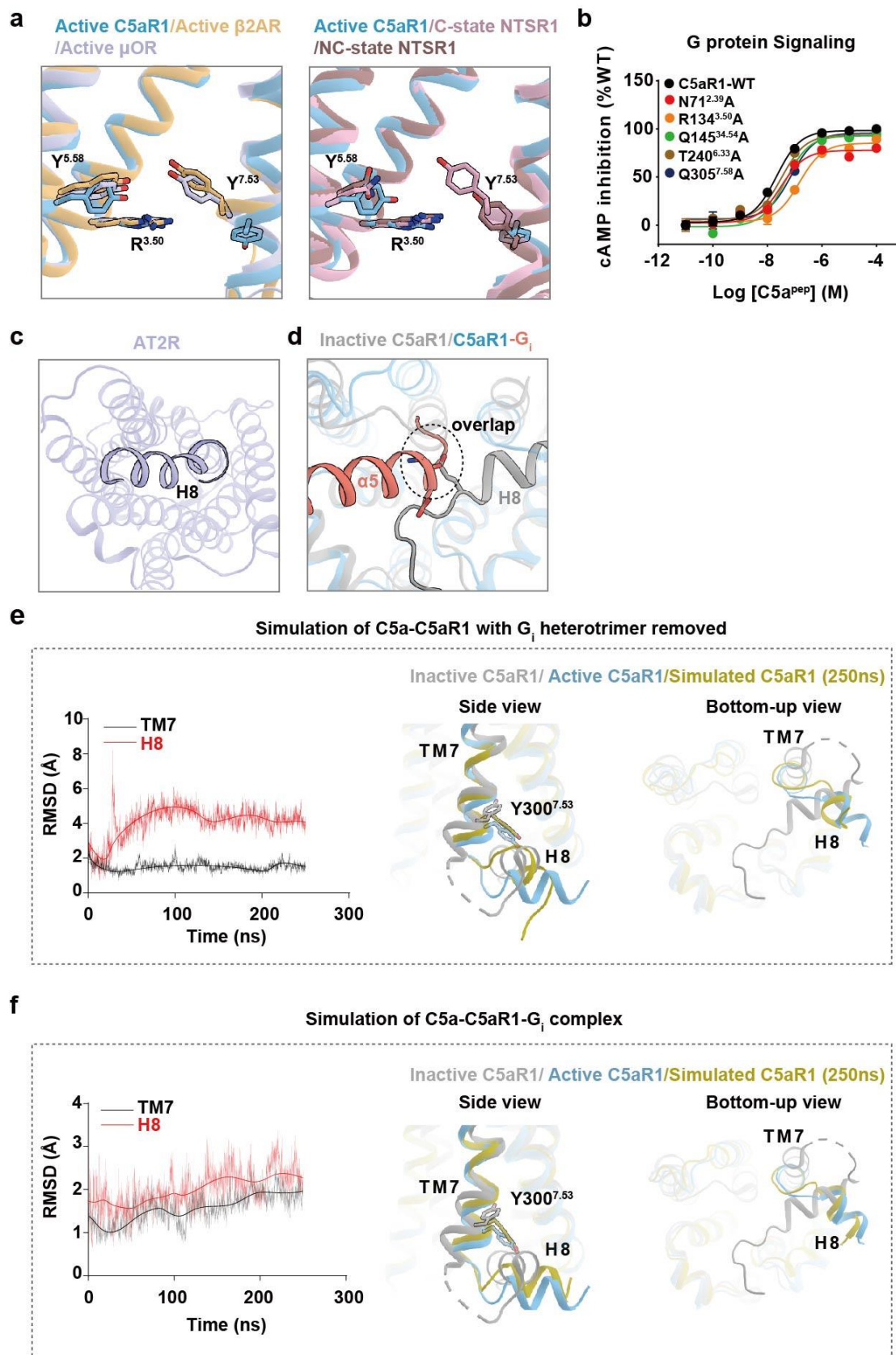


Fig. S15. Noncanonical conformation of TM7 and H8 in C5aR1.

a, Structural superimposition of C5a-bound active C5aR1 with active β 2AR (PDB:3SN6), μ OR (PDB:6DDE), C-state NTSR1(PDB:6OS9) and NC-state NTSR1 (PDB: 6OSA) showing a unique conformation of Y^{7.53}.

b, Representative curve for effects of the N71^{2.39}A, R134^{3.50}A, Q145^{34.54}, T240^{6.33}A and Q305^{7.58}A mutations in C5aR1 on C5a^{pep} induced G protein signaling detected by cAMP inhibition assay. Data are presented as the mean \pm SEM of three independent experiments performed in triplicate.

c, The noncanonical conformation of H8 of AT2R (PDB: 5UNG).

d, Structural alignment of inactive C5aR1 and C5aR1-G_i complex showing that the α 5 helix of G α _i and H8 in the inactive state occupied overlapped cytoplasmic cavity of C5aR1.

e-f, MD simulation study of C5aR1 using C5a-C5aR1 with G_i heterotrimer removed (**e**) or C5a-C5aR1-G_i complex (**f**) as the starting model. Root Mean Square Deviation (RMSD) of TM7 and H8 relative to the first snapshot during 250 ns classical MD simulation were shown in the left panel. Structural alignment of the simulated C5aR1 at 250 ns with inactive C5aR1 (PDB: 5O9H) and active C5aR1 (cryo-EM structure of C5a-bound C5aR1) were shown in the right panel.