

Supplementary information, Figure S10

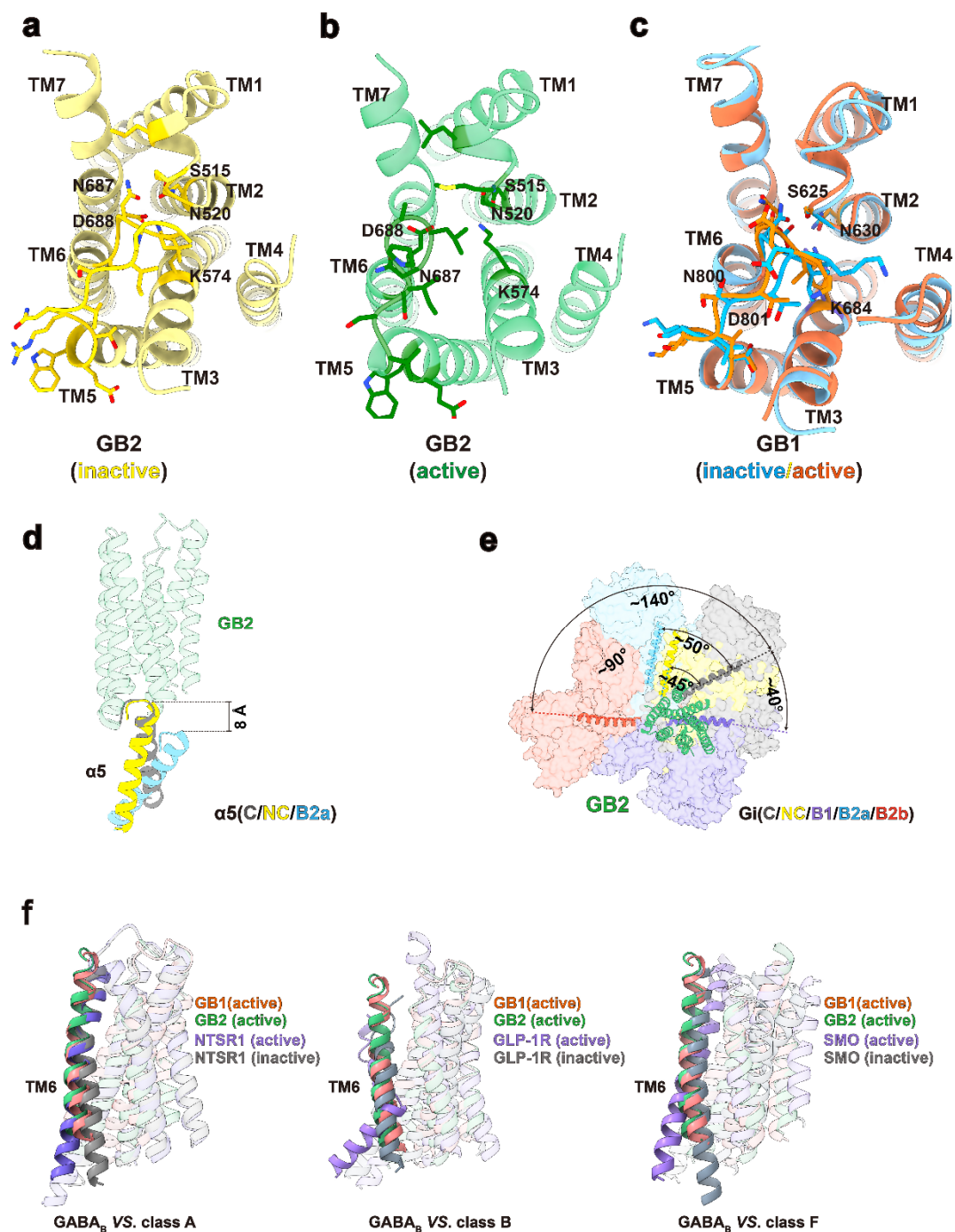


Fig. S10 Conformation of ICL3 in inactive and active GABA_B structures and the α5-receptor interface in GABA_B-Gi₁₁ complex. **a-c** Interactions of the ICL3 with other residues of TM domain in GABA_B in GB2 inactive (**a**), active state (**b**) and GB1 in both

states(c). **d** Comparison of the $G\alpha_{i1}$ $\alpha 5$ -helix binding position between GB2 (B2a state) and the NTSR1– G_{i1} protein complex in canonical (C; PDB code: 6OS9) and noncanonical (NC; PDB code: 6OSA) states. The position of $\alpha 5$ -helix from GABA_B– G_i complex in different states show around 8 Å downward movement compared with that of NTSR1– G_{i1} complex. Structures were aligned by the TM domains and only GB2 TM domain is shown for clarity. Color usage for $\alpha 5$: C state, grey; NC state, gold; B2a state, cyan. **e** Orientations of the G_i protein when coupling to GABA_B and NTSR1 receptors. Rotation of G_i protein are measured by the αN domains. Color usage for G proteins: C state, grey; NC state, gold; B1 state, purple; B2a state, cyan; and B2b state, red. **f** Comparison of the active GB1 and GB2 TM domains with the inactive and active structures of class A GPCR NTSR1 (PDB code: 4BUO and 6OS9 for inactive and active states, respectively), class B GPCR glucagon-like peptide-1 receptor (GLP-1R; PDB code: 5VEW and 6B3J for inactive and active states, respectively) and class F GPCR Smoothed receptor (SMO; PDB code: 6JKV and 6OT0 for inactive and active states, respectively), showing the positions of TM6 helices of GB1 and GB2 subunits are similar to that of the representative class A, B and F GPCR in the inactive state.