A hydrogen-bonded polar network in the core of the glucagon-like peptide-1 receptor is a fulcrum for biased agonism: lessons from class B crystal structures.

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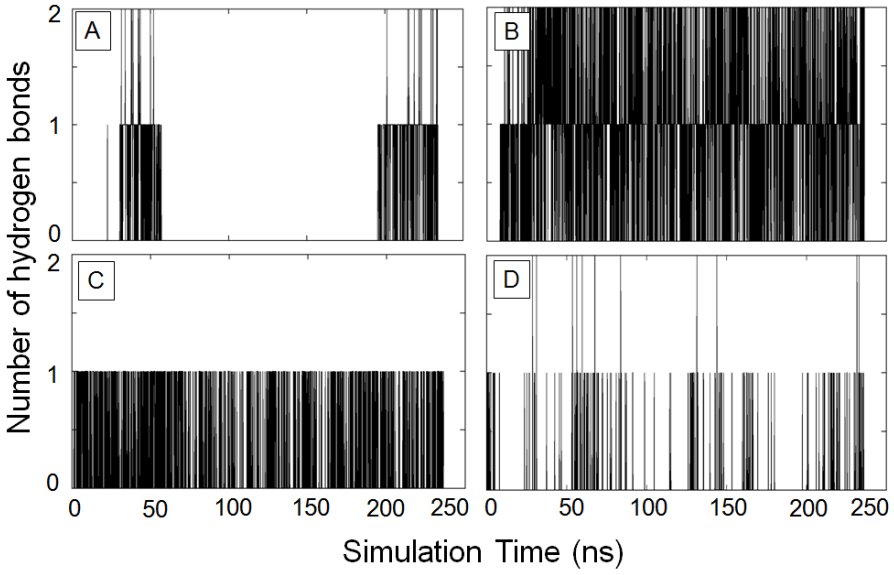
MOLECULAR PHARMACOLOGY



Supplementary Figure 1. Hydrogen bonds for the polar network residues of the GLP-1R apo inactive receptor during the 240 ns molecular dynamics simulation. A) R2.60-N3.43; B) R2.60-E.6.53; C) E6.53-Q7.49; D) H6.52-E6.53. Hydrogen bonds were defined with the donor-acceptor distance < 3.0 Å, and an angle cutoff of 20° (B and C) or with the donor-acceptor distance < 3.75 Å, and an angle cutoff of 30° (A and D); this was particularly necessary for (D)

as the neighboring residues H6.52 and E6.53 are angled away from each other. The R2.60-N3.43 and the H6.52 and E6.53 heavy atom distances rarely exceed 4 Å.

Supplemental Movie Legend

Close up of the polar network residues of GLP-1R during the molecular dynamics simulations. View from the extracellular side with transmembrane helices (TM) depicted as cylinders. TM 2, 3, 6 and 7 are color coded in blue, magenta, green and orange, respectively. Polar network residues are depicted as ball and stick, with carbon, nitrogen, oxygen and hydrogen atoms colored in cyan, blue, red and white, respectively.

Supplementary Data

Molecular modelling PDB files

Data Supplement 1

GLP1R apo.pdb

Inactive transmembrane domain model of the human GLP-1 receptor

Data Supplement 2

GLP1R_full-length_GLP1 bound_G protein peptide bound.pdb

Full-length, peptide bound model of the human GLP-1 receptor