

Supplementary information, Fig. S4| The structures of active and inactive human  $\beta_1 AR$  are similar to those of the human  $\beta_2 AR$ .

a, The overall structure of the T4L- $\beta_1$ AR bound with carazolol. b, The overall structures of the T4L- $\beta_1$ AR bound with BI-167107 (cyan), norepinephrine (yellow) and epinephrine (magenta). The receptors are stabilized in active conformation by Nb6B9. c, Comparison of the PIF motif of the inactive state  $\beta_1$ AR (carazolol bound, green) and  $\beta_2$ AR (carazolol bound, orange. PDB code: 2RH1). d, Comparison of the PIF motif of the active state  $\beta_1$ AR (BI-167107 bound, cyan) and  $\beta_2$ AR (BI-167107 bound, pink. PDB code: 4LDE). e, Comparison of the positions of Y<sup>5.58</sup> and Y<sup>7.53</sup> of the inactive state  $\beta_1$ AR (carazolol bound, green) and  $\beta_2$ AR (carazolol bound, orange. PDB code: 2RH1). f, Y<sup>5.58</sup> and Y<sup>7.53</sup> form a water-mediated hydrogen bond in the active state  $\beta_1$ AR (BI-167107 bound, cyan) and  $\beta_2$ AR (BI-167107 bound, pink. PDB code: 4LDE). g, The norepinephrine binding pocket in the simulated  $\beta_2$ AR-norepinephrine complex structure. h, The norepinephrine binding pocket in