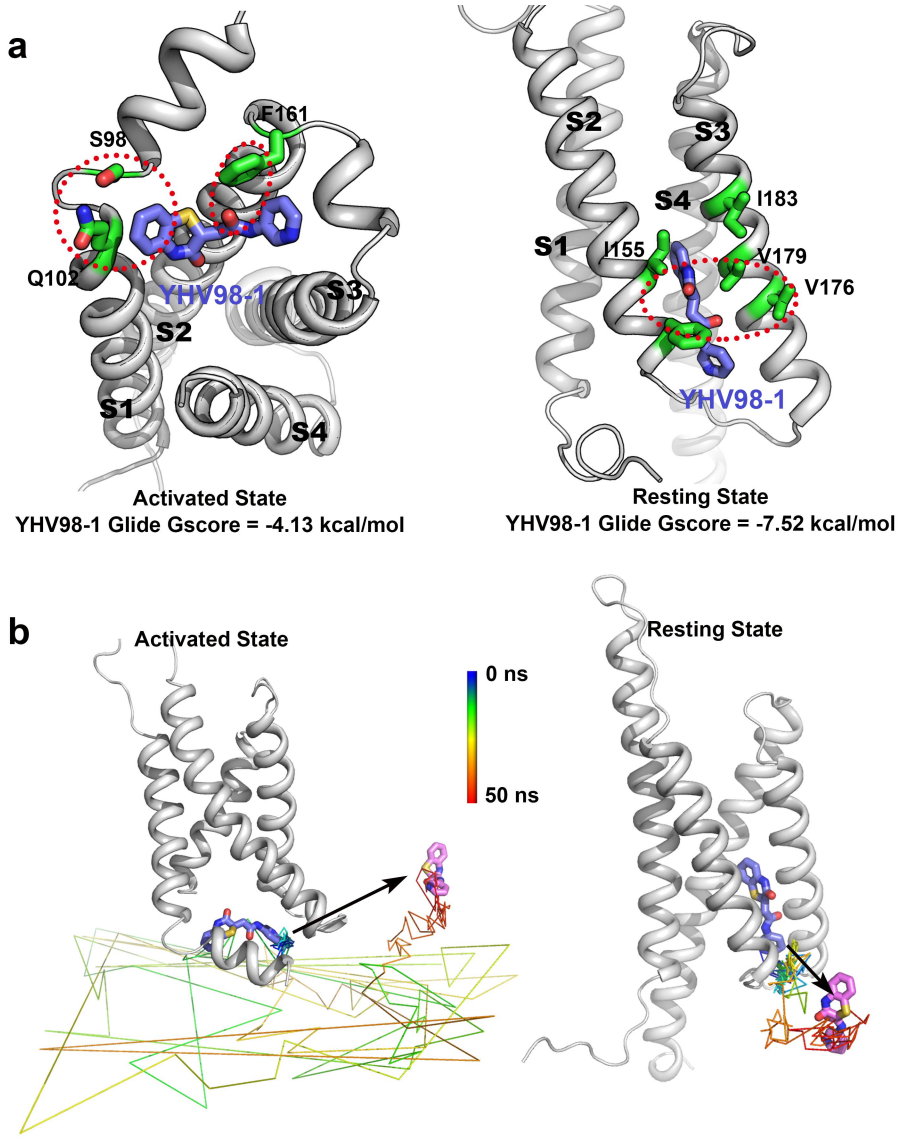

Fig. S7. Molecular docking and MD simulations showing the compound YHV98-1 binding unstable in the activated-state or resting-state Hv1 channel. a Docking of YHV98-1 to the activated-state (left) and resting-state (right) Hv1 channel. (left) the view from the intracellular side looking along the pore axis and (right) the side view perpendicular to the pore axis. The optimal docking conformations in the Hv1 channel is shown as blue sticks. Hv1 channel is shown as grey cartoon, and the red ellipses mark the areas where YHV98-1 does not binding properly with Hv1 channel. **b** Trajectories of YHV98-1 molecules

in the MD simulations on the activated-state (left) and resting-state (right) Hv1 channel. The initial snapshot and the last snapshot of YHV98-1 were shown as blue and pink stick, respectively. The gradient arrow and curve represented the direction and process of YHV98-4 escaping from the docking pocket of Hv1 channel in MD simulations, respectively.