Identification Mechanism of BACE1 on Inhibitors Probed by Using Multiple Separate Molecular Dynamics Simulations and Comparative Calculations of Binding Free Energies

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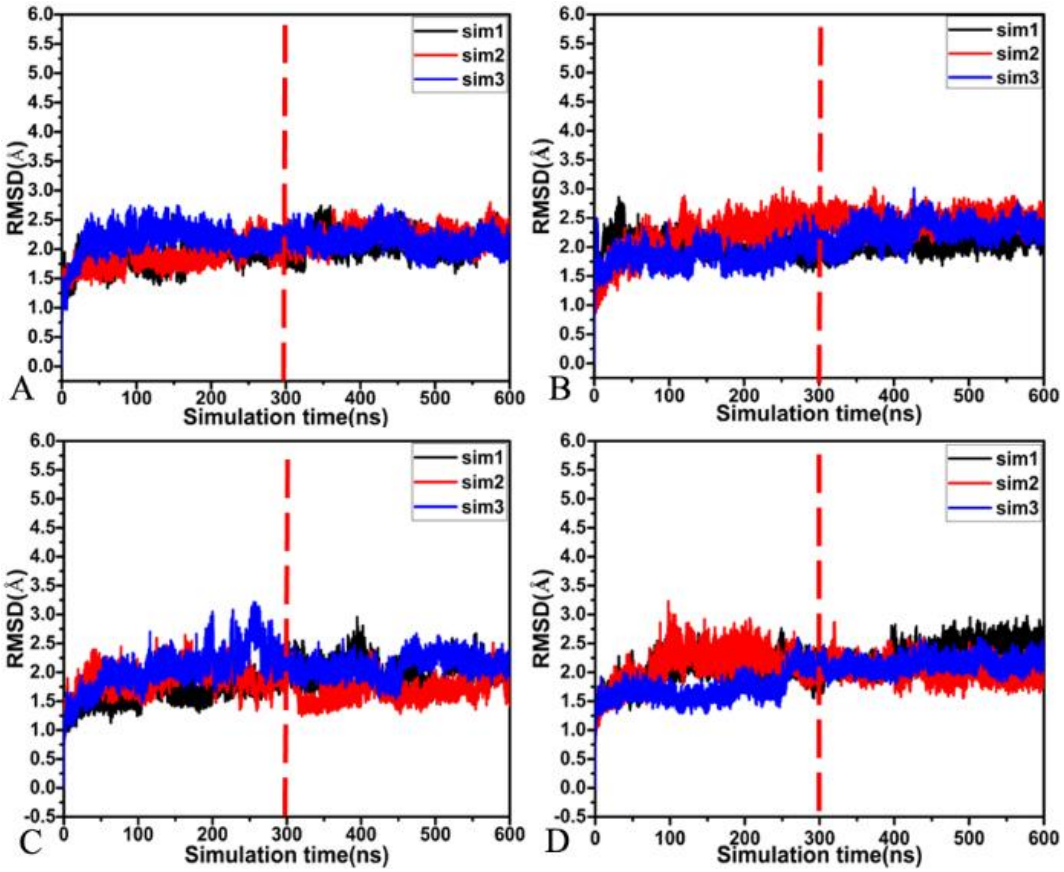

Figure S1. RMSDs of backbone atoms in BACE1 calculated by using three separate MD trajectories: (A) the *apo* BACE1, (B) the 60W-BACE1 complex, (C) the 954-BACE1 complex and (D) the 60X-BACE1 complex.

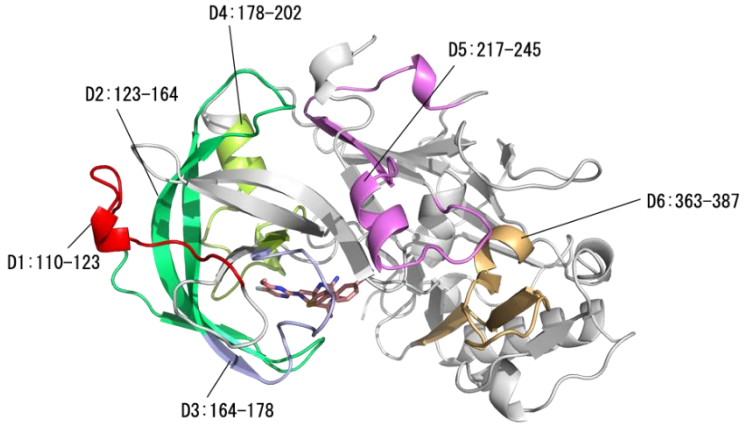

Figure S2. Structural domains corresponding to the obvious changes in RMSFs due to inhibitor binding.

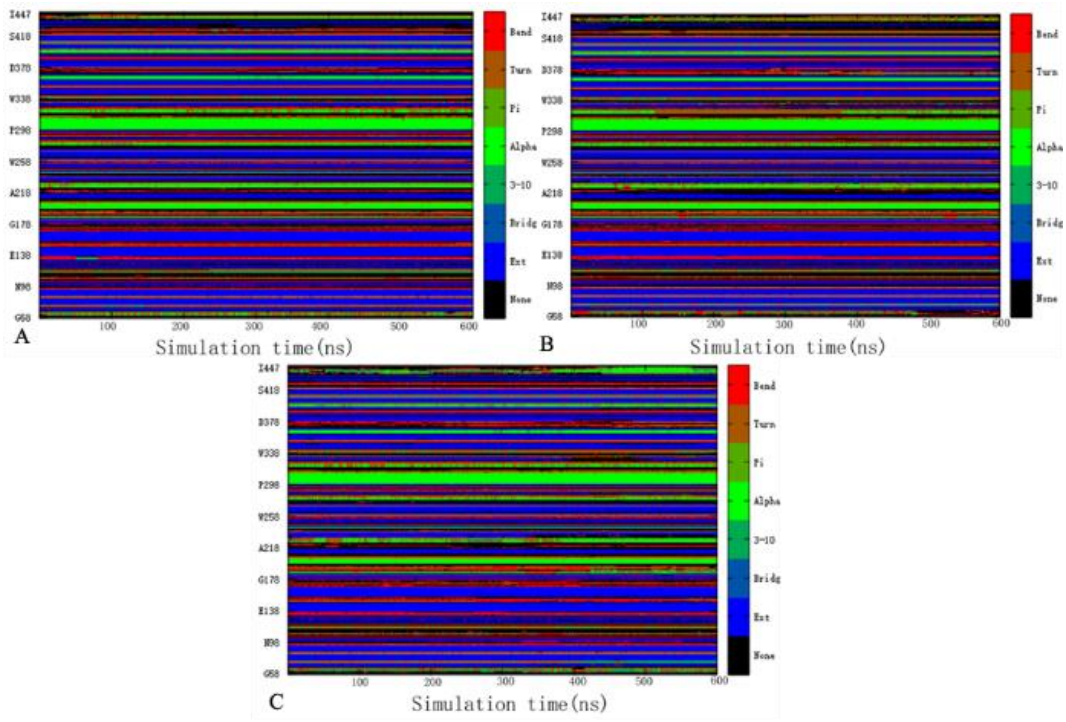

Figure S3. Stability of secondary structures for the 60W-bound BACE1 in three separate MD simulations: (A) the simulation 1, (B) the simulation 2 and (C) the simulation 3.

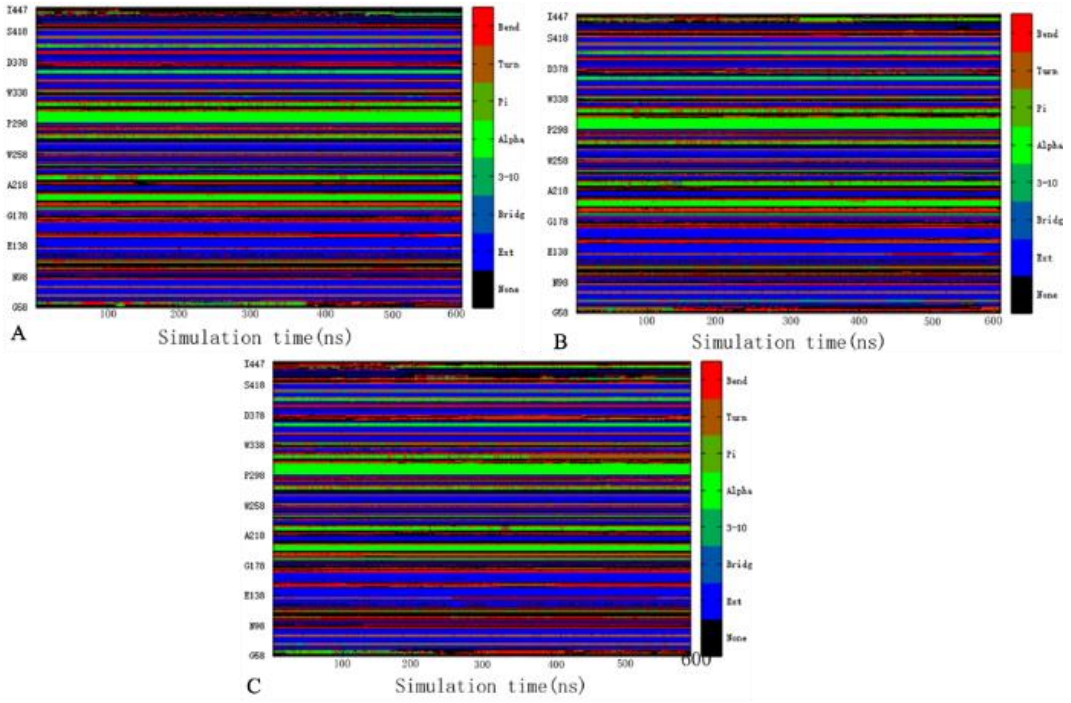

Figure S4. Stability of secondary structures for the 954-bound BACE1 in three separate MD simulations: (A) the simulation 1, (B) the simulation 2 and (C) the simulation 3.

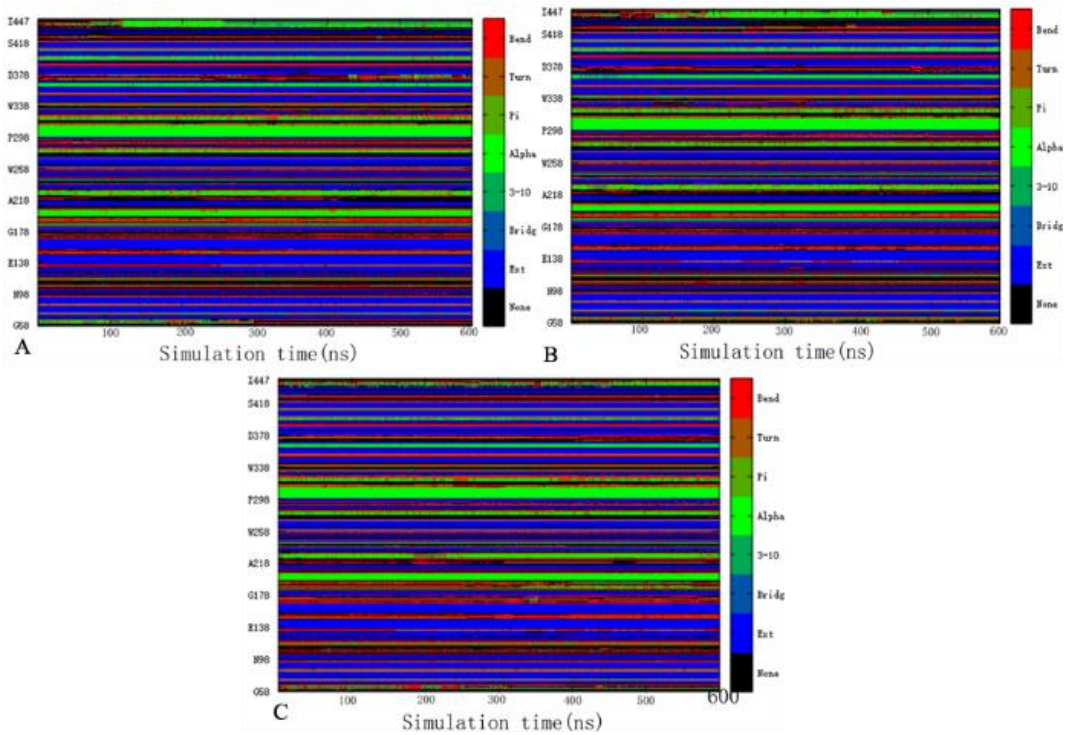

Figure S5. Stability of secondary structures for the 60X-bound BACE1 in three separate MD simulations: (A) the simulation 1, (B) the simulation 2 and (C) the simulation 3.

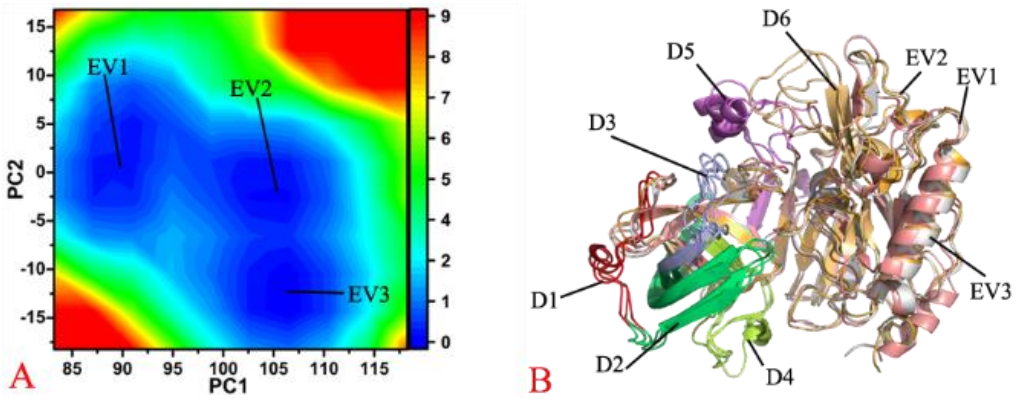

Figure S6. (A) Free energy landscapes of the *apo* BACE1 constructed by using the PC1 and PC2 as reaction coordinates and (B) structural superimposition of the *apo* BACE1 situated at the energy valleys EV1-EV3.