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# Pharmacophore-driven Identification of Human Glutaminyl Cyclase Inhibitors from Foods, Plants and Herbs Unveil the Bioactive Property and Potential of Azaleatin for the Treatment of Alzheimer's Disease

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# Supporting information

## Figures

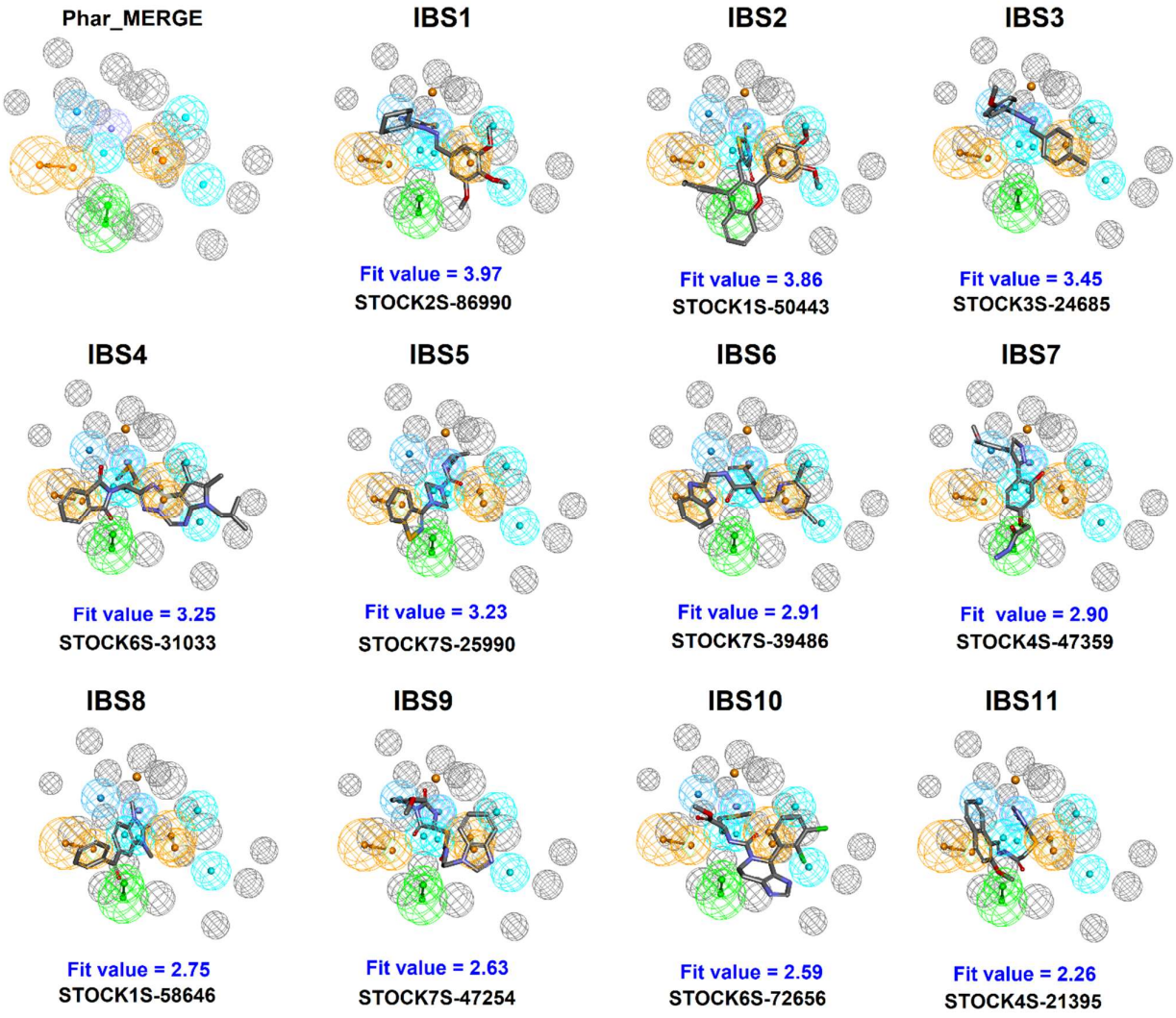


**Figure S1. The results of ligand-pharmacophore (Phar-MERGE) mapping of TOP 11 hits screened from Natural Product database.** The top 11 candidates identified from IBS database are mapped with pharmacophore model, **Phar-MERGE.** The fitting values and the compound named by IBS database are shown. (Pharmacophore features are color-coded as follows: cyan, hydrophobic; green, hydrogen-bond acceptor; orange, ring aromatic; purple, zinc ion binder and dark gray, excluded volume.)

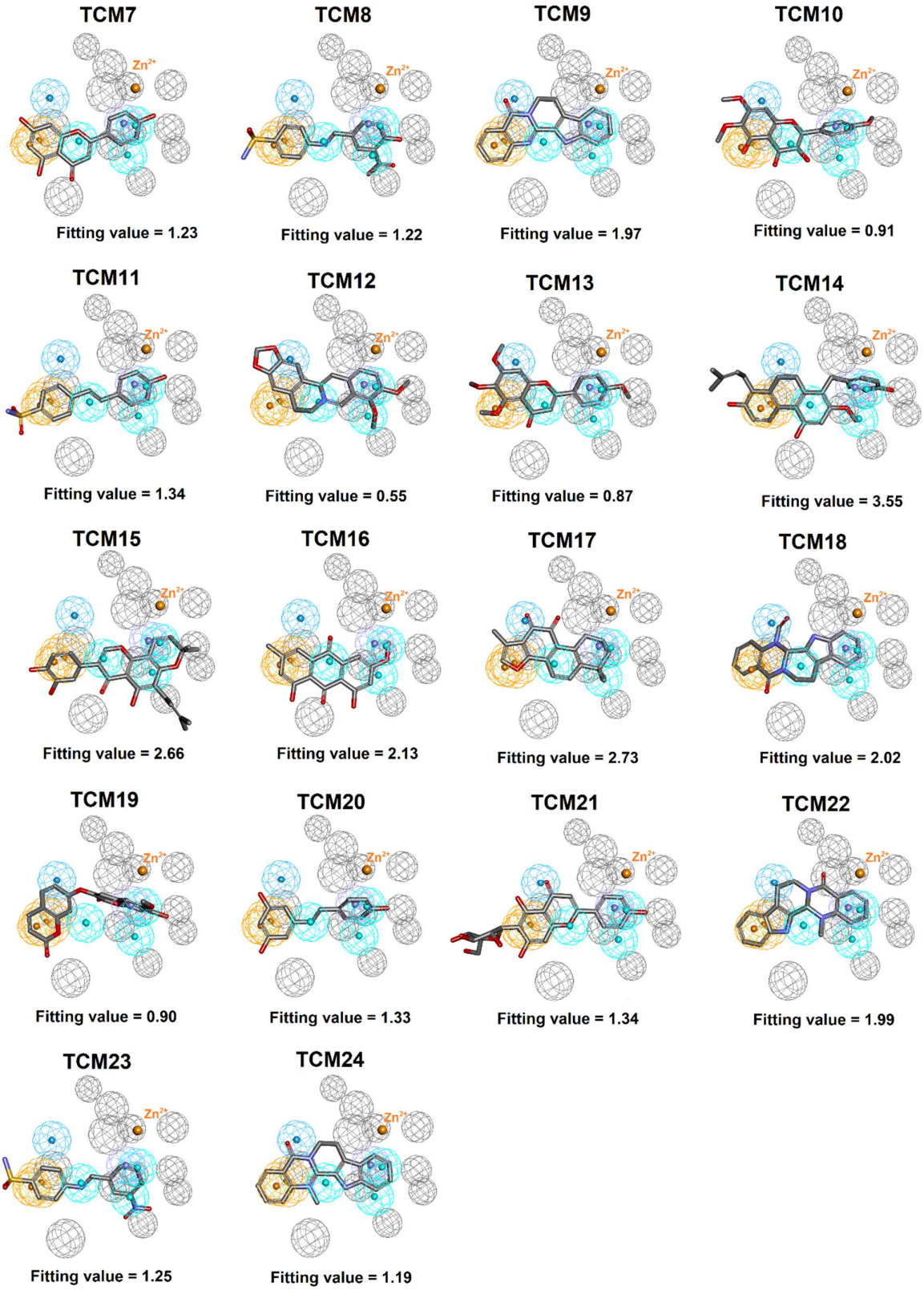


**Figure S2. The results of ligand-pharmacophore (Phar-SEN) mapping of hits screened from Traditional Chinese Medicine database.** The chemical structures of identified 18 candidates (TCM7~TCM24) mapped with **Phar-SEN**. (Pharmacophore features are color-coded as follows: cyan, hydrophobic; green, hydrogen-bond acceptor; orange, ring aromatic; purple, zinc ion binder and dark gray, excluded volume.)

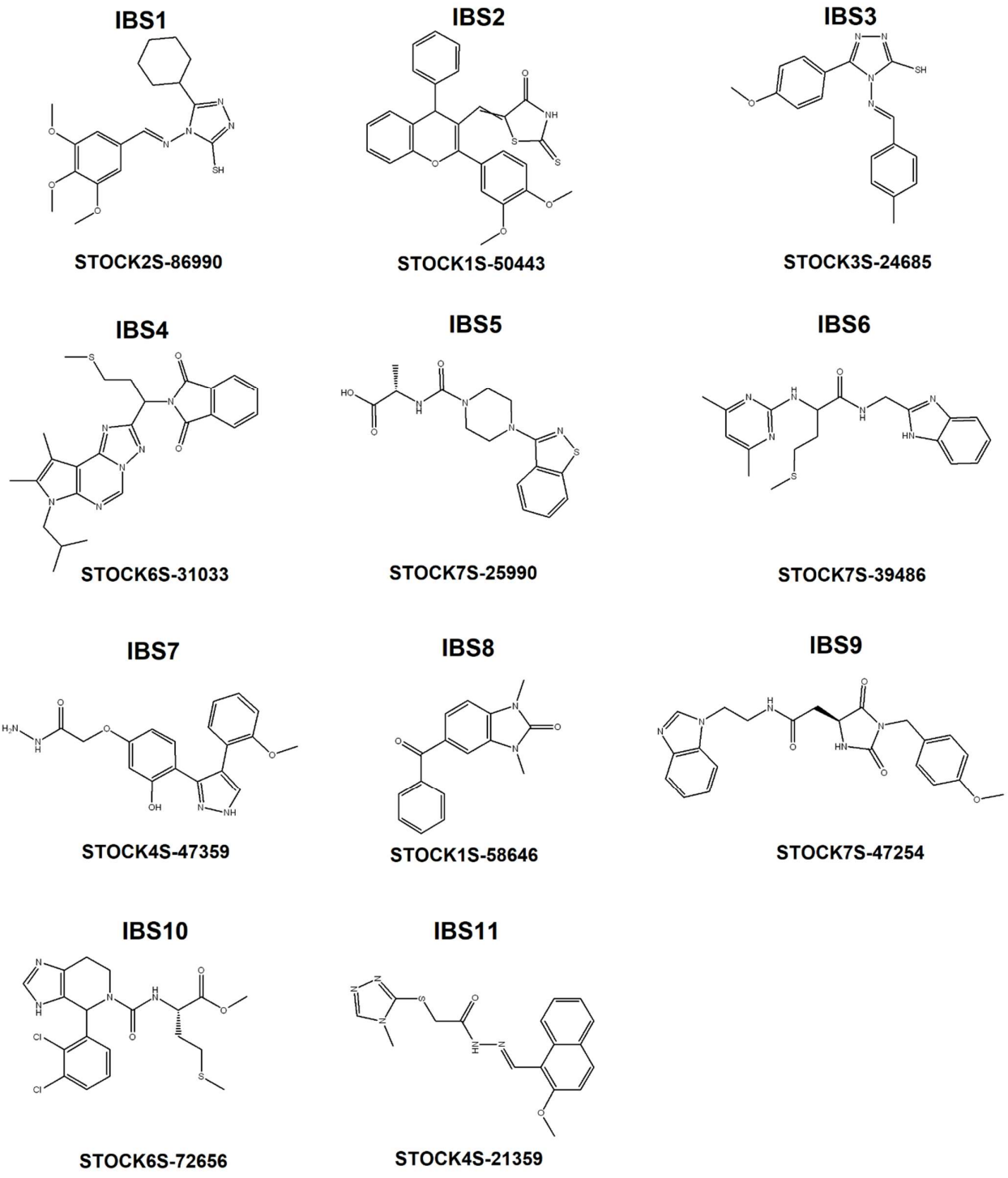


**Figure S3. The detailed chemical structures of hits screened by Phar-MERGE from IBS database.**

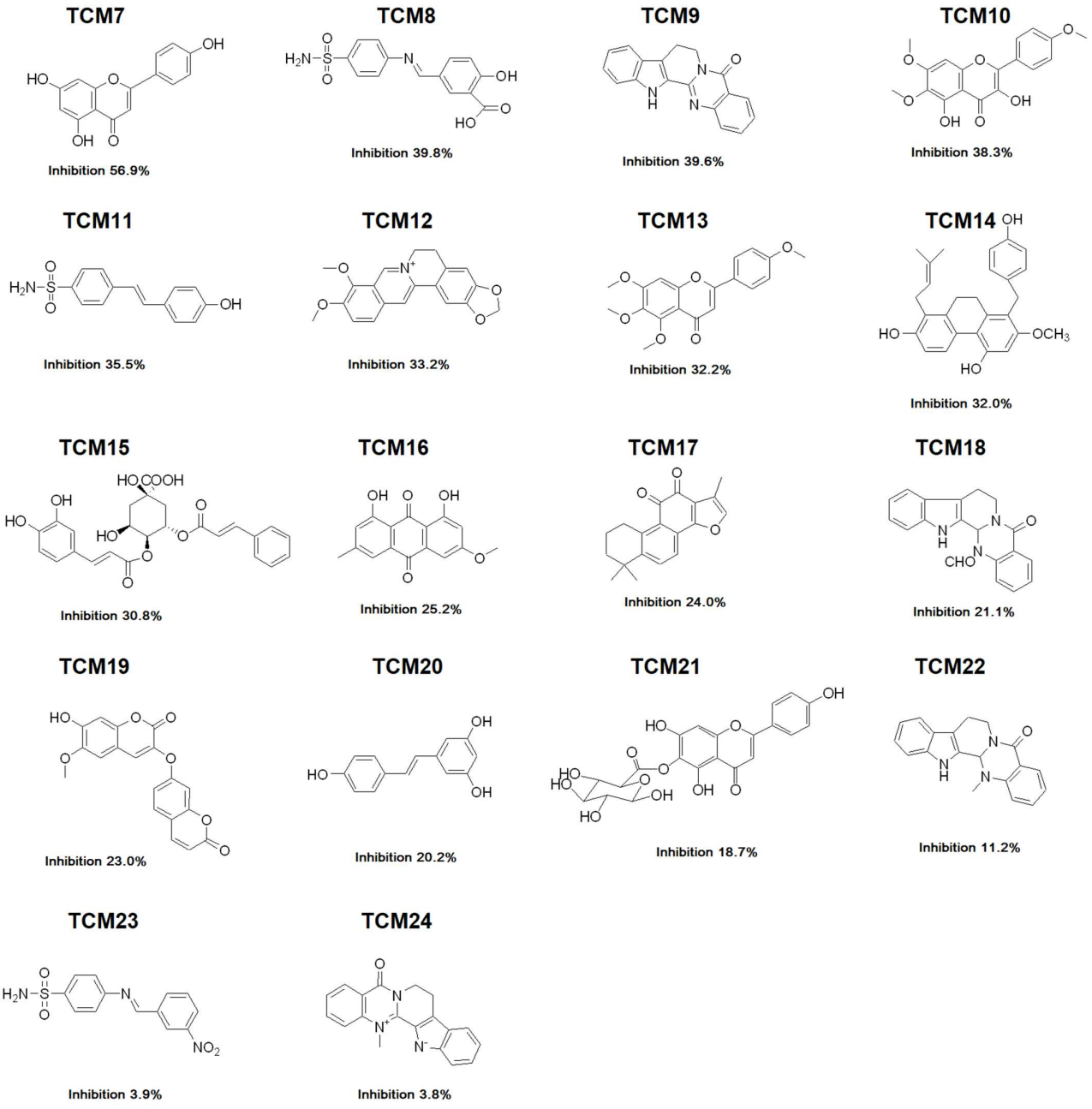


**Figure S4. The detailed chemical structures of hits screened by Phar-SEN from TCM database.** The 2D chemical structures and inhibition % (at 100 μM) of TCM7~TCM24 against hQC are shown.

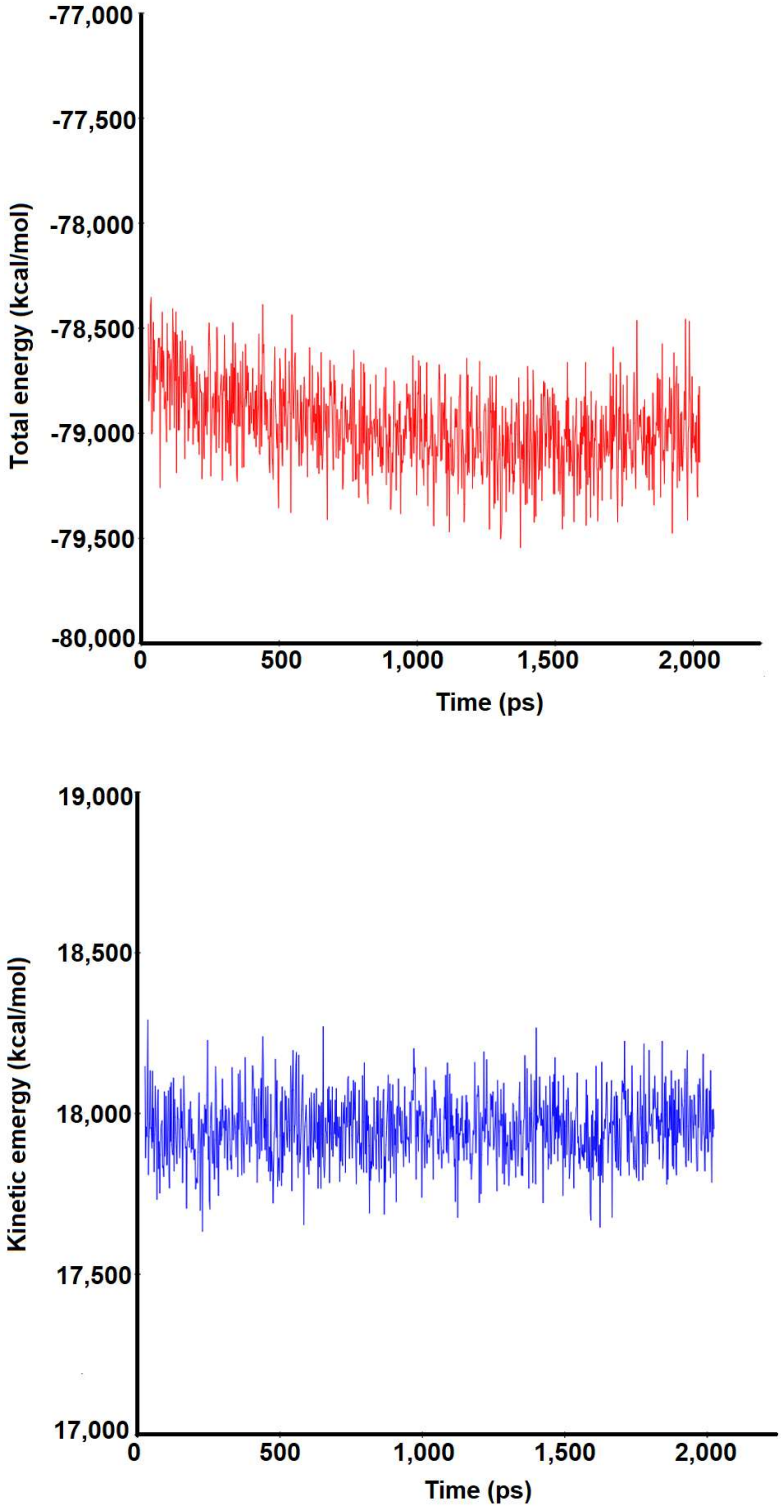


**Figure S5. The molecular dynamics simulations of hQC-TCM1.** The trajectory profiles of total energy and kinetic energy of hQC in complex with TCM1 during MD simulation time for 2,000 ps are presented.

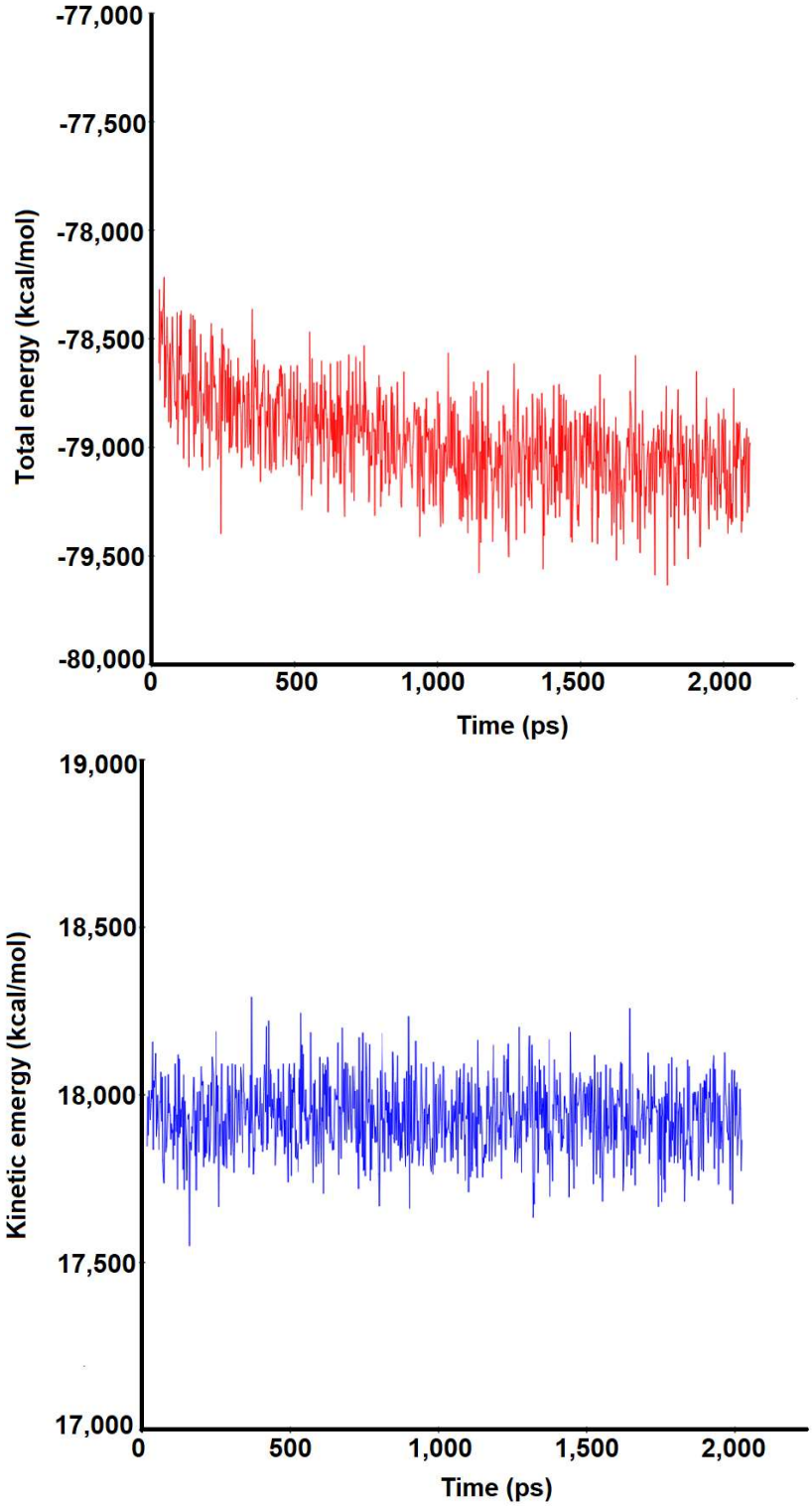


**Figure S6. The molecular dynamics simulations of hQC-TCM2 complex.** The total energy and kinetic energy as a function of simulation time for 2,000 ps are shown.

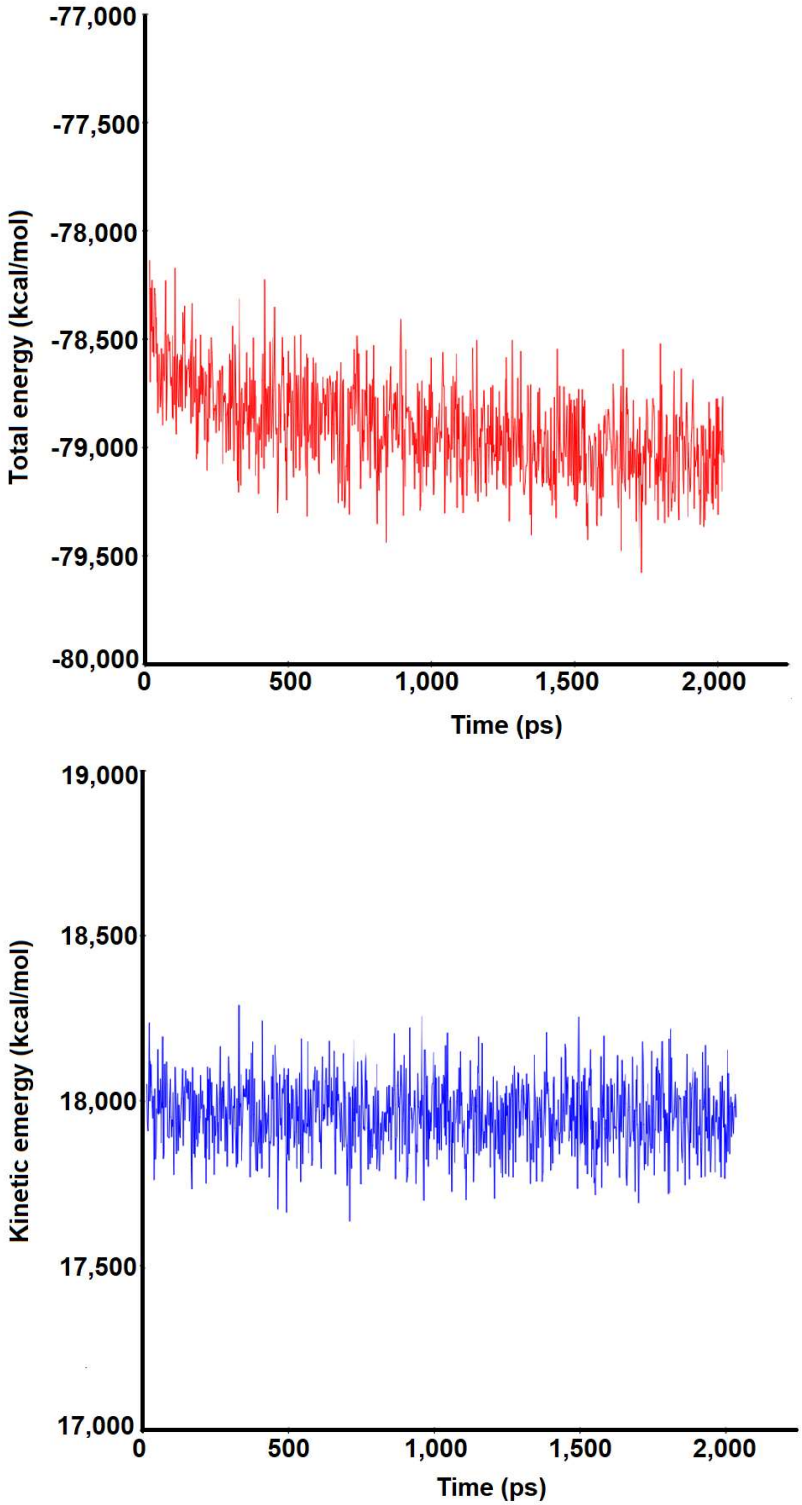


**Figure S7. The molecular dynamics simulations of hQC-TCM3.** The trajectory profiles of total energy and kinetic energy of hQC in complex with TCM3 during MD simulation time for 2,000 ps are presented.

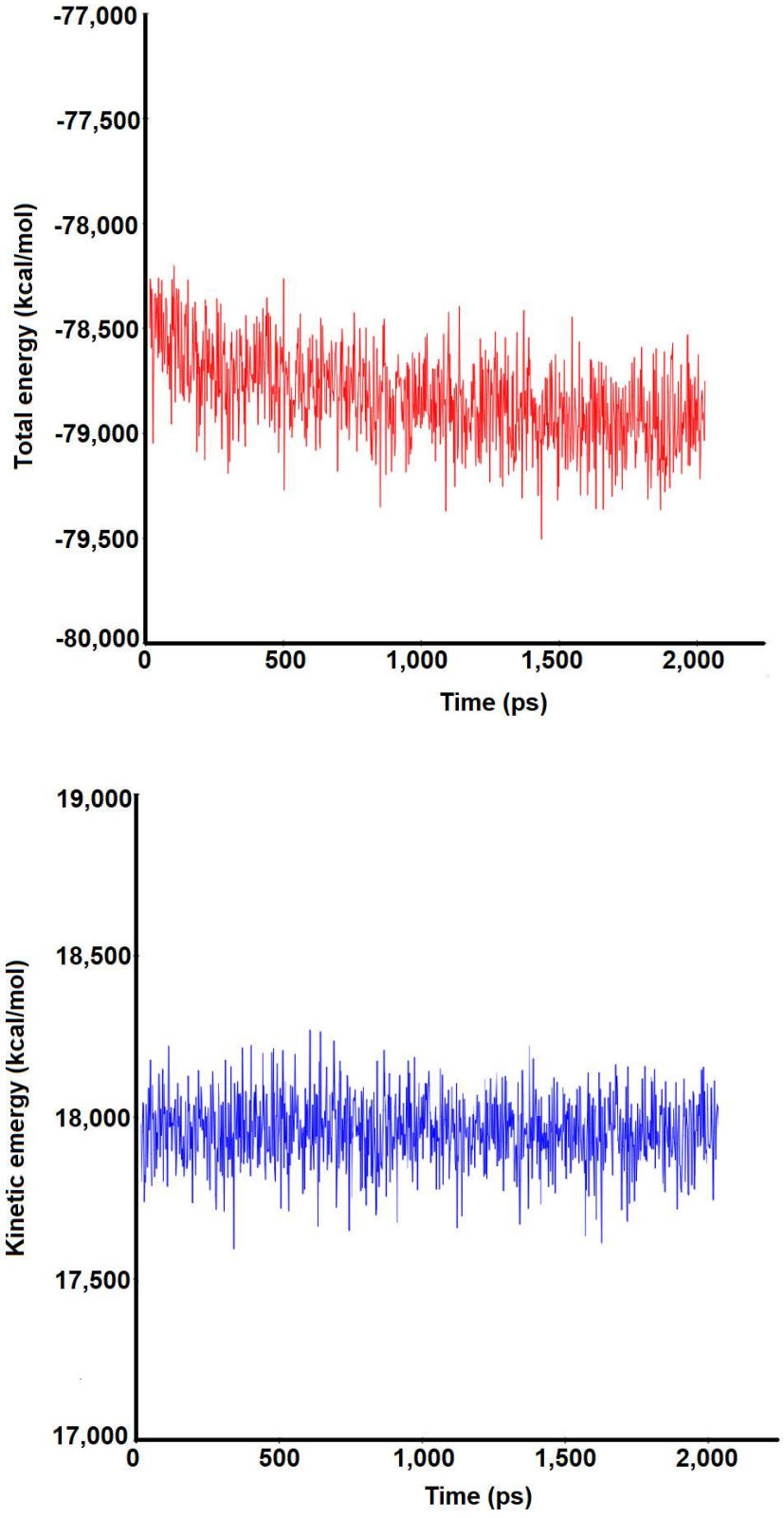


**Figure S8. The molecular dynamics simulations of hQC-TCM4 complex.** The total energy and kinetic energy as a function of simulation time for 2,000 ps are shown.

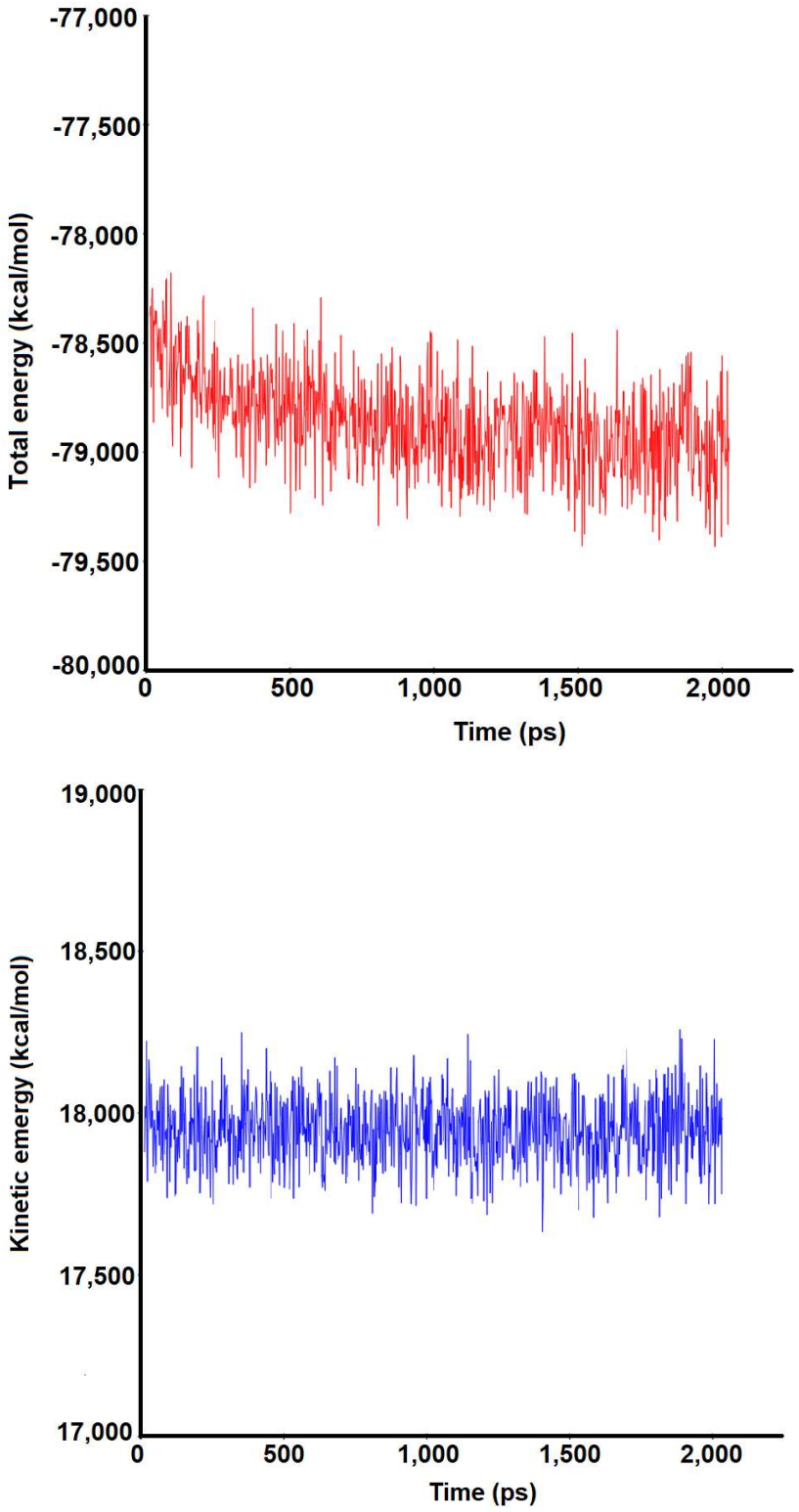


**Figure S9. The molecular dynamics simulations of hQC-TCM5.** The trajectory profiles of total energy and kinetic energy of hQC in complex with TCM5 during MD simulation time for 2,000 ps are presented.

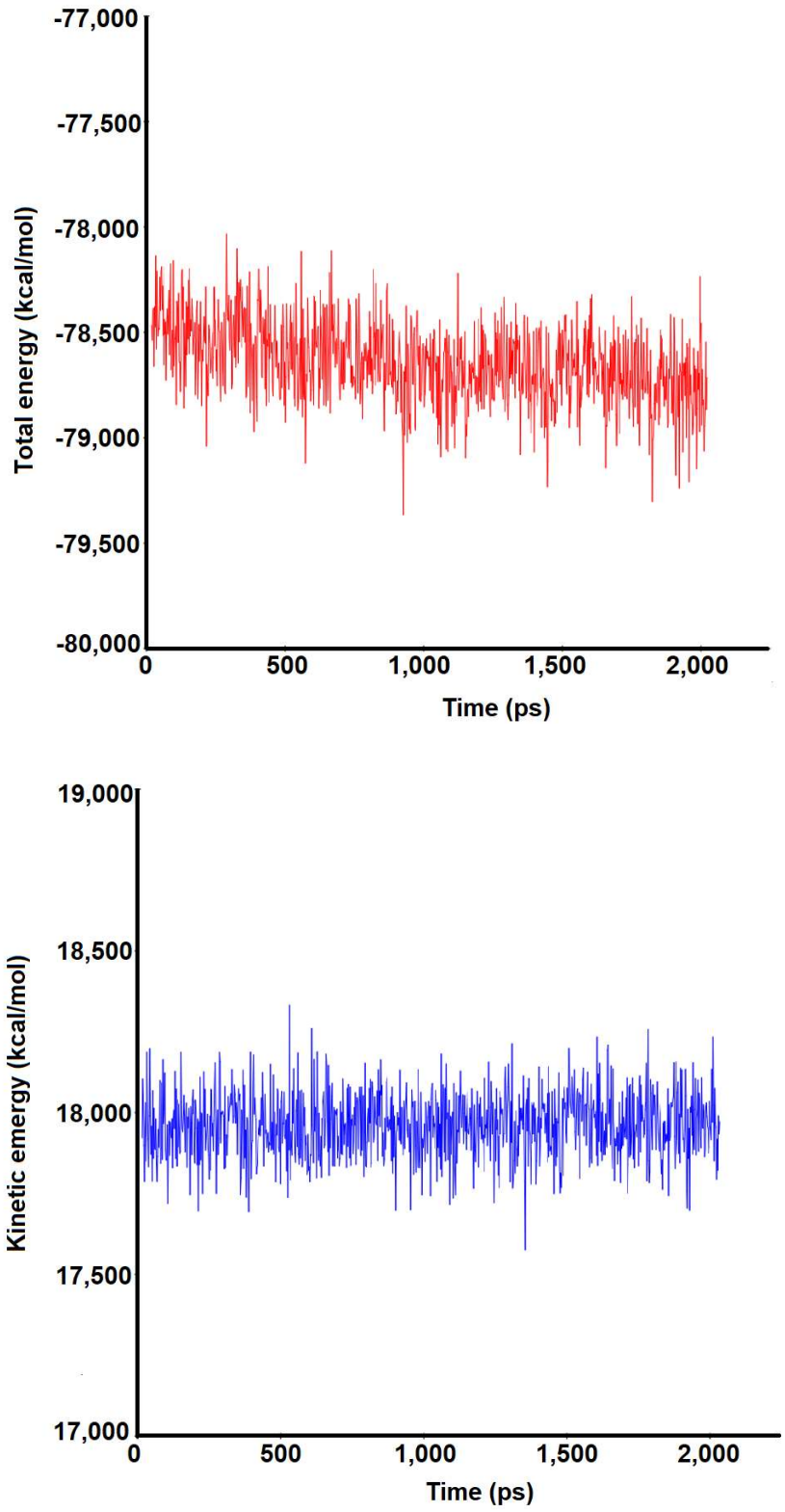


**Figure S10. The molecular dynamics simulations of hQC-TCM6 complex.** The total energy and kinetic energy as a function of simulation time for 2,000 ps are shown.

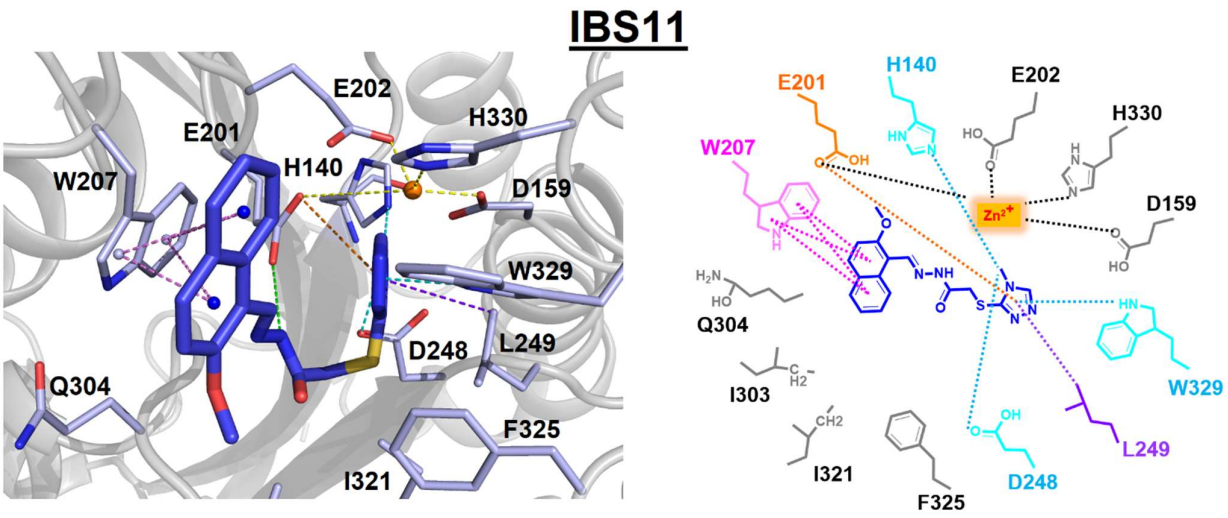


**Figure S11. The detailed molecular interactions of IBS11 targeting hQC.** The detailed molecular interactions of IBS11 binding to hQC was analyzed and shown. In the left panel, IBS11 is presented as stick (deep-blue); hQC is shown as ribbon (gray); zinc ion is displayed as spheres (orange). In the right panel, IBS11 is colored in deep-blue and the active site residues of hQC are labeled. The dash lines colored in magenta, orange, black, cyan, and purple denote the hydrophobic interaction, anion-pi interaction, and coordination with zinc ion, pi-donor hydrogen bond, and pi-sigma interaction, respectively.