Supplementary Material

Rational design of selective HDAC2 inhibitors for liver cancer treatment: computational insights into the selectivity mechanism through molecular dynamics simulations and QM/MM calculation

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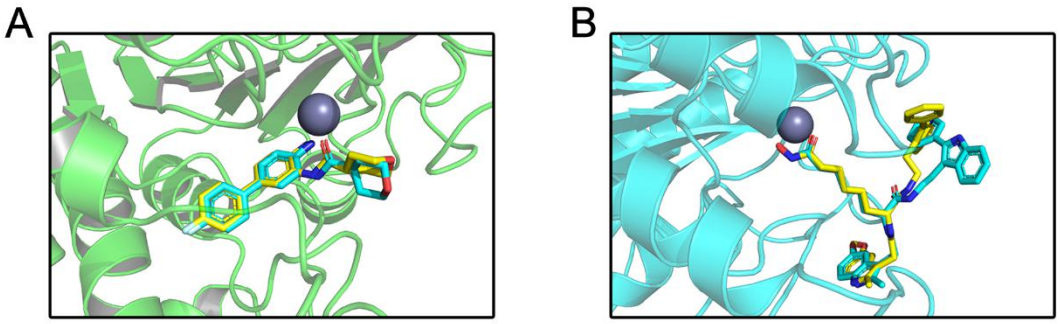

Figure S1. Comparison of the docked and experimental crystallographic conformations for (A) HDAC2, RMSD 0.341 Å (PDB code:5IWG) and (B) HDAC8, RMSD 0.462 Å (PDB code: 2V5X). The original conformation of the co-crystal ligands obtained from X-ray diffraction were indicated as blue sticks, and the docked poses were represented as yellow sticks.

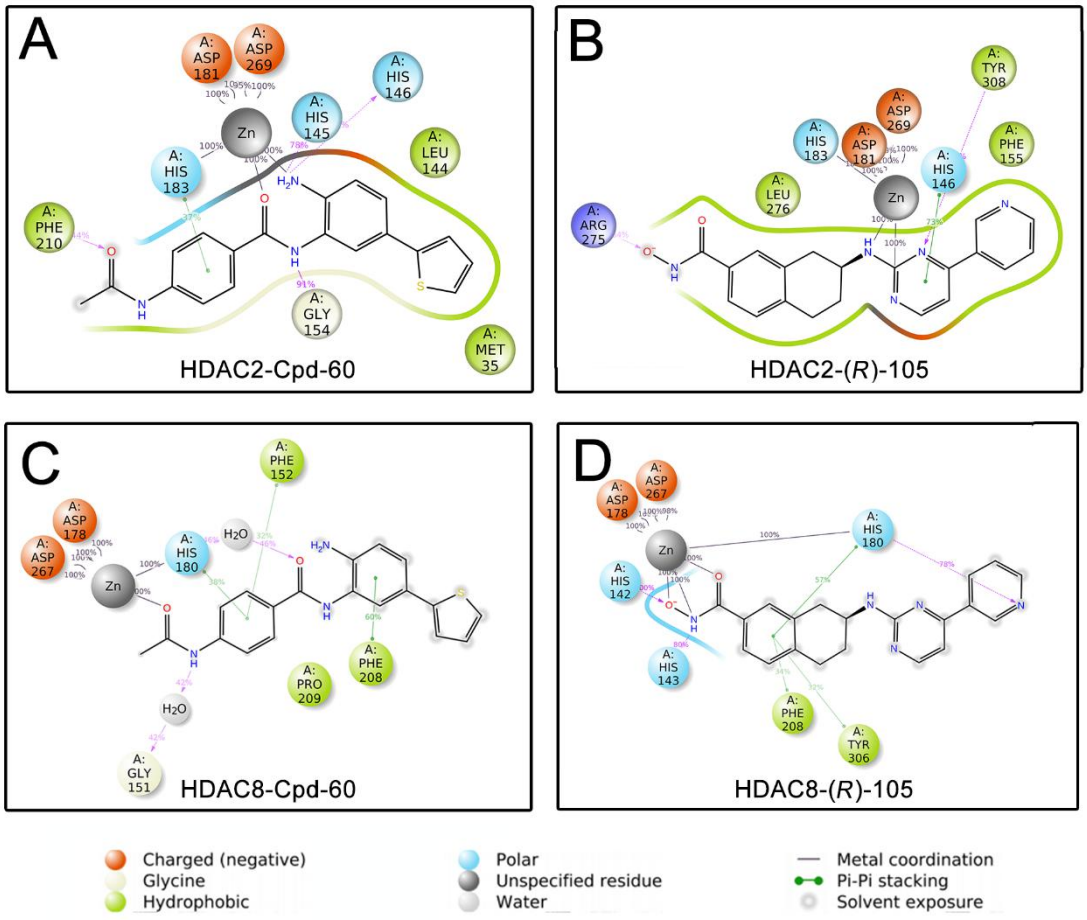

Figure S2. 2D-ligand contact image of ligand-protein complex in the active cavity. (A)HDAC2/Cpd-60; (B)HDAC2/(*R*)-105; (C)HDAC8/Cpd-60; (D) HDAC8/(*R*)-105.

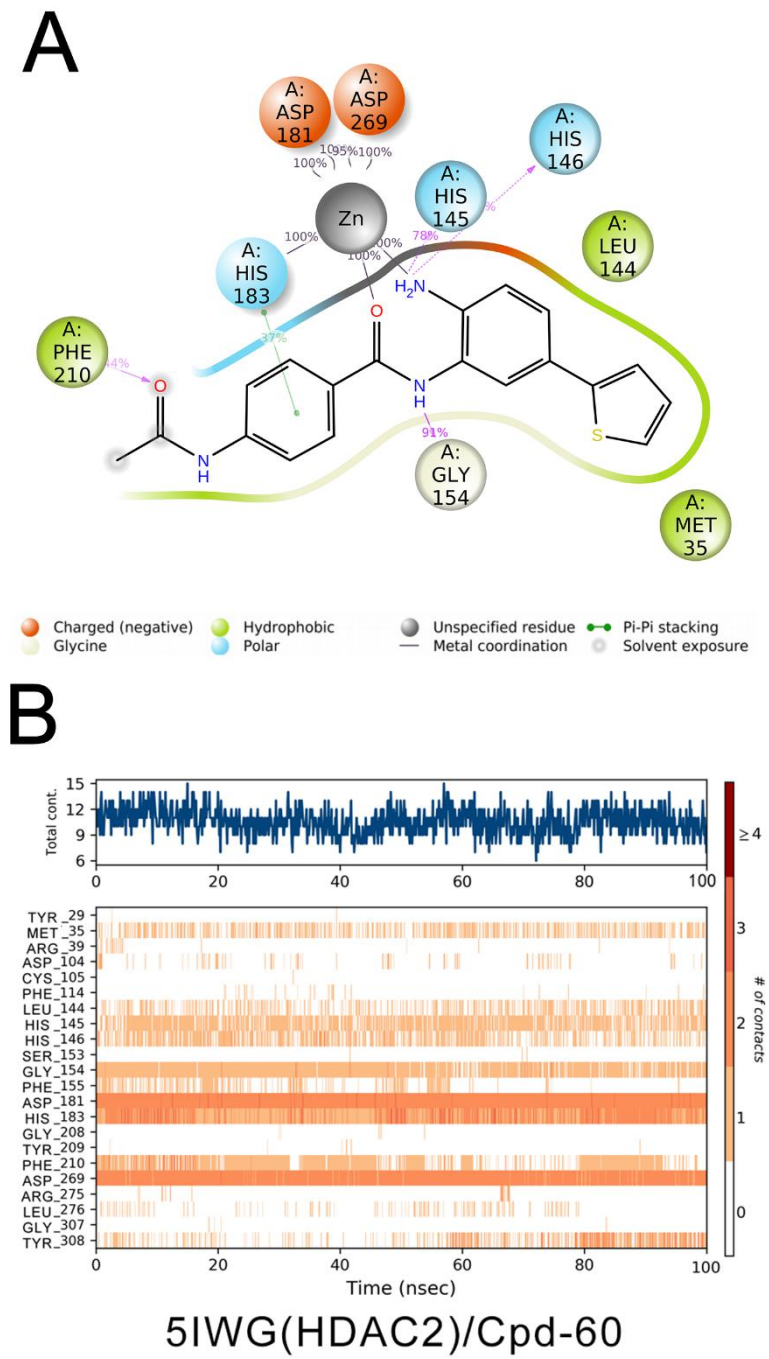

Figure S3. Ligand-Protein contacts of HDAC2/Cpd-60 complex obtained from MD simulation over the entire 100 ns. (A) 2D-ligand contact image of ligand-protein complex in the active cavity. (B) The top graph showed the total number of specific protein-ligand interactions during the simulation. The bottom panel indicated specific residues which interact with the ligand during the simulation. Some residues made more than one specific contact with the ligand, which was represented by a darker degree of orange, according to the scale on the right of the plot.

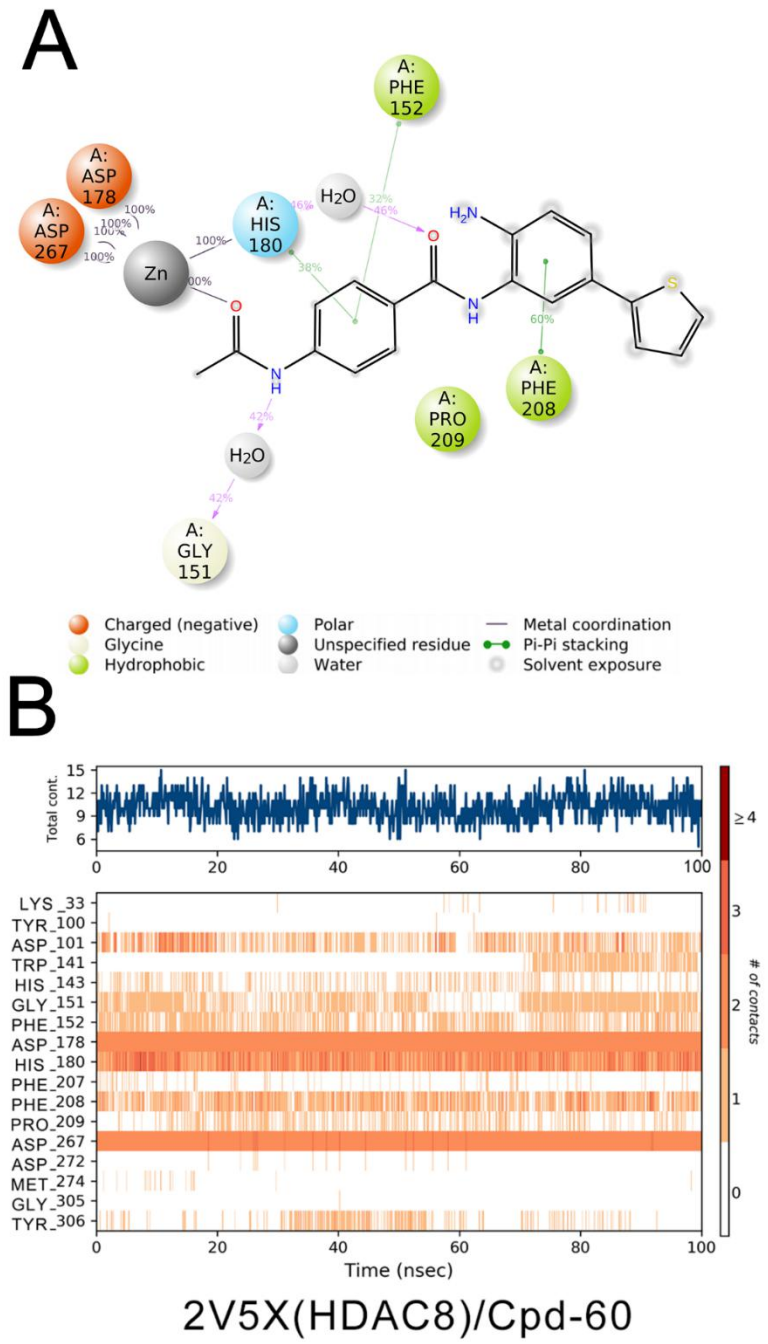

Figure S4. Ligand-Protein contacts of HDAC8/Cpd-60 complex obtained from MD simulation over the entire 100 ns. (A) 2D-ligand contact image of ligand-protein complex in the active cavity. (B) The top graph showed the total number of specific protein-ligand interactions during the simulation. The bottom panel indicated specific residues which interact with the ligand during the simulation. Some residues made more than one specific contact with the ligand, which was represented by a darker degree of orange, according to the scale on the right of the plot.

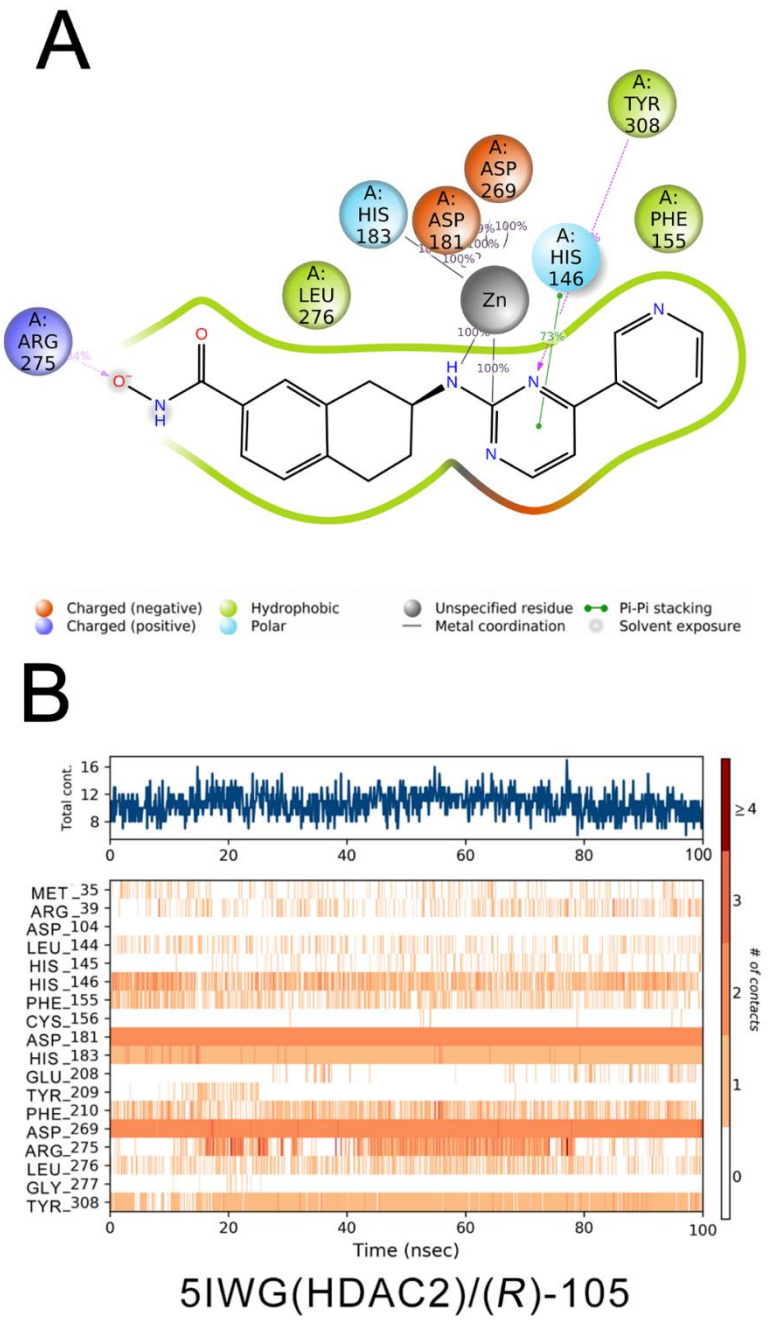

Figure S5. Ligand-Protein contacts of HDAC2/(*R*)-105 complex obtained from MD simulation over the entire 100 ns. (A) 2D-ligand contact image of ligand-protein complex in the active cavity. (B) The top graph showed the total number of specific protein-ligand interactions during the simulation. The bottom panel indicated specific residues which interact with the ligand during the simulation. Some residues made more than one specific contact with the ligand, which was represented by a darker degree of orange, according to the scale on the right of the plot.

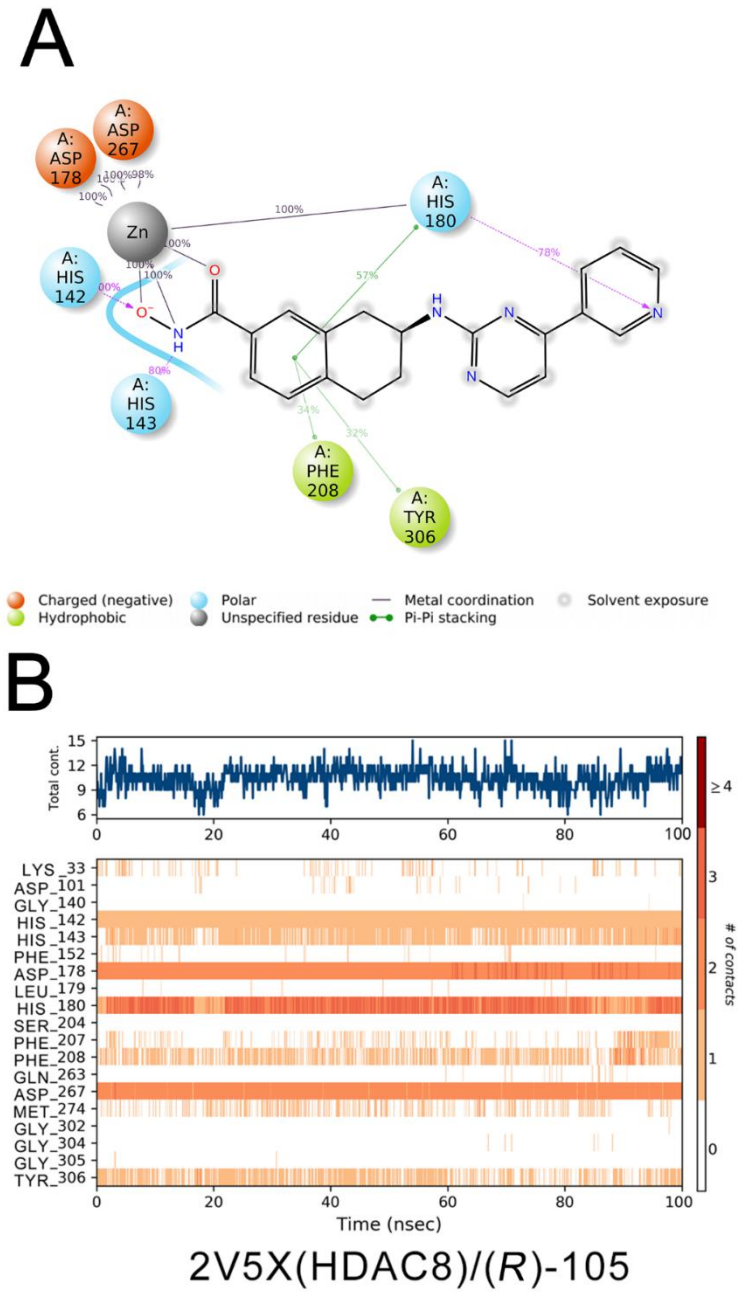

Figure S6. Ligand-Protein contacts of HDAC8/(*R*)-105 complex obtained from MD simulation over the entire 100 ns. (A) 2D-ligand contact image of ligand-protein complex in the active cavity. (B) The top graph showed the total number of specific protein-ligand interactions during the simulation. The bottom panel indicated specific residues which interacted with the ligand during the simulation. Some residues made more than one specific contact with the ligand, which was represented by a darker degree of orange, according to the scale on the right of the plot.

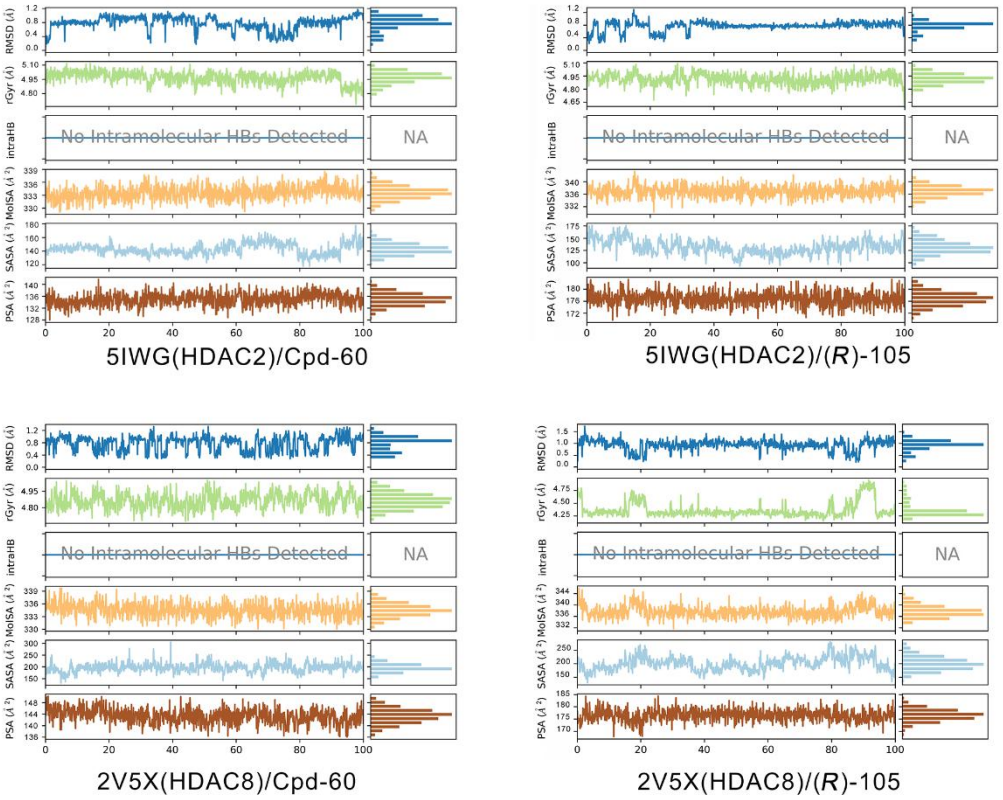

Figure S7. Ligands' five properties obtained from MD simulation over the entire 100 ns for complexes.

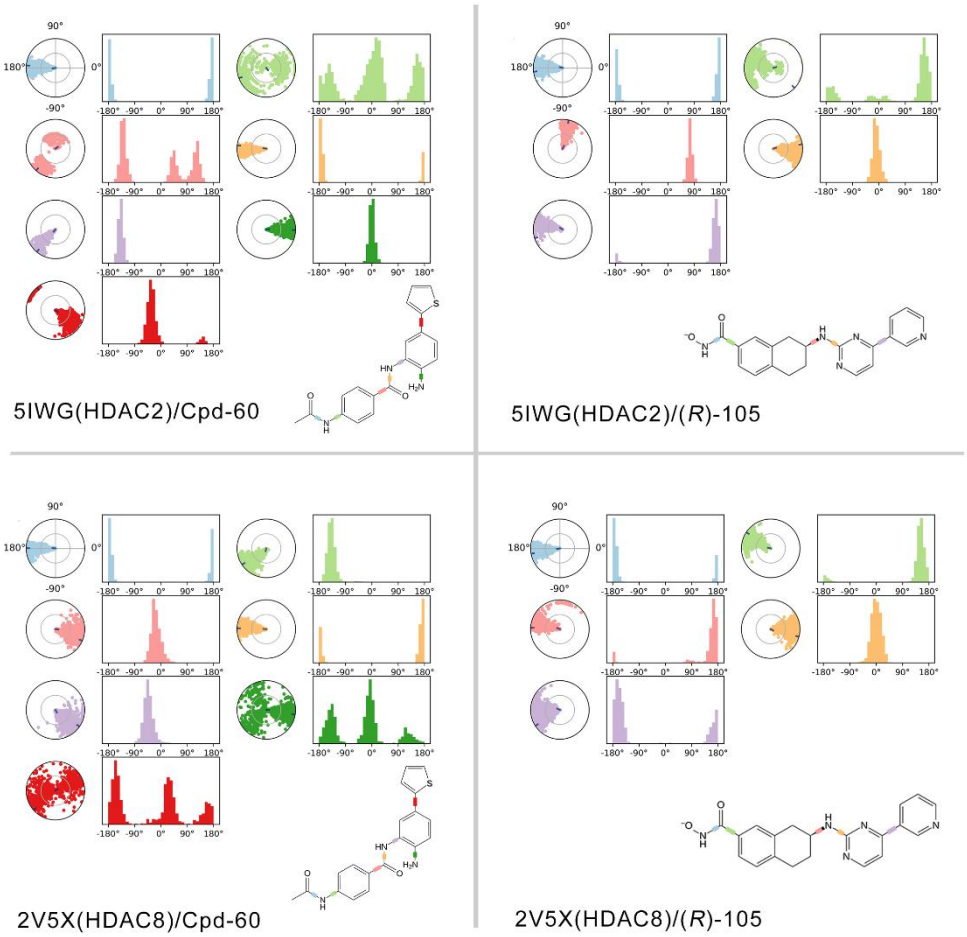

Figure S8. Ligand Torsion Profile obtained from MD simulation over the entire 100 ns for complexes.