Support Information

Prediction of the binding affinities and selectivity for CB1 and CB2 ligands using homology modeling, molecular docking, molecular dynamics simulations, and MM-PBSA binding free energy calculations

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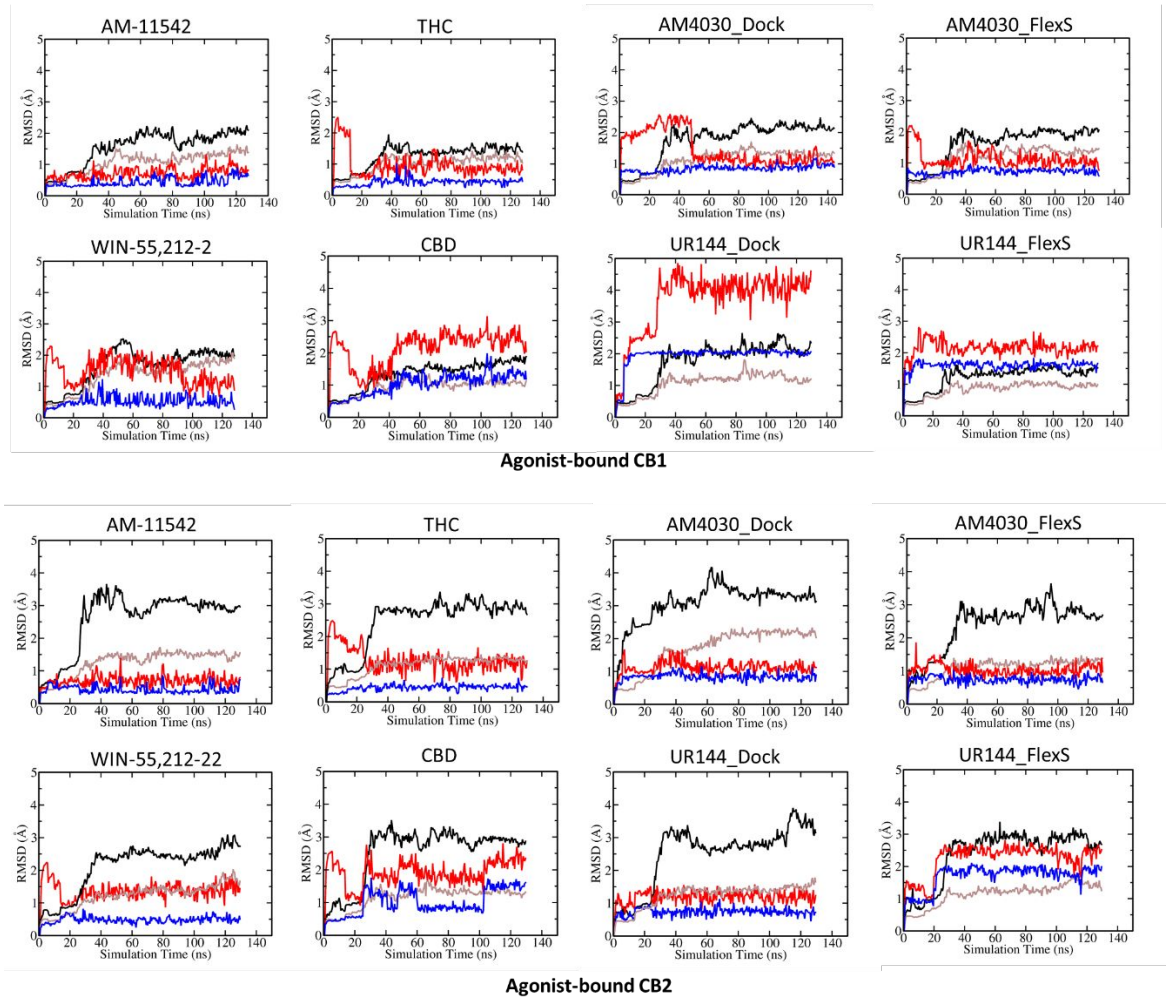

Figure S1. RMSD values of agonist-bound CB1 and agonist-bound CB2 systems along the MD simulation time. Black curves represent the RMSD value of the backbone atoms of the whole CB1/CB2 protein, brown curves represent the backbone atoms of the transmembrane helices of CB1/CB2; red and blue curves are the RMSD ligand without (non-LS-fitting) and with least-square fittings (LS-fitting), respectively.

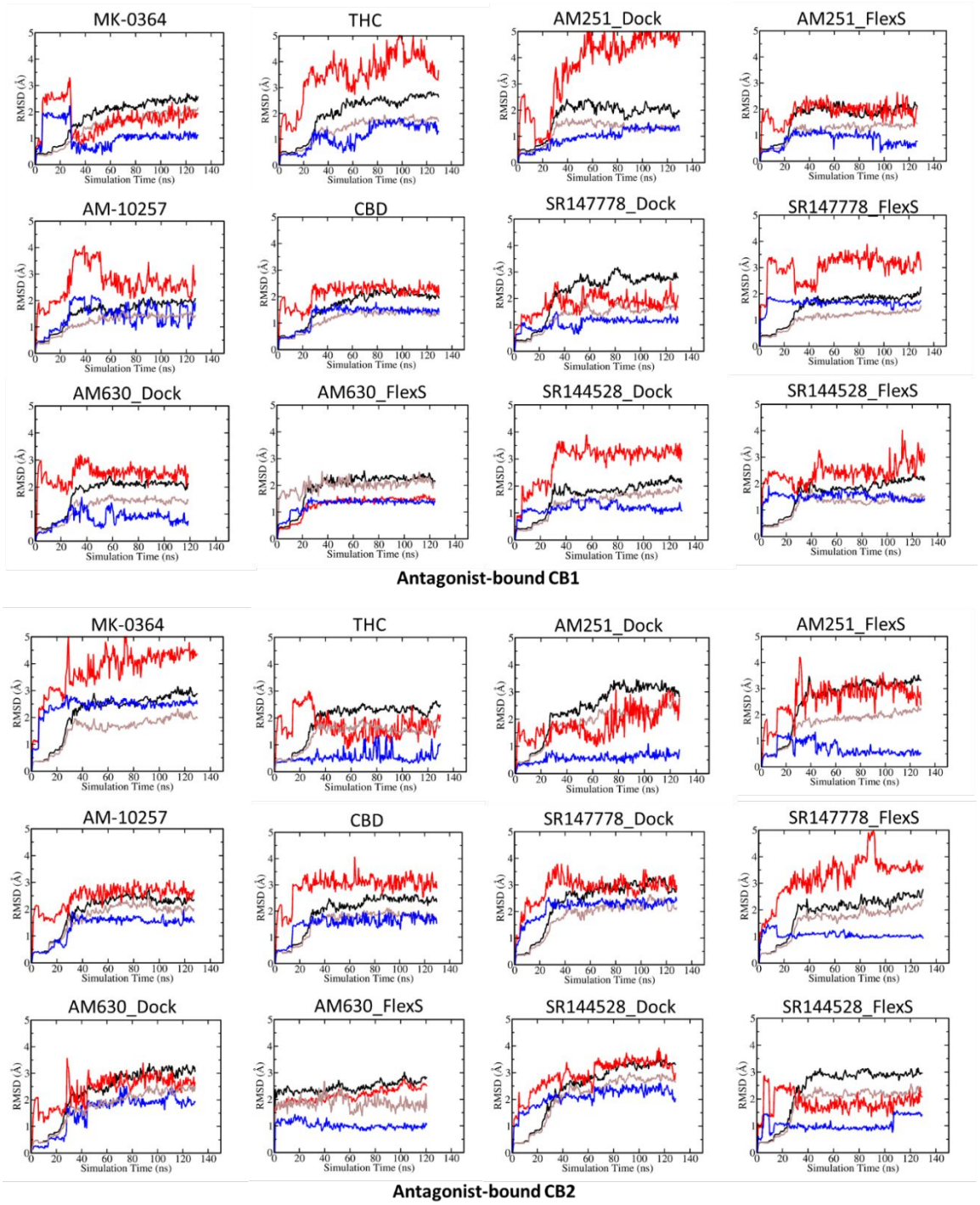

Figure S2. RMSD values of antagonist-bound CB1 and antagonist-bound CB2 systems along the MD simulation time. Black curves represent the RMSD value of the backbone atoms of the whole CB1/CB2 protein, brown curves represent the backbone atoms of the transmembrane helices of CB1/CB2; red and blue curves are the RMSD ligand without (non-LS-fitting) and with least-square fittings (LS-fitting), respectively.

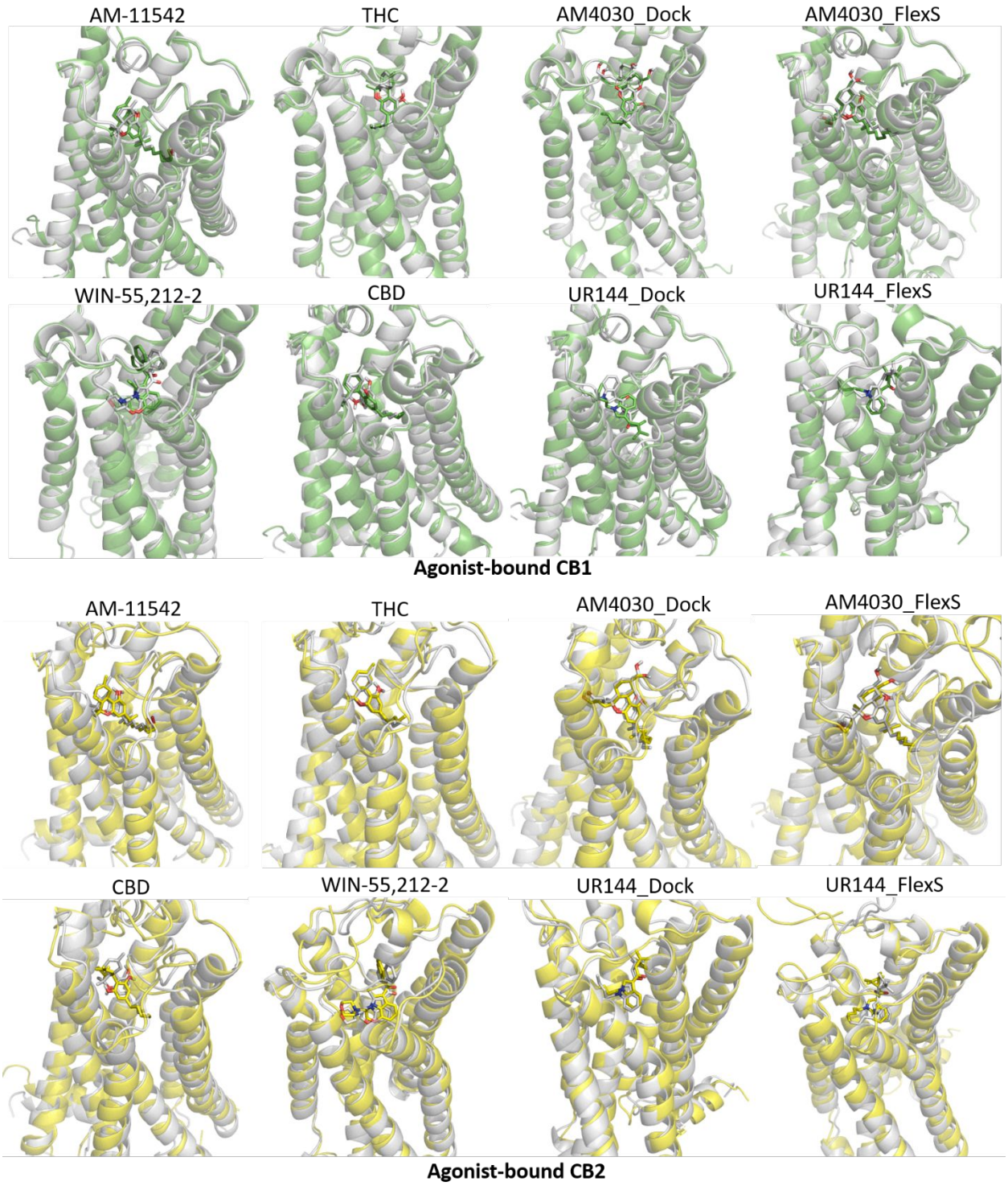

Figure S3. Comparison of the initial structure (in grey) with the representative structure of MD simulation in agonist-bound CB1 (in green) and agonist-bound CB2 systems (in yellow).

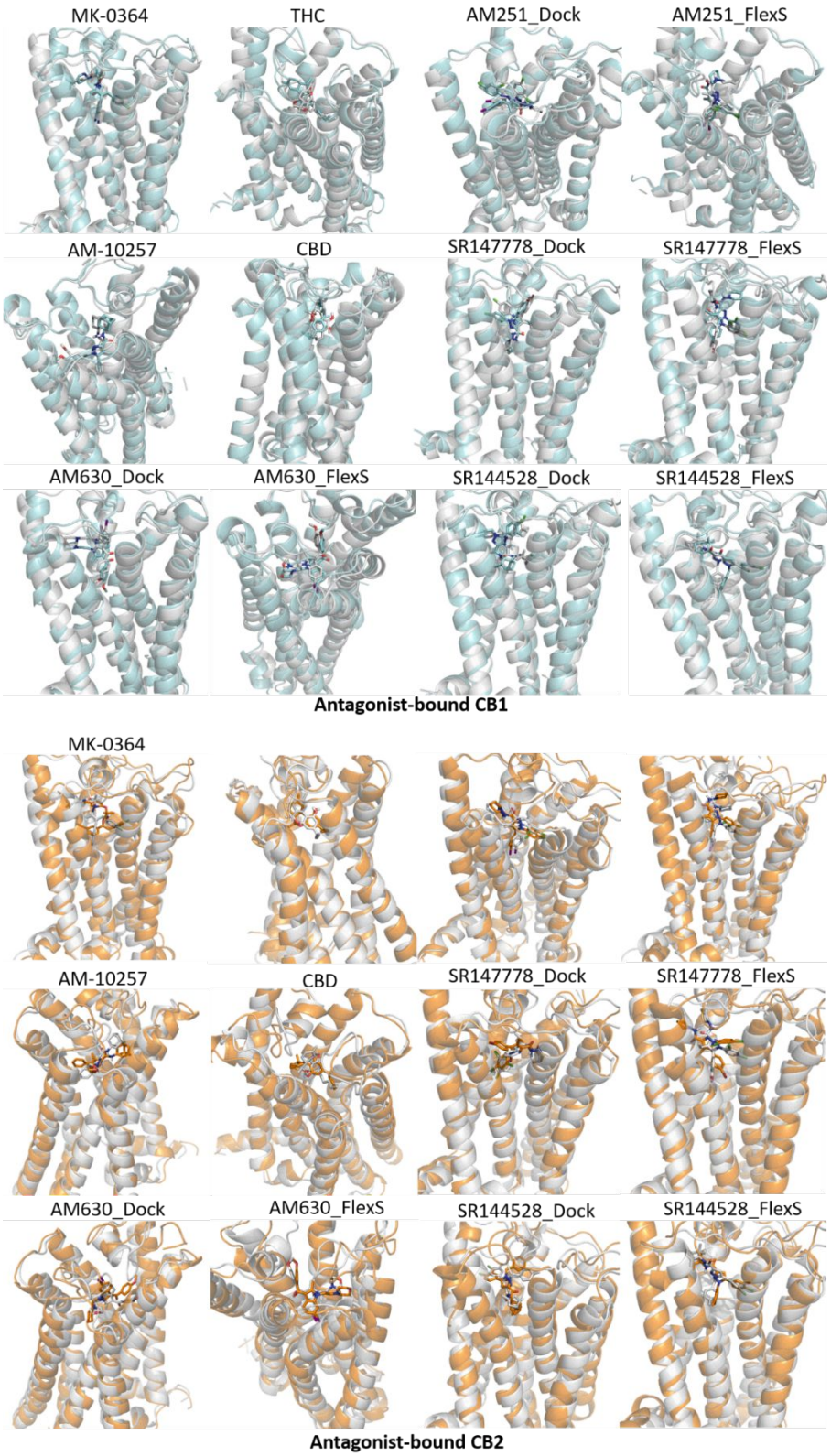

Figure S4. Comparison of the initial structure (in grey) with the representative structure of MD simulation in antagonist-bound CB1 (in cyan) and antagonist-bound CB2 systems (in orange).

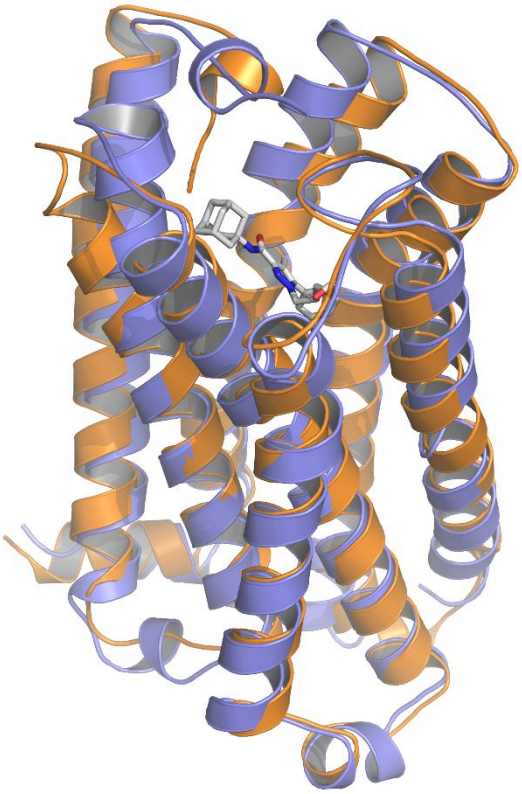

Figure S5. The comparison between antagonist-bound CB2 homology model (in orange) and antagonist-bound CB2 crystal structure (entry code: 5ZTY) (in slate blue) and its co-crystallized ligand AM-10257 (grey sticks).