Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.


# Molecular mechanism under binding selectivity of inhibitors toward FABP5 and FABP7 explored by multiple short molecular dynamics simulations and free energy analysis

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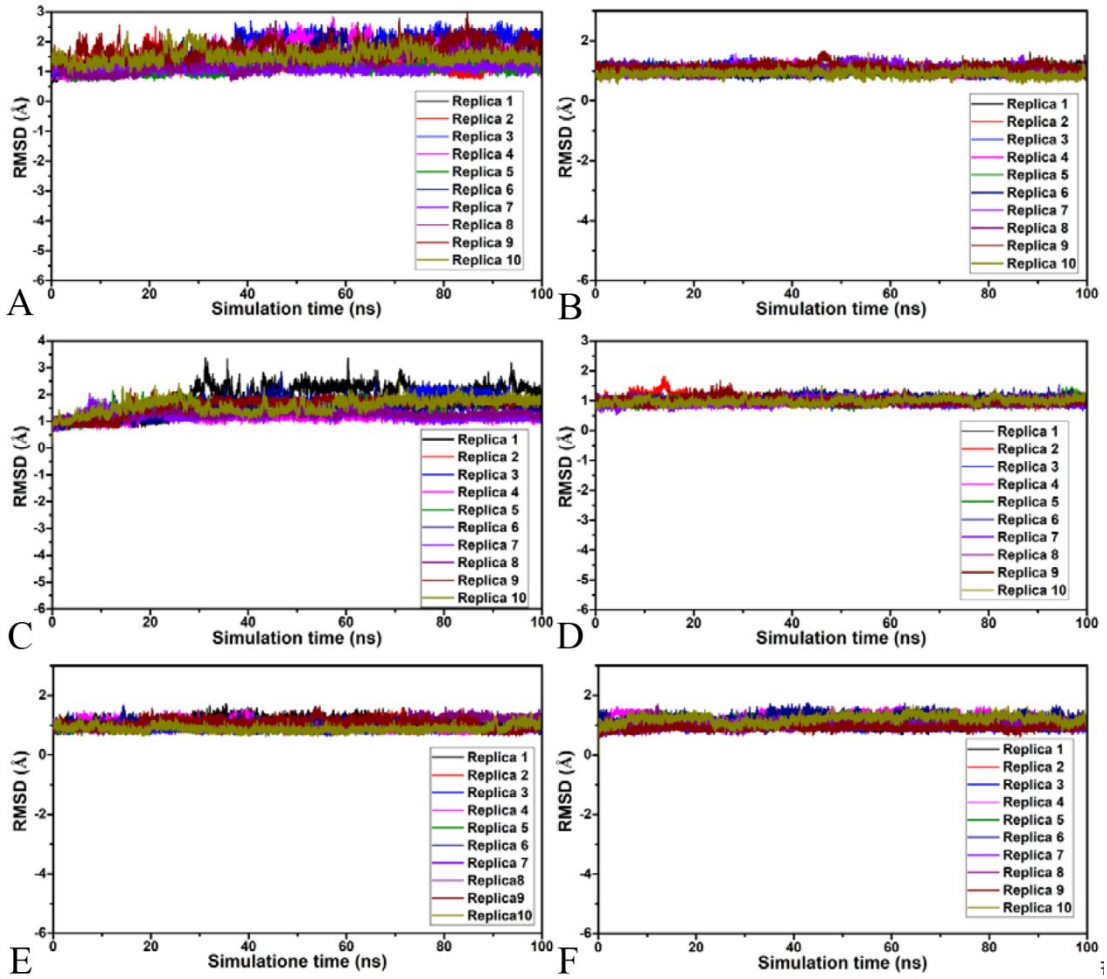


Fig. S1. Root-mean-square deviations (RMSDs) of backbone atoms in FABP5 and FABP7: (A) the 65X-FABP5, (B) the 65X-FABP7, (C) the 8KS-FABP5, (D) the 8KS-FABP7, (E) the 5M8-FABP5 and (F) the 5M8-FABP7.

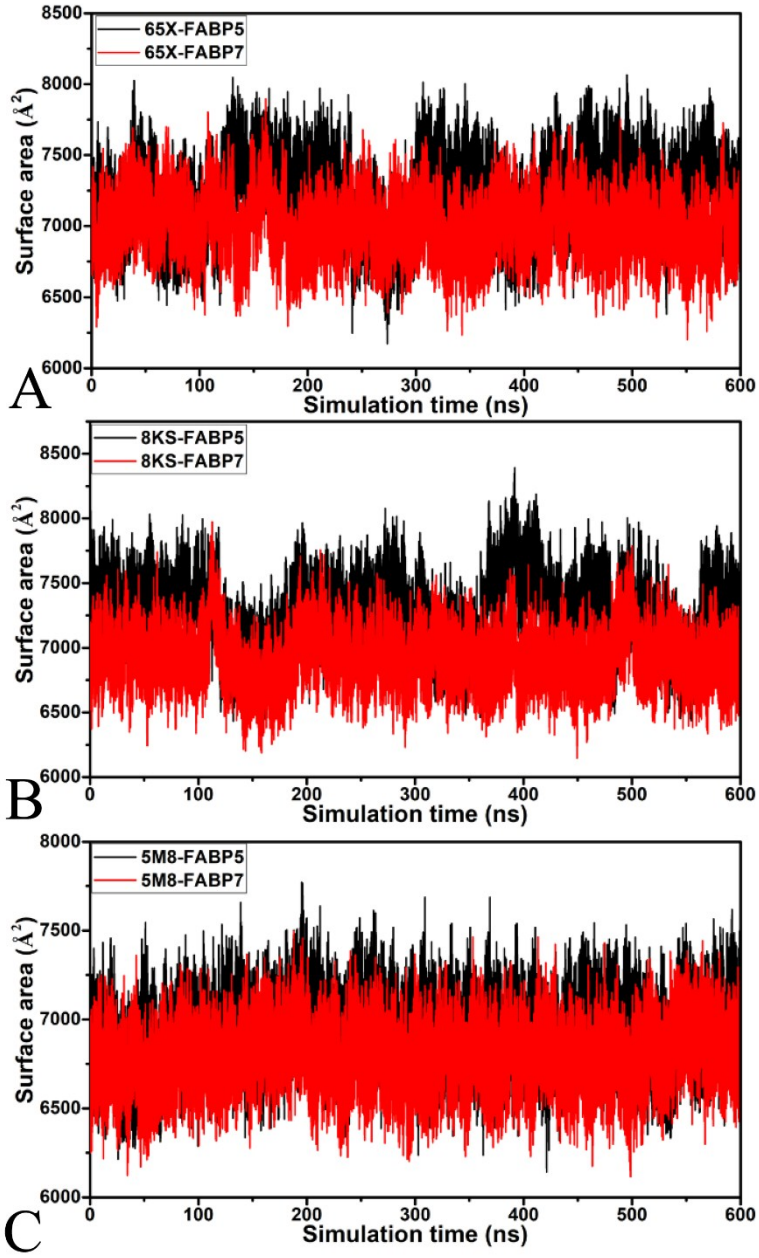


Fig. S2. Evolution of surface area for the inhibitor-FABP5/FABP7 complexes as the simulation time of the MSMD jointed trajectories: (A) the 65X-FABP5 and 65X-FABP7 complexes; (B) the 8KS-FABP5 and 8KS-FABP7 complexes and (C) the 5M8-FABP5 and 5M8-FABP7 complexes.

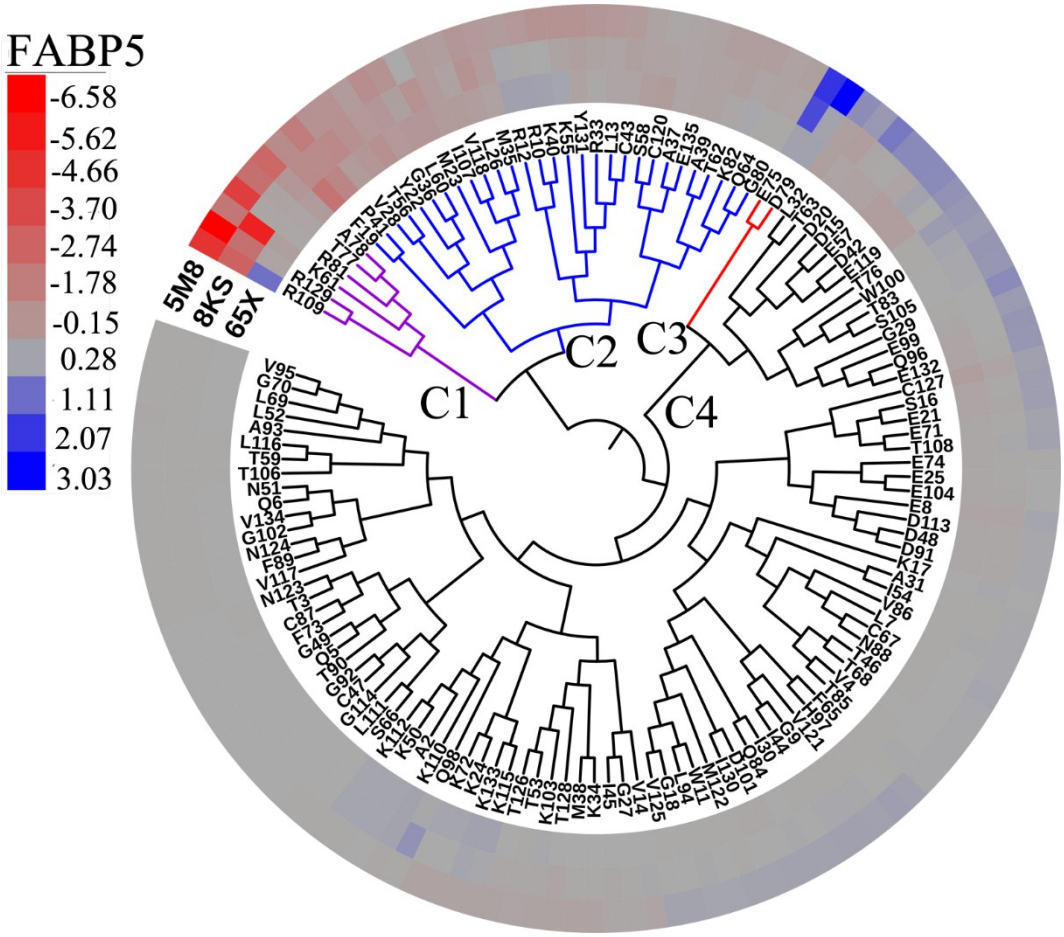


Fig. S3. Hierarchical clustering tree of residues providing contributions to bindings of inhibitors to FABP5 based on interaction energies of separate residues. Binding energy contributions favoring inhibitor associations are shown in red, with the highest contribution (-6.58 kcal/mol) is indicated by exact red and lower contributions gradually fading towards gray (an indicator of -0.15 kcal/mol). Nevertheless, energy contributions weakening inhibitor associations are reflected by blue, with the highest contributions (3.03 kcal/mol) are presented by exact blue and lower ones gradually fading towards gray.

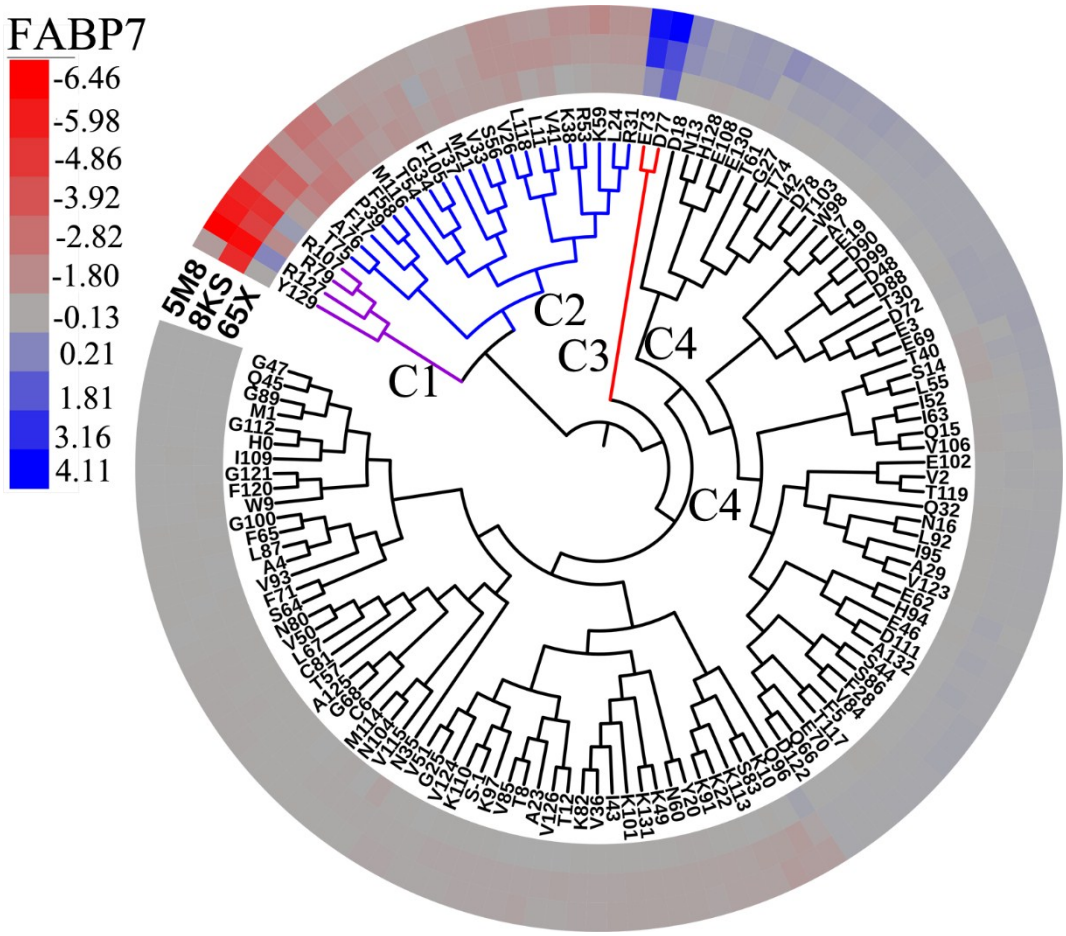


Fig. S4. Hierarchical clustering tree of residues contributing significant information to identification of hot interaction spots of inhibitors with FABP7 based on energetic contributions of separate residues. Favorable energy contributions favoring inhibitor associations are shown in red, with the highest contribution (-6.46 kcal/mol) is indicated by exact red and lower contributions gradually fading towards gray (an indicator of -0.13 kcal/mol). While energy contributions weakening inhibitor associations are reflected by blue, with the highest contributions (4.11 kcal/mol) are presented by exact blue and lower ones gradually fading towards gray.

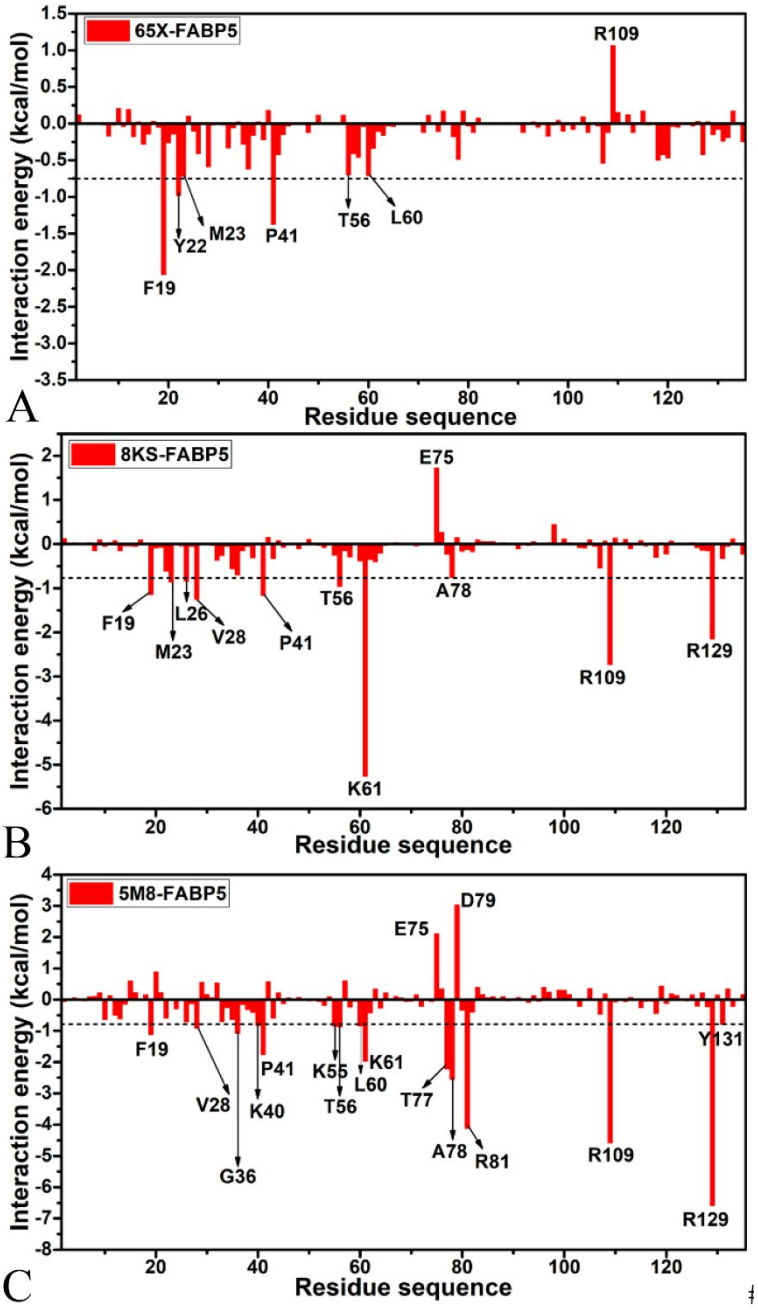


Fig. S5. Interaction spectrum of three inhibitors with separate residues in FABP5: (A) 65X, (B) 8KS and (C) 5M8.

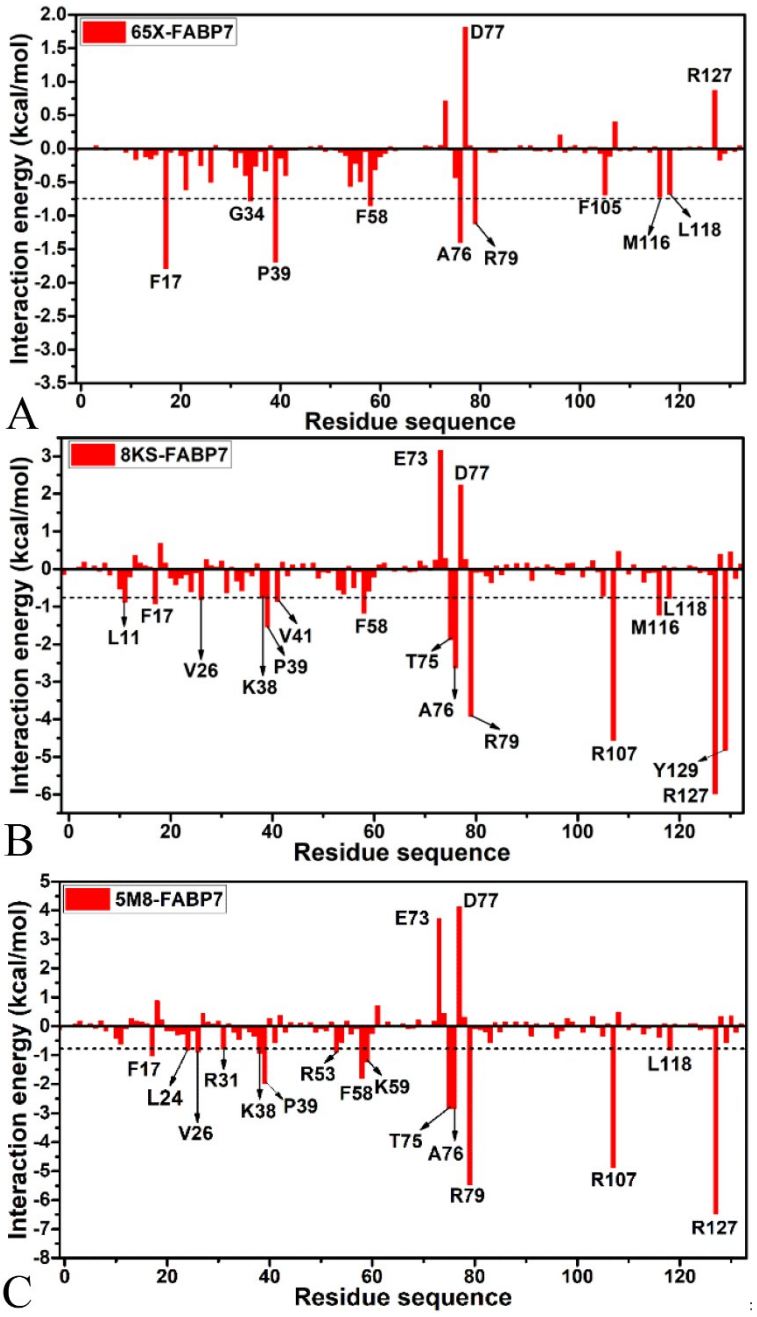


Fig. S6. Interaction spectrum of three inhibitors with separate residues in FABP7: (A) 65X, (B) 8KS and (C) 5M8.

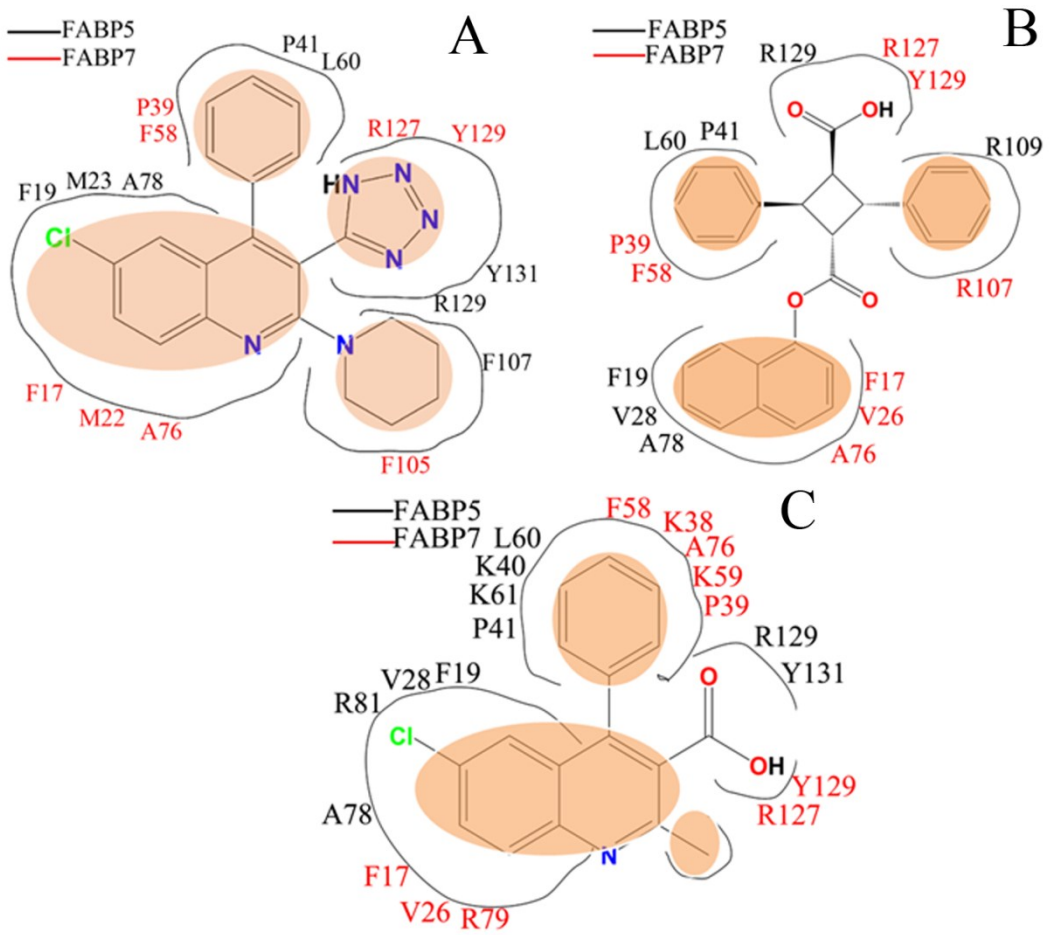


Fig. S7 Common binding modes of three inhibitors to FABP5 and FABP7: (A) the 65X-FABP5/FABP7 complexes, (B) the 8KS-FABP5/FABP7 complexes and (C) the 5M8-FABP5/FABP7 complexes.

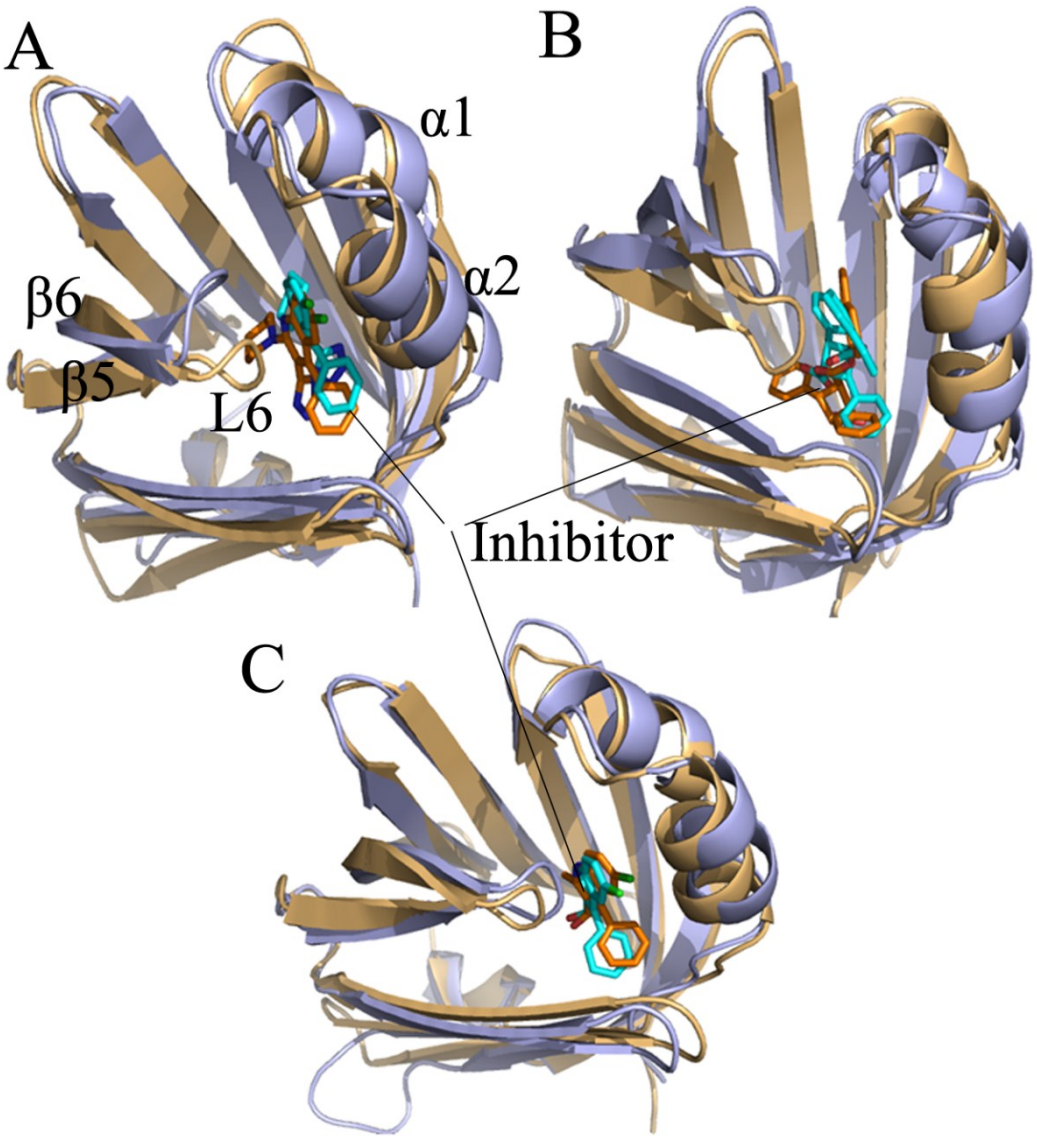


Fig. S8 Superimpositions of structures for the inhibitor-FABP5 and the inhibitor-FABP7 complexes extracted from the equilibrated MSMD trajectories: (A) the 65X-FABP5/FABP7 complexes, (B) the 8KS-FABP5/FABP7 complexes and (C) the 5M8-FABP5/FABP7 complexes. Two proteins FABP5 and FABP7 are shown in cartoon modes, in which FABP5 is represented in the light blue and FABP7 is characterized in the light orange. Inhibitors are displayed in stick modes, among which the inhibitors binding to FABP5 are indicated in the cyan, while the inhibitors binding with FABP7 are shown in the orange.