Supporting information for

Molecular Dynamics Exploration of Selectivity of Dual Inhibitors 5M7, 65X and 65Z toward Fatty Acid Binding Proteins 4 and 5

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Table S1. Comparison of energy contribution of individual component in inhibitor-FABP4 and inhibitor-FABP5 systems by MM-GBSA method[a]

Energy	$\Delta\Delta E_{ele}$	$\Delta\Delta E_{vdw}$	$\Delta\Delta G_{pol}$	$\Delta\Delta G_{nopol}$	[b]$\Delta\Delta G_{ele+pol}$
5M7-FABP4/5	-7.30	3.06	1.19	0.03	-6.12
	-6.84	3.02	1.46	0.04	-5.27
	-7.35	3.45	1.22	0.01	-6.03
	-7.63	3.08	1.54	0.04	-6.09
	-7.66	3.14	1.97	0.07	-5.69
AVE	-7.36	3.15	1.48	0.04	-5.84
SD	0.30	0.15	0.28	0.02	0.32
65X-FABP4/5	-14.26	1.95	8.66	0.04	-5.60
	-14.01	1.64	8.80	0.04	-5.21
	-13.10	1.85	7.02	0.03	-6.08
	-14.24	1.45	8.22	0.07	-6.02
	-14.08	1.35	8.30	0.06	-5.77
AVE	-13.94	1.68	8.2	0.05	-5.74
SD	0.43	0.23	0.63	0.01	0.31
65Z-FABP4/5	-13.33	1.68	8.65	0.29	-4.68
	-14.12	1.44	9.47	0.33	-4.65
	-14.61	1.52	9.10	0.31	-5.51
	-12.84	2.05	8.45	0.32	-4.39
	-14.21	1.70	9.51	0.31	-4.70
AVE	-13.82	1.68	9.04	0.31	-4.79
SD	0.64	0.21	0.43	0.01	0.38

[a]All values are in kcal/mol.

$\Delta\Delta E=\Delta E^{FABP4}-\Delta E^{FABP5}$

$SD=\sqrt{\frac{1}{5}\sum_{i=1}^{5}\left(\Delta\Delta E^{i}-\Delta\Delta E^{ave}\right)^{2}}$

Table S2. Energy contribution of substituted residues in FABP4 and FABP5 calculated by MM-GBSA method[a].

	5M7-FABP4/5		[b]ΔΔE	65X-FABP4/5		[b]ΔΔE	65Z-FABP4/5		[b]ΔΔE
Ser12/Asp15	0.02	0.16	-0.14	0.02	0.18	-0.16	0.02	0.17	-0.15
Glu14/Lys17	0.18	0.17	0.01	-0.18	-0.09	-0.09	0.18	0.09	0.09
Asp18/Glu21	0.11	0.11	0	0.12	0.12	0	0.11	0.12	-0.01
Val23/Leu26	-0.34	-0.3	-0.04	-0.51	-0.38	-0.13	-0.52	-0.35	-0.17
Phe27/Ile30	-0.01	-0.01	0	-0.01	-0.01	0	-0.01	-0.01	0
Thr29/Leu32	-0.43	-0.47	0.04	-0.32	-0.43	0.11	-0.34	-0.45	0.11
Val32/Met35	-0.23	-0.41	0.18	-0.16	-0.27	0.11	-0.29	-0.22	-0.07
Ala33/Gly36	-1.01	0.79	-0.22	-1.43	-0.47	-0.96	-1.27	-0.44	-0.82
Gly34/Ala37	0.01	-0.05	0.06	-0.02	-0.04	0.02	0	-0.03	0.03
Asn39/Asp42	-0.01	0.17	-0.18	-0.05	-0.22	0.17	-0.01	-0.2	0.19
Met40/Cys43	-0.13	-0.09	-0.04	-0.1	-0.07	-0.03	-0.1	-0.07	-0.03
Ser53/Thr56	-0.61	-0.78	0.17	-0.71	-0.89	0.18	-0.49	-0.63	0.14
Phe57/Leu60	-1.12	-0.77	-0.35	-1.38	-0.99	-0.39	-1.08	-0.67	-0.41
Asn59/Thr62	-0.1	-0.16	0.06	0.01	0.01	0	-0.03	0	-0.03
Glu61/Gln64	0.16	0.02	0.14	0.15	0.02	0.13	0.15	0.02	0.13
Ile62/Phe65	-0.02	0.02	-0.04	-0.03	-0.01	-0.02	-0.01	0.01	-0.02
Val73/Thr76	-0.04	-0.02	-0.02	-0.01	-0.01	0	-0.04	-0.02	-0.02
Asp77/Gly80	0.23	0.4	-0.17	0.28	0.11	0.17	-0.21	-0.02	-0.19
Ser101/Glu104	-0.01	0.1	-0.11	0.01	0.11	-0.1	-0.01	0.11	-0.12
Lys120/Asn123	-0.08	0.01	-0.09	-0.07	-0.01	-0.06	-0.08	0.01	-0.09
Ser124/Cys127	-0.03	-0.22	0.19	-0.04	-0.15	0.11	0.02	-0.08	0.1
Val127/Ile130	-0.02	-0.02	0	-0.02	-0.02	0	-0.02	-0.02	0

[a]All values are in kcal/mol.

[b]$\Delta\Delta E=\Delta E^{FABP4}-\Delta E^{FABP5}$.

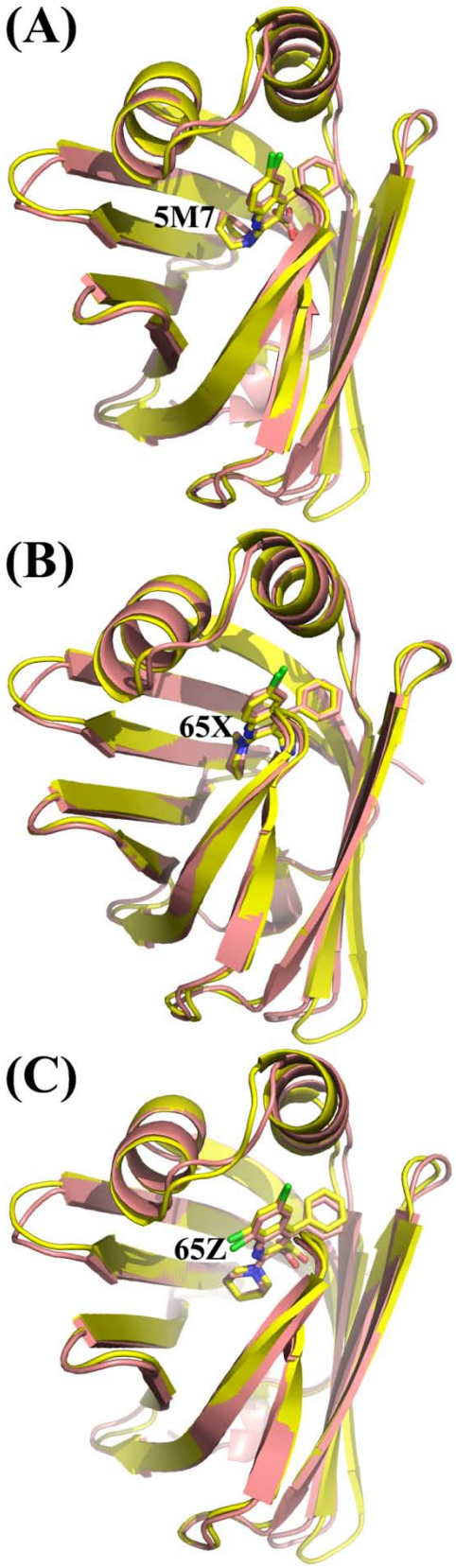

Figure S1. Superposition of conformations used in the experimental studies between inhibitor-FABP4 (yellow) and inhibitor-FABP5 (pink) complexes. **(A)** 5M7-FABP4/FABP5, **(B)** 65X-FABP4/FABP5 and **(C)** 65Z-FABP4/FABP5.

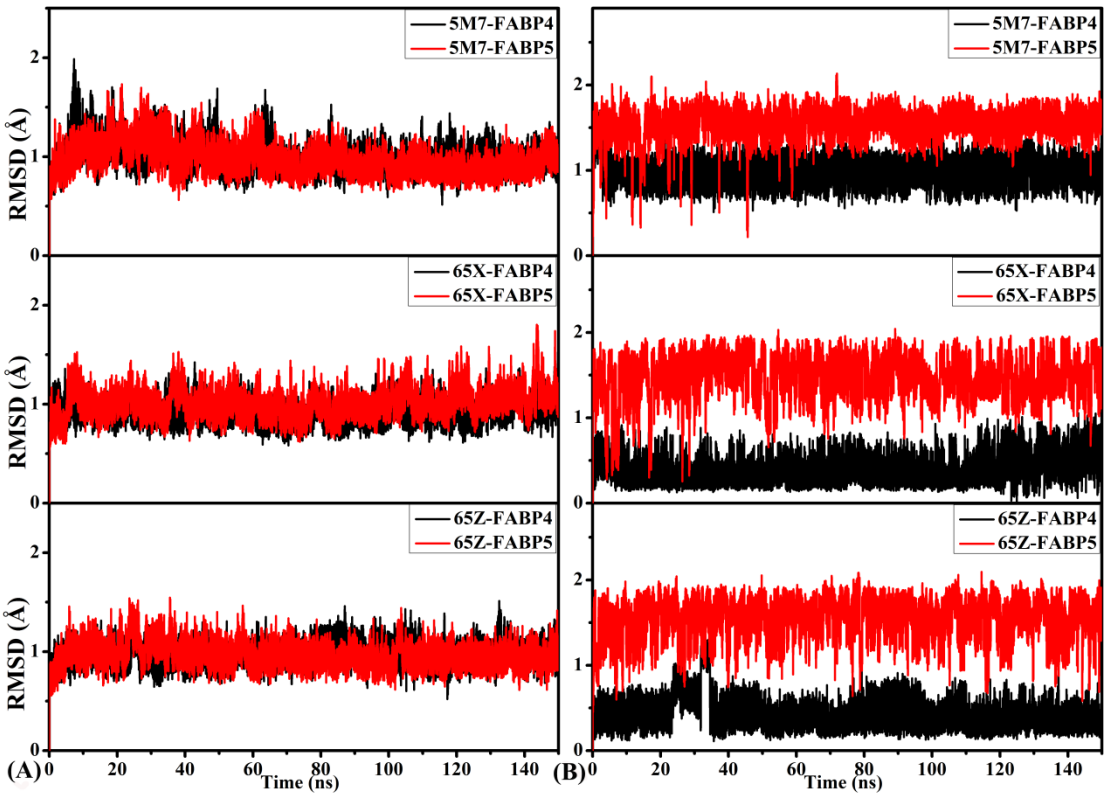

Figure S2. Root-mean-square-deviations (RMSDs) of the backbone atoms in FABP4/FABP5 **(A)** and three inhibitors **(B)** relative to their starting structures during the MD simulation as function as time.

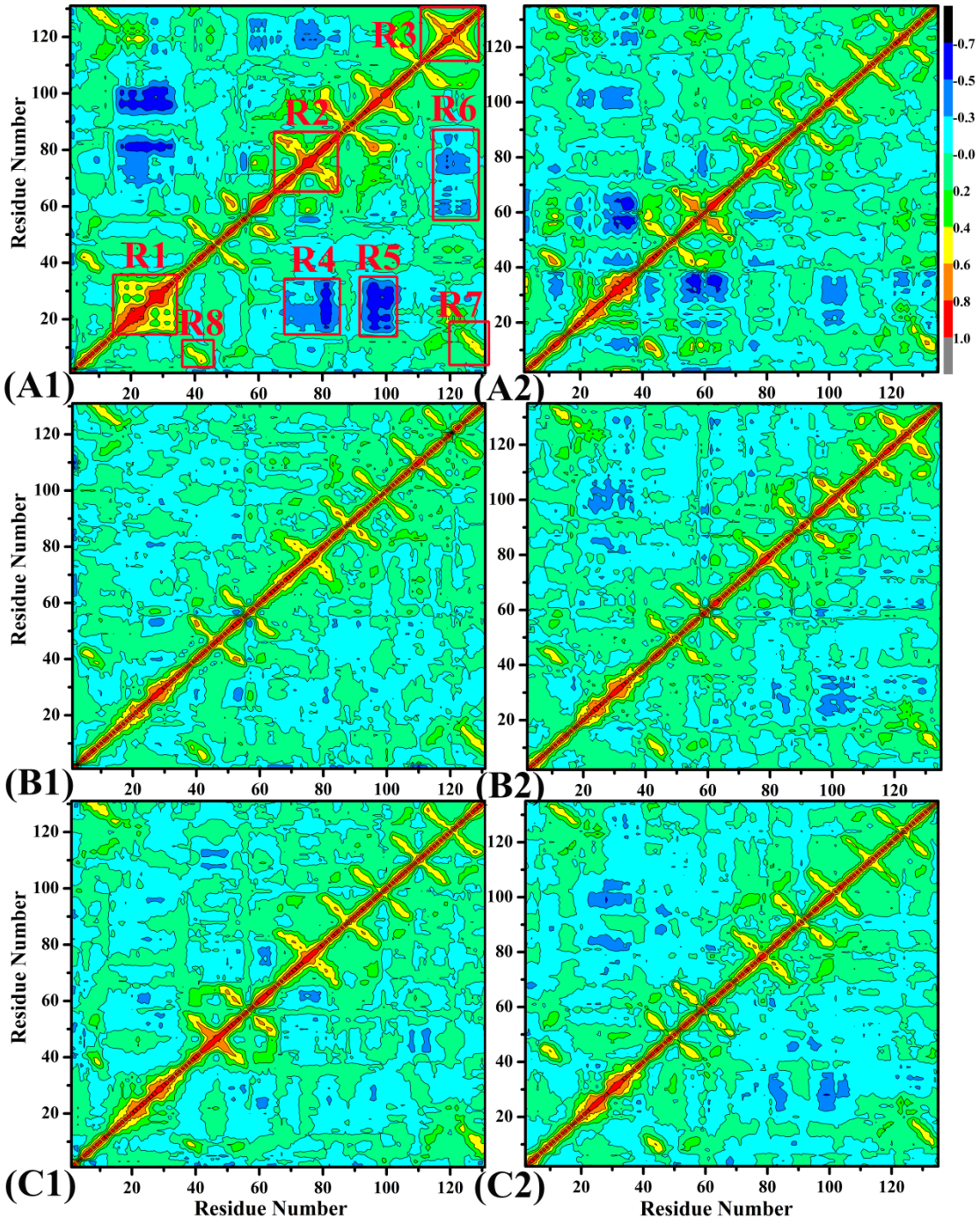

Figure S3. Cross-correlation matrices of fluctuations of Cα atoms relative to their average positions in six systems: **(A1/A2)** 5M7-FABP4/FABP5, **(B1/B2)** 65X-FABP4/FABP5 and **(C1/C2)** 65Z-FABP4/FABP5.

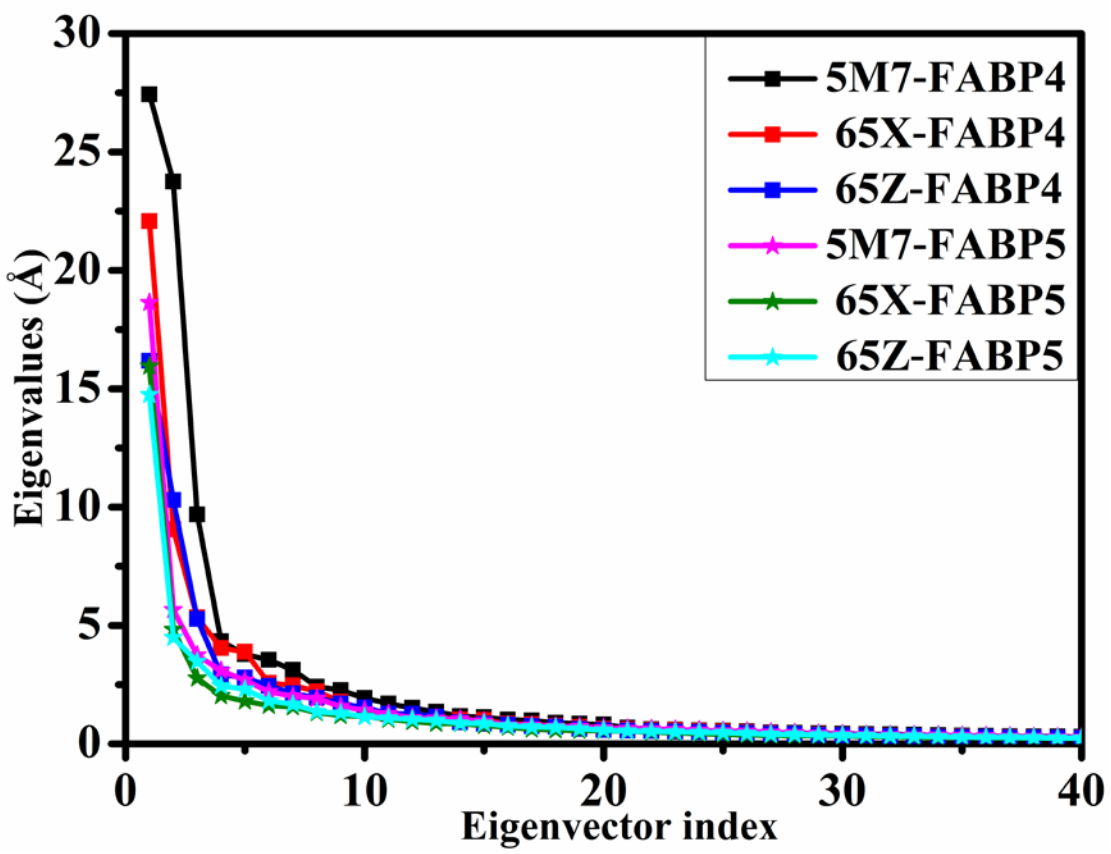

Figure S4. Comparison of the eigenvalues plotted against the corresponding eigenvector indices originated from the diagonalization of covariance matrix of Cα atoms.