

Supplementary Material

Steered molecular dynamics simulations study on FABP4 inhibitors

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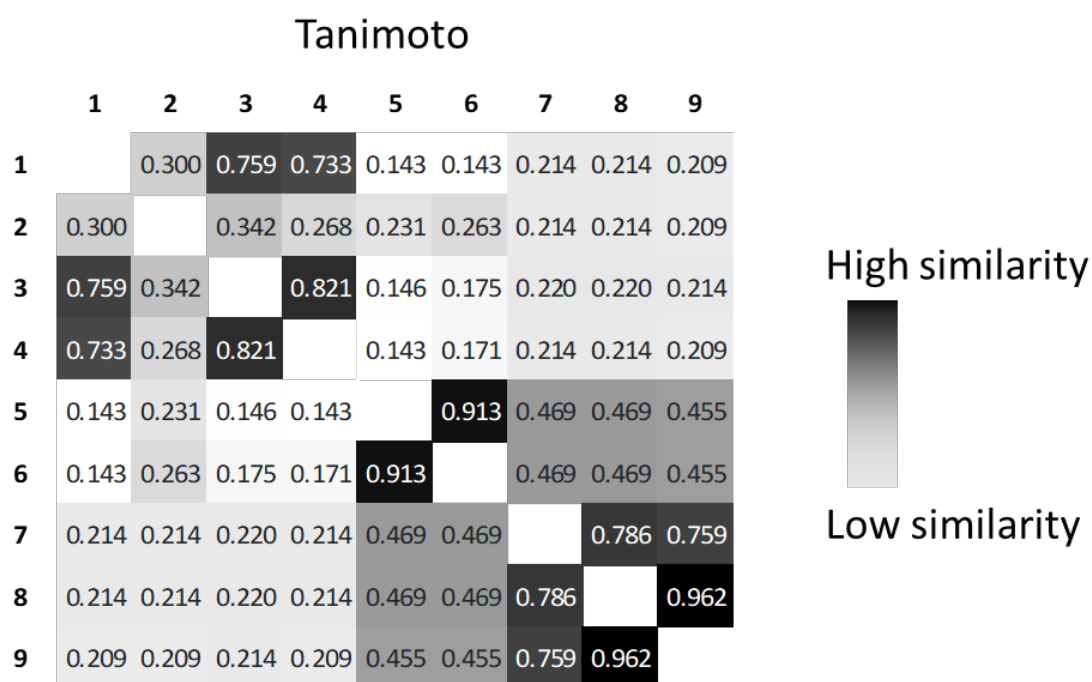


Figure S1. Similarity matrix calculated by Tanimoto index for molecules 1–9.

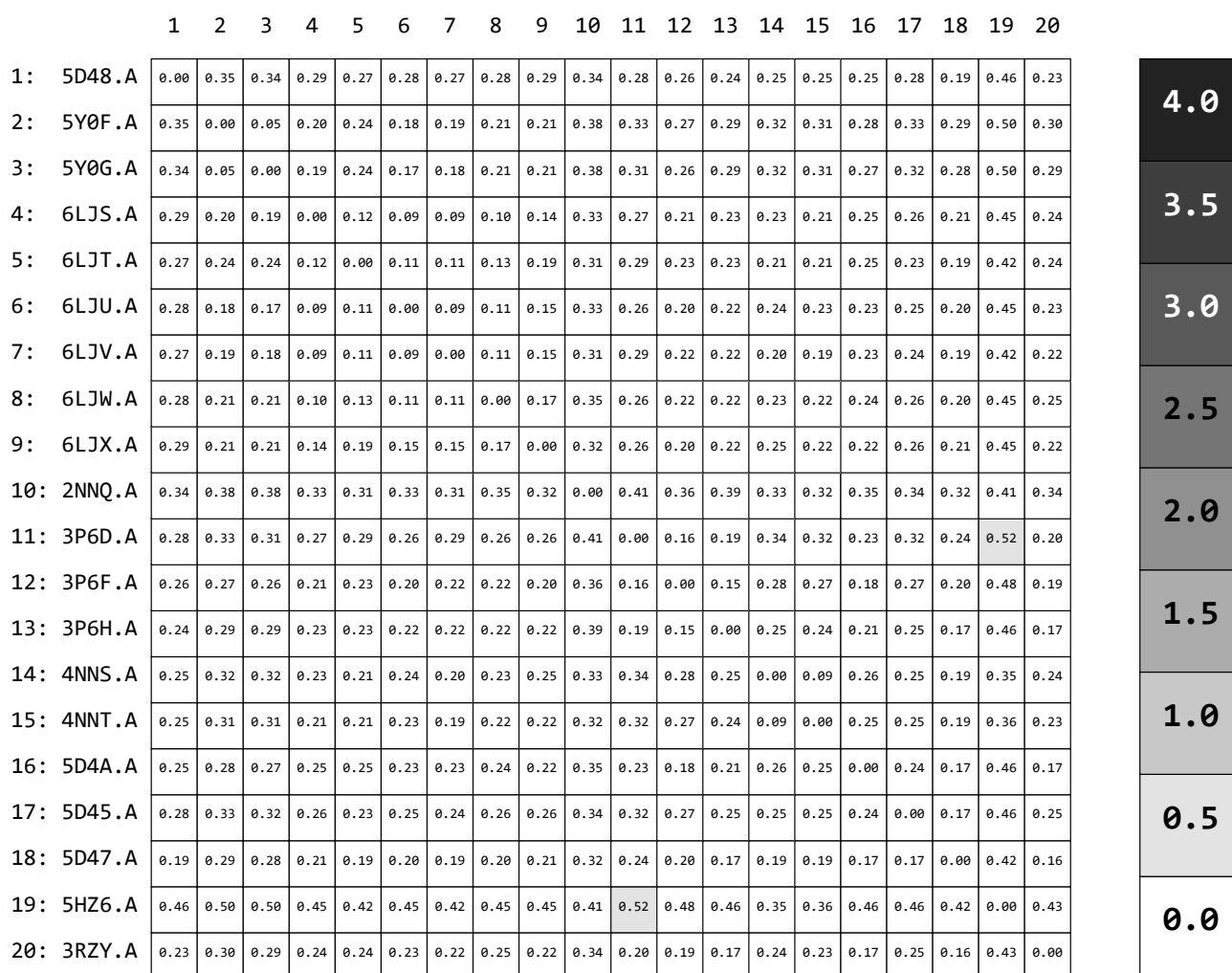


Figure S2. RMSD matrix for the selected FABP4 from the Protein Data Bank (PDBids are reported in the Figure).

	1	2	3	4	5	6	7	8	9	
1: 6LJX ligand in 6LJX protein: average	0.00	0.61	0.64	0.84	0.55	1.93	0.24	0.68	0.76	4.0
2: 6LJX ligand in 6LJX protein: energy min	0.61	0.00	0.87	1.14	0.48	2.05	0.66	0.50	0.90	3.5
3: 6LJX ligand in 6LJX protein: 100 ns	0.64	0.87	0.00	0.95	0.74	1.83	0.75	0.89	1.12	3.0
4: 6LJX ligand in 2NNQ protein: average	0.84	1.14	0.95	0.00	1.02	1.35	0.91	1.09	1.19	2.5
5: 6LJX ligand in 2NNQ protein: energy min	0.55	0.48	0.74	1.02	0.00	1.94	0.63	0.51	0.95	2.0
6: 6LJX ligand in 2NNQ protein: 100 ns	1.93	2.05	1.83	1.35	1.94	0.00	1.98	1.99	2.10	1.5
7: 6LJX ligand in 6LJV protein: average	0.24	0.66	0.75	0.91	0.63	1.98	0.00	0.73	0.64	1.0
8: 6LJX ligand in 6LJV protein: energy min	0.68	0.50	0.89	1.09	0.51	1.99	0.73	0.00	1.00	0.5
9: 6LJX ligand in 6LJV protein: 100 ns	0.76	0.90	1.12	1.19	0.95	2.10	0.64	1.00	0.00	0.0

Figure S3. RMSD matrix for the selected FABP4 structures from the PDB (PDBids are reported in the Figure). Average structure during MD simulation, minimum energy structure during the simulation, and final structure at 100 ns of simulation.

Table S1. Molecules from the first scaffold hopping replacement.

Rank	Structure	Field Score
molecule (16) 1	<chem>O=C1C(NC(=O)N)=CC(=NN1CC)c2ccccc2</chem>	0.963
molecule (17) 2	<chem>O=C1C(NC(=O)N)=CC(=NN1)c2ccccc2</chem>	0.935
molecule (18) 3	<chem>O=C(Nc1cc(nnc1OC)-c2ccccc2)N</chem>	0.911
molecule (19) 4	<chem>O=C(NC1=CC(=CN(C1=O)C)c2ccccc2)N</chem>	0.873
molecule (20) 5	<chem>O=C(Nc1cc(nn2cnc12)-c3ccccc3)N</chem>	0.882
6	<chem>O=C(N)/C=C/C=C(C=C(C1=O)C)c2ccccc2</chem>	0.853
7	<chem>O=C(Nc1cc(nn2c(nnc12)C)-c3ccccc3)N</chem>	0.894
8	<chem>O=C(Nc1cc(nc(OC)n1)-c2ccccc2)N</chem>	0.883
9	<chem>O=C(N)Cc1cc(nc(n1)C)-c2ccccc2</chem>	0.863
10	<chem>O=C(Nc1cc(nc(n1)C)-c2ccccc2)N</chem>	0.859
11	<chem>O=C(Nc1cc(nc([n+][O-])N)-c2ccccc2)N</chem>	0.829
12	<chem>O=C(Nc1cc(nc2ccnn21)-c3ccccc3)N</chem>	0.859
13	<chem>Clc1nc(NC(=O)N)cc(n1)-c2ccccc2</chem>	0.856
14	<chem>O=C(Nc1cc(nc(n1)CC)-c2ccccc2)N</chem>	0.857
15	<chem>Oc1nc(NC(=O)N)cc(n1)-c2ccccc2</chem>	0.837
16	<chem>O=C1C(NC(=O)N)=C(C(=NN1C)c2ccccc2)C=C</chem>	0.879
17	<chem>O=C(Nc1cc(nc(SC)n1)-c2ccccc2)N</chem>	0.856
18	<chem>O=C(n1c2cc(nc(N)c2nn1)-c3ccccc3)N</chem>	0.827
19	<chem>O=C1/C(C(=NN1)c2ccccc2)=C\NC(=O)N</chem>	0.855
20	<chem>O=C(Nc1cc(nc(N)c1[N+])([O-])=O)-c2ccccc2)N</chem>	0.846
21	<chem>O=C(Nc1cc(n2c(n1)ccn2)-c3ccccc3)N</chem>	0.85
22	<chem>O=C(N)Cc1cc(ncn1)-c2ccccc2</chem>	0.85
23	<chem>O=C1C(NC(=O)N)=CC(c2ccccc2)=CN1</chem>	0.839

24	<chem>O=C(Nc1cc(ncn1)-c2ccccc2)N</chem>	0.847
25	<chem>O=C(Nc1cc(nc(n1)NC)-c2ccccc2)N</chem>	0.842
26	<chem>O=C(Nc1cc(nc(n1)N)-c2ccccc2)N</chem>	0.82
27	<chem>O=C(Oc1cc(nc(n1)C)-c2ccccc2)N</chem>	0.823
28	<chem>O=C(Nc1cc(nc(c1C#N)C)-c2ccccc2)N</chem>	0.825
29	<chem>O=C(c1cc(nn1CC)-c2ccccc2)C(=O)N</chem>	0.839
30	<chem>O=C(Nc1cc(nc(c1)C)-c2ccccc2)N</chem>	0.81
31	<chem>O=C(N)Cc1cc(nc(O)n1)-c2ccccc2</chem>	0.81
32	<chem>O=C(Nc1cc(nc2cc(nn21)C)-c3ccccc3)N</chem>	0.851
33	<chem>O=C(Nc1cn(nc1CC)-c2ccccc2)N</chem>	0.831
34	<chem>O=C1C(c2ccccc2)=CC(OC(=O)N)=NN1C</chem>	0.816
35	<chem>O=C(Nc1cc(nc(n1)C2CC2)-c3ccccc3)N</chem>	0.864
36	<chem>O=C1C(NC(=O)N)=CC(c2ccccc2)=C(O1)C</chem>	0.845
37	<chem>Clc1nc(OC(=O)N)cc(n1)-c2ccccc2</chem>	0.814
38	<chem>O=C(/C=C(/OC(=O)N)C)c1ccccc1</chem>	0.847
39	<chem>O=C(Nc1cc(cc(n1)C)-c2ccccc2)N</chem>	0.789
40	<chem>FC(F)(F)c1nc(NC(=O)N)cc(n1)-c2ccccc2</chem>	0.844
41	<chem>O=C(Nc1cc(nc2c1cc[nH]2)-c3ccccc3)N</chem>	0.812
42	<chem>O=C(Nc1cc(nc(n1)N(C)C)-c2ccccc2)N</chem>	0.842
43	<chem>O=C(Nc1cc(nc(n1)COC)-c2ccccc2)N</chem>	0.839
44	<chem>Clc1cc(NC(=O)N)cc(n1)-c2ccccc2</chem>	0.799
45	<chem>O=C(N)/C=C(/C(OC)=O)C(Oc1ccccc1)=O</chem>	0.817
46	<chem>O=C(N)c1cnc2c(c(nn2C)-c3ccccc3)c1</chem>	0.813
47	<chem>O=C(Nc1cc(nc(n1)C(C)C)-c2ccccc2)N</chem>	0.853
48	<chem>O=C(Nc1c(C)cnc(-c2ccccc2)c1)N</chem>	0.812
49	<chem>O=C(N)/C=C\1C(OC(c2ccccc2)=C1)=O</chem>	0.836
50	<chem>O=C(NC=1C=C(C(=O)N(C1)C)c2ccccc2)N</chem>	0.791

Table S2. Molecules from the second scaffold hopping replacement.

Rank	Structure	Field Score
molecule (21) 1	<chem>O=C(N)c1c(NC(=O)N)cn(n1)-c2ccccc2</chem>	0.803
molecule (22) 2	<chem>O=C(Nc1cc(nnc1OC)-c2ccccc2)CC</chem>	0.786
molecule (23) 3	<chem>Fc1ccc(cc1NC(=O)C)-c2ccccc2</chem>	0.756
molecule (24) 4	<chem>Oc1ccc(cc1NC(=O)C)-c2ccccc2</chem>	0.748
molecule (25) 5	<chem>O=C(Nc1cc(-c2ccccc2)ccn1)C</chem>	0.77
6	<chem>Clc1ccc(cc1NC(=O)C)-c2ccccc2</chem>	0.761
7	<chem>CO/N=C(/c1ccccc1)c2ccccc2</chem>	0.818
8	<chem>O=C(Nc1cccc(-c2ccccc2)c1)N</chem>	0.745
9	<chem>O=C(Nc1cccc(-c2ccccc2)c1)C</chem>	0.733
10	<chem>Oc1ccc(-c2ccccc2)cc1NC=O</chem>	0.747
11	<chem>O=CNc1cccc(-c2ccccc2)c1</chem>	0.749
12	<chem>O=C(Nc1cc(-c2ccccc2)ccc1OC)C</chem>	0.739
13	<chem>O=C(N)c1cc(nc2ccccc21)-c3ccccc3</chem>	0.762
14	<chem>n12cnnc1c(nc3ccccc32)-c4ccccc4</chem>	0.791
15	<chem>O=C(Nc1cc(-c2ccccc2)ccn1)CC</chem>	0.755
16	<chem>O=C1c2ccccc2C(=NN1C)c3ccccc3</chem>	0.732
17	<chem>O=C(Nc1cncc(c1)-c2ccccc2)C</chem>	0.722

18	<chem>Nc1cc2c(c(ncn2)-c3ccccc3)cn1</chem>	0.751
19	<chem>O=C(N)c1cc2c(s1)c(ncn2)-c3ccccc3</chem>	0.781
20	<chem>O=C(Nc1cccc(-c2ccccc2)c1)CC</chem>	0.744
21	<chem>O=C(Nc1cc(-c2ccccc2)ccn1)C3CC3</chem>	0.766
22	<chem>O=C1NN=C(N1/N=C/c2ccccc2)C</chem>	0.782
23	<chem>O=C1C=2CCCCC2C(=NN1C)c3ccccc3</chem>	0.713
24	<chem>Oc1ccc(c2c1NC(S2)=O)-c3ccccc3</chem>	0.745
25	<chem>Clc1nc(nc(NCC)n1)-c2ccccc2</chem>	0.706
26	<chem>Cc1nc(-c2ccccc2)cc(-n3cccn3)n1</chem>	0.726
27	<chem>Cc1nc(cc(NC2CC2)n1)-c3ccccc3</chem>	0.691
28	<chem>CN(c1nc(OC)nc(n1)-c2ccccc2)C</chem>	0.716
29	<chem>Oc1ccc(NC(=O)C)cc1-c2ccccc2</chem>	0.718
30	<chem>O=C(c1ccccc1)c2nnc(s2)N</chem>	0.789
31	<chem>Clc1cc(cc(CC([O-])=O)c1)-c2ccccc2</chem>	0.706
32	<chem>Oc1c(cc(cc1C)-c2ccccc2)C</chem>	0.723
33	<chem>O=C1C(N)=C(C(=NN1c2ccccc2)C)C=C</chem>	0.764
34	<chem>O=C1c2cc(ncc2N=CN1)-c3ccccc3</chem>	0.781
35	<chem>O=C1c2c(C(=CN1C)c3ccccc3)cc[nH]2</chem>	0.715
36	<chem>Cc1cc(Nc2cc(ncn2)-c3ccccc3)no1</chem>	0.771
37	<chem>O=C(N)c1ccnc(-c2ccccc2)c1</chem>	0.757
38	<chem>O=C(Nc1cc(-c2ccccc2)ccn1)COC</chem>	0.748
39	<chem>Fc1ccc(NC(=O)C)cc1-c2ccccc2</chem>	0.705
40	<chem>O=C(Nc1cc(ncn1)-c2ccccc2)C3CC3</chem>	0.753
41	<chem>O=C(Nc1cc(-c2ccccc2)ccn1)CCC</chem>	0.752
42	<chem>O=C(Nc1cc(cc(c1)-c2ccccc2)C([O-])=O)C</chem>	0.682
43	<chem>O=S(=O)(Nc1c(O)ccc(c1)-c2ccccc2)C</chem>	0.71
44	<chem>n1ccc(-c2c[nH]nn2)cc1-c3ccccc3</chem>	0.764
45	<chem>O=C(Nc1c(ccc(-c2ccccc2)c1)C)CC</chem>	0.713
46	<chem>Oc1c(c(nc2cncc12)-c3ccccc3)C#N</chem>	0.765
47	<chem>Oc1ccc(cc1C(=O)NC)-c2ccccc2</chem>	0.73
48	<chem>O=C1C=C(OC)C(=O)c2c(cn(c12)C)-c3ccccc3</chem>	0.722
49	<chem>O=C1C(=CC(=NN1C)c2ccccc2)C</chem>	0.691
50	<chem>O=C(Nc1ccc(c(c1)-c2ccccc2)CC)C</chem>	0.735