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Design of Novel Anti-MRSA Inhibitors: A Computational Study Integrating QSAR, ADMET, and Molecular Dynamics Simulation

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Table S1: All results of the 3D-QSAR model's internal validation.

		Statistical parameters					Fraction of field contributions (%)				
	Model	q^{2} [a]	ONC[b]	SEE[c]	r^{2} [d]	F[e]	S	E	H	D	A
Alignment	(Atom-based)										
CoMFA	**S+E**	**0.642**	**8**	**0.172**	**0.958**	**162.009**	**39.8**	**60.2**			
CoMSIA	S+E	0.514	4	0.199	0.954	83.716	28.4	71.6			
	S+D	0.573	3	0.375	0.812	53.426	52.0			48.0	
	S+A	0.502	3	0.341	0.845	67.308	24.3				75.7
	S+H	0.547	10	0.176	0.967	86.879	29.4		70.6		
	E+D	0.505	9	0.253	0.929	44.975		75.4		24.6	
	E+A	0.515	3	0.325	0.859	75.221		41.1			58.9
	E+H	0.554	8	0.177	0.964	107.502		51.1	48.9		
	D+A	0.524	3	0.336	0.850	69.932				31.2	68.8
	D+H	0.517	5	0.332	0.861	43.322			67.4	32.6	
	A+H	0.565	5	0.192	0.960	72.218			56.1		43.9
	S+E+D	0.556	8	0.214	0.947	71.651	22.2	59.1		18.7	
	S+E+A	0.536	3	0.323	0.861	76.276	15.2	34.4			50.5
	S+E+H	**0.590**	**5**	**0.250**	**0.907**	**122.767**	**15.4**	**56.6**	**28.0**		
	S+D+A	0.527	3	0.333	0.852	71.239	15.7			24.3	60.0
	S+D+H	0.589	5	0.329	0.864	44.452	27.7		46.5	25.7	
	S+A+H	0.556	10	0.181	0.965	82.043	16.6		46.4		37.0
	E+D+A	0.518	3	0.323	0.861	76.469		30.9		20.9	48.2
	E+A+H	0.532	5	0.206	0.953	69.287		34.5	32.3		33.2
	D+A+H	0.567	5	0.190	0.961	74.016			46.3	15.8	37.9
	D+H+E	0.553	5	0.195	0.956	87.782		45.7	39.5	14.8	
	S+E+D+A	0.565	6	0.227	0.942	56.350	14.5	36.3		14.2	35.0
	S+E+D+H	0.544	4	0.180	0.963	103.558	14.0	40.4	33.6	12.1	
	S+E+A+H	0.751	5	0.195	0.957	77.419	11.8	30.8	27.3		30.1
	S+D+A+H	0.742	5	0.203	0.954	71.496	13.7		37.3	15.2	33.7

Table S1 Continued

E+D+A+H	0.745	5	0.211	0.950	66.067		30.6	27.3	12.2	30.0
S+E+D+A+H	0.576	5	0.196	0.957	77.195	10.4	27.8	24.0	10.3	27.6

Table S2 The list of all the molecules with their SMILES notation

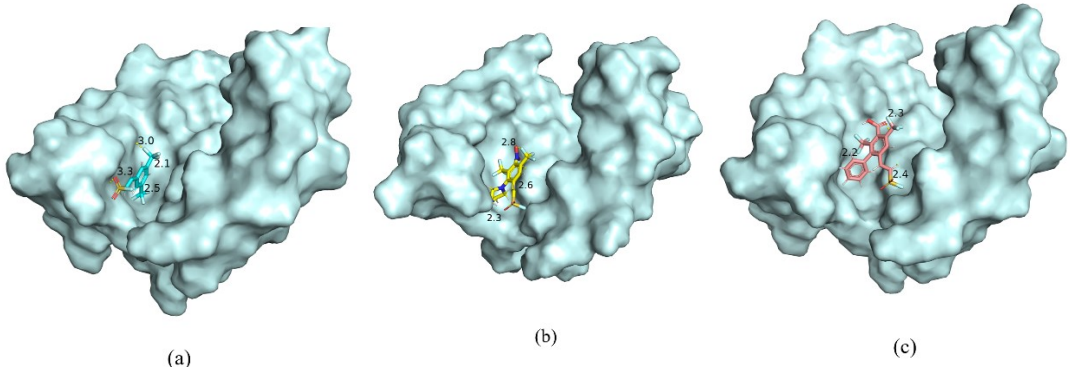
No	SMILES
01	FS(=O)(=O)\C=C\C1=CC=CC=C1
02	CC1=CC=C(\C=C\S(F)(=O)=O)C=C1
03	CCC1=CC=C(\C=C\S(F)(=O)=O)C=C1
04	FS(=O)(=O)\C=C\C1=CC=C(OC2=CC=CC=C2)C=C1
05	COC1=CC=C(\C=C\S(F)(=O)=O)C=C1
06	FS(=O)(=O)\C=C\C1=CC=C(C=C1)C1=CC=CC=C1
07	FC1=CC=C(\C=C\S(F)(=O)=O)C=C1
08	FS(=O)(=O)\C=C\C1=CC=C(Cl)C=C1
09	FS(=O)(=O)\C=C\C1=CC=C(Br)C=C1
10	FS(=O)(=O)\C=C\C1=CC=C(I)C=C1
11	FC(F)(F)OC1=CC=C(\C=C\S(F)(=O)=O)C=C1
12	FC(F)(F)C1=CC=C(\C=C\S(F)(=O)=O)C=C1
13	CC(=O)C1=CC=C(\C=C\S(F)(=O)=O)C=C1
14	[O-][N+](=O)C1=CC=C(\C=C\S(F)(=O)=O)C=C1
15	FS(=O)(=O)\C=C\C1=CC=C(C=C1)C#N
16	OC(=O)C1=CC=C(\C=C\S(F)(=O)=O)C=C1
17	CCOC(=O)C1=CC=C(\C=C\S(F)(=O)=O)C=C1
18	FS(=O)(=O)\C=C\C1=CC=C(C=O)C=C1
19	OC1=CC=C(\C=C\S(F)(=O)=O)C=C1
20	CSC1=CC=C(\C=C\S(F)(=O)=O)C=C1
21	CS(=O)(=O)C1=CC=C(\C=C\S(F)(=O)=O)C=C1
22	CC(C)S(=O)(=O)C1=CC=C(\C=C\S(F)(=O)=O)C=C1
23	COC1=CC(\C=C\S(F)(=O)=O)=CC=C1
24	CC1=CC(\C=C\S(F)(=O)=O)=CC=C1
25	CC(C)C1=CC(\C=C\S(F)(=O)=O)=CC=C1
26	FS(=O)(=O)\C=C\C1=CC=CC(=C1)C1=CC=CC=C1
27	FC1=CC(\C=C\S(F)(=O)=O)=CC=C1
28	FS(=O)(=O)\C=C\C1=CC=CC(Br)=C1
29	FS(=O)(=O)\C=C\C1=CC=CC(I)=C1
30	FC(F)(F)C1=CC(\C=C\S(F)(=O)=O)=CC=C1
31	FS(=O)(=O)\C=C\C1=CC=CC(C=O)=C1
32	CC(=O)C1=CC(\C=C\S(F)(=O)=O)=CC=C1
33	[O-][N+](=O)C1=CC(\C=C\S(F)(=O)=O)=CC=C1
34	OC1=CC(\C=C\S(F)(=O)=O)=CC=C
35	CCOC(=O)C1=CC(\C=C\S(F)(=O)=O)=CC=C1

36	CS(=O)(=O)C1=CC(\C=C\S(F)(=O)=O)=CC=C1
37	COC1=CC=CC=C1\C=C\S(F)(=O)=O
38	CC1=CC=CC=C1\C=C\S(F)(=O)=O
39	FS(=O)(=O)\C=C\C1=CC=CC=C1Br
40	CC(=O)C1=CC=CC=C1\C=C\S(F)(=O)=O
41	FS(=O)(=O)\C=C\C1=CC=CC=C1C=O
42	OC1=CC=CC=C1\C=C\S(F)(=O)=O
43	FS(=O)(=O)C=CC1=CC=CC2=CC=CC=C12
44	FS(=O)(=O)\C=C\C1=CC=C2C=CC=CC2=C1
45	CC1=CC=C(\C=C\S(F)(=O)=O)C(C)
46	FC1=CC=C(\C=C\S(F)(=O)=O)C(F)=C1
47	CC1=CC(\C=C\S(F)(=O)=O)=CC(C)=C1
48	COC1=CC(\C=C\S(F)(=O)=O)=CC(OC)=C1
49	FC(F)(F)C1=CC(=CC(\C=C\S(F)(=O)=O)=C1)C(F)(F)F
50	OC1=CC(\C=C\S(F)(=O)=O)=CC(O)=C1
51	FS(=O)(=O)\C=C\C1=CC(Cl)=CC(Cl)=C1
52	COC1=CC=C(Cl)C=C1\C=C\S(F)(=O)=O
53	CC1=C(Br)C=CC(\C=C\S(F)(=O)=O)=C1
54	FS(=O)(=O)\C=C\C1=CC(\C=C\S(F)(=O)=O)=CC=C1
55	FS(=O)(=O)\C=C\C1=CC=C(O1)C=O
56	FS(=O)(=O)\C=C\C1=CC=CC2=C1OC1=CC=CC=C21
57	FS(=O)(=O)\C=C\C1=COC2=CC=CC=C12
58	FS(=O)(=O)\C=C\C1=CC=CS1
59	FS(=O)(=O)\C=C\C1=CSC=C1
60	FS(=O)(=O)\C=C\C1=CC2=CC=CC=C2S1
61	FS(=O)(=O)\C=C\C1=CC=CC2=C1SC1=CC=CC=C21
62	S=[3H]N1C(\C=C\S(F)(=O)=O)=CC2=CC=CC=C12
63	S=[3H]N1C=CC2=CC(\C=C/S(F)(=O)=O)=CC=C12
64	S=[3H]N1C2=CC=CC=C2C2=C1C=CC(\C=C\S(F)(=O)=O)=C2
65	FS(=O)(=O)\C=C\C1=CN(N=C1)C1=CC=CC=C1
66	FC(F)(F)C1=CC=C(\C=C\S(F)(=O)=O)C=N1
67	FS(=O)(=O)\C=C\C1=CC(Cl)=NC(Cl)=C1
68	FS(=O)(=O)\C=C\C=C\C1=CC=CC=C1
69	CC1=CC=C(\C=C\C=C\S(F)(=O)=O)C=C1
70	CC(C)(C)C1=CC=C(\C=C\C=C\S(F)(=O)=O)C=C1
71	FS(=O)(=O)\C=C\C=C\C1=CC=C(Br)C=C1
72	FC(F)(F)C1=CC=C(\C=C\C=C\S(F)(=O)=O)C=C1
73	FS(=O)(=O)\C=C\C=C\C1=CC=CC(Br)=C1
74	FC1=CC(\C=C\C=C\S(F)(=O)=O)=CC=C1
75	FS(=O)(=O)\C=C\C=C\C1=CC=CC(=C1)C#N
76	[O-][N+](=O)C1=CC=CC=C1\C=C\C=C\S(F)(=O)=O
77	CC1=CC=CC=C1\C=C\C=C\S(F)(=O)=O
78	FS(=O)(=O)\C=C\C=C\C1=CC2=C(C=CC=C2)C=C1

79	COC1=CC(\C=C\C=C\S(F)(=O)=O)=CC(OC)=C1
80	FC1=CC=C(\C=C\C=C\S(F)(=O)=O)C=C1F
81	CCOC(=O)\C=C\C=C\S(F)(=O)=O
82	CCOC(=O)\C=C\C=C\S(F)(=O)=O

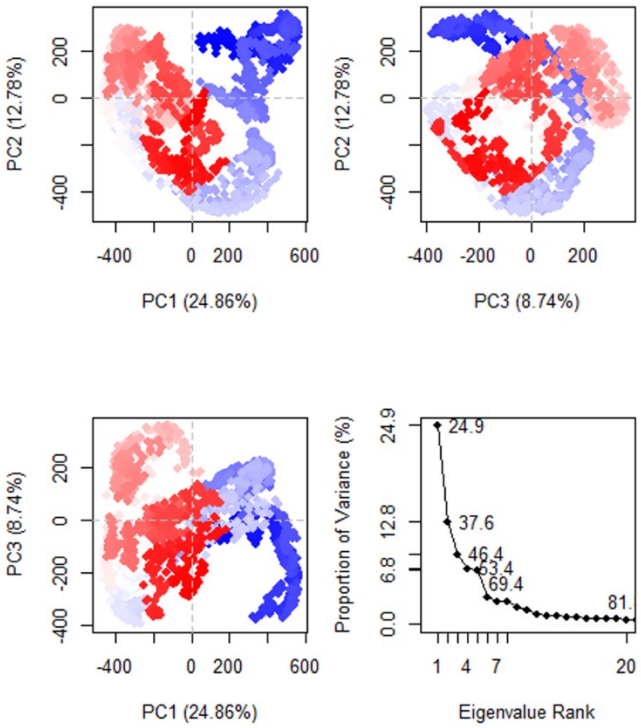
Table S2 Continued (New designed molecules)

N01	OC(=O)C1=C(C=C(\C=C\S(F)(=O)=O)C(C2=CC=CC=C2)=C1C(F)(F)F)C(F)(F)F
N02	[O]S(=O)(=O)C1=C(C=C(\C=C\S(F)(=O)=O)C(C2=CC=NC=C2)=C1C(F)(F)F)C(F)(F)F
N03	[O]S(=O)(=O)C1=C(C=C(\C=C\S(F)(=O)=O)C(C2=CC=CC=C2)=C1C(F)(F)F)C(F)(F)F
N04	[O]S(=O)(=O)C1=C(C=C(\C=C\S(F)(=O)=O)C(N2CC[N]CC2)=C1C(F)(F)F)C(F)(F)F
N05	OC(=O)C1=C(C=C(\C=C\S(F)(=O)=O)C(C2=CC=NC=C2)=C1C(F)(F)F)C(F)(F)F
N06	CC(C)(C)C1=C(C(=C(C=C1\C=C\S(F)(=O)=O)C(F)(F)F)[N+]([O-])=O)C(F)(F)F
N07	CC(C)(C)C1=C(C(=C(C=C1\C=C\S(F)(=O)=O)C(F)(F)F)S([O])(=O)=O)C(F)(F)F
N08	[O-][N+](=O)C1=C(C=C(\C=C\S(F)(=O)=O)C(N2CC[N]CC2)=C1C(F)(F)F)C(F)(F)F

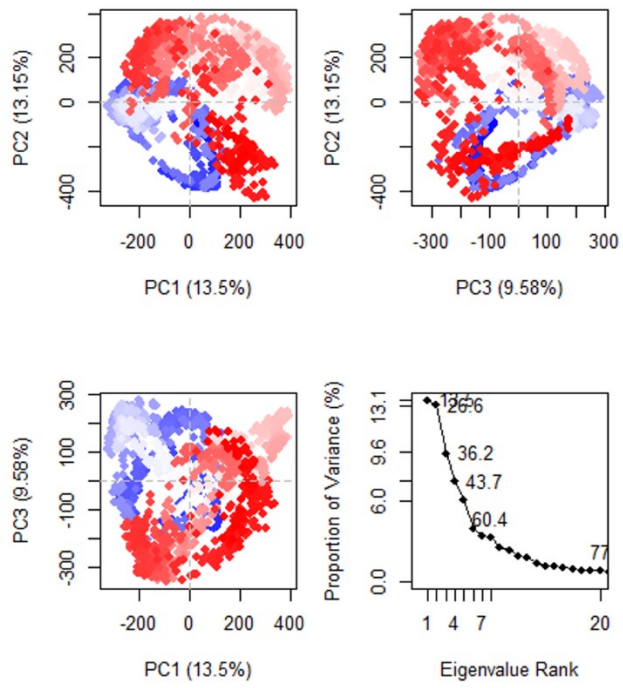


(a) (b) (c)

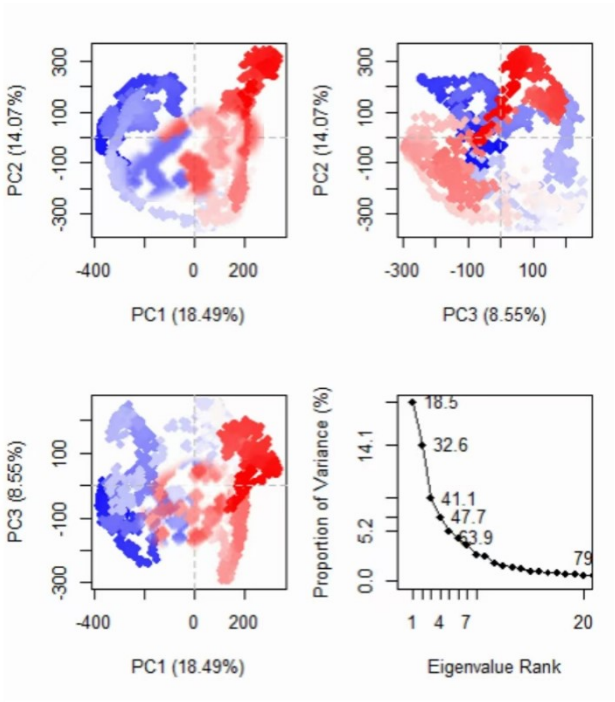
Fig. S1 Root Mean Square Deviation (RMSD) of both the ligand and the binding cavity. (a)2FNP-49. (b)2FNP-N06. (c)2FNP-N07


PC2 (12.78%)
PC1 (24.86%)
PC3 (8.74%)
PC1 (24.86%)
PC2 (12.78%)
PC3 (8.74%)
Proportion of Variance (%)
Eigenvalue Rank
24.9
37.6
46.4
69.4
81.

(a)


PC2 (13.15%)
PC1 (13.5%)
PC3 (9.58%)
PC1 (13.5%)
PC2 (13.15%)
PC3 (9.58%)
Proportion of Variance (%)
Eigenvalue Rank
26.6
36.2
43.7
60.4
77

(b)



(c)

Fig. S2 Principal component analysis (PCA) of composite components. (a)2FNP-49. (b)2FNP-N06. (c)2FNP-N07