Supporting information.

Systematic study on the interaction mechanism between PARP1 and its inhibitors by molecular dynamics simulation

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Table S1. The binding models between CAT and ligands with binding affinity (nmol).

PDB ID	Binding affinity		PDB ID	Binding affinity		PDB ID	Binding affinity	
	Ki	IC50		Ki	IC50		Ki	IC50
1efy[α]	6	-	4gv7[β]	-	1210~5600	4rv6[γ]	1.4	0.7~500
1pax[α]	70	160~420	4pjt[β]	1.2	0.57~7.2	4und[γ]	1.2	0.57~7.2
2pax[α]	-	22~180	4zzz[β]	-	5300	4uxb[γ]	-	9.1~481
3pax[α]	-	1.70e+4	5a00[β]	-	10~40	5wry[γ]	-	-
4pax[α]	48~52	400	5ha9[β]	-	79	5xsr[γ]	-	17
6i8m[α]	-	27~50	6ghk[β]	-	-	5xst[γ]		27
6i8t[α]	-	162	7kk3[β]	-	0.58	5xsu[γ]		244
1uk0[β]	-	8~16	7kk6[β]	5.2	-	6vkk[γ]	1.4	-
1uk1[β]	-	60	3gjw[γ]	5	-	7aab[γ]	-	45
1wok[β]	-	33	3gn7[γ]	4~5	-	7aac[γ]	5.2	-
2rcw[β]	8	-	3l3m[γ]	6	-	7cmw[γ]	-	0.9
2rd6[β]	5	1~355	4l6s[γ]	-	3			

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Table S2. Standard deviation and standard error of the mean of the binding free energies for all models.

Model	ΔG_{vdw}^{sd}	ΔG_{vdw}^{se}	ΔG_{ele}^{sd}	ΔG_{ele}^{se}	ΔG_{polar}^{sd}	ΔG_{polar}^{se}	ΔG_{nonpol}^{sd}	ΔG_{nonpol}^{se}	ΔG^{sd}	ΔG^{se}
1efy	2.66	0.26	3.95	0.39	2.92	0.29	-4.47	0.02	2.87	0.29
1pax	1.79	0.18	3.21	0.32	2.15	0.21	0.09	0.01	2.53	0.25
2pax	2.57	0.26	4.20	0.42	2.32	0.23	0.13	0.01	3.01	0.30
3pax	1.84	0.18	8.16	0.81	6.40	0.64	0.16	0.02	2.89	0.29
4pax	1.99	0.20	3.17	0.32	2.08	0.21	0.08	0.01	2.10	0.21
6i8m	2.72	0.27	10.12	1.01	9.94	0.99	0.15	0.02	2.93	0.29
6i8t	2.90	0.29	10.91	1.09	8.86	0.88	0.17	0.02	4.14	0.41
1uk0	2.74	0.27	10.85	1.08	10.37	1.03	0.12	0.01	4.26	0.42
1uk1	2.65	0.26	8.01	0.80	7.79	0.78	0.13	0.01	3.18	0.32
1wok	2.16	0.21	4.38	0.44	2.80	0.28	0.10	0.01	2.77	0.28
2rcw	2.17	0.22	11.91	1.18	11.62	1.16	0.10	0.01	2.98	0.30
2rd6	3.11	0.31	11.67	1.16	9.33	0.93	0.17	0.02	4.41	0.44
4gv7	2.25	0.22	3.24	0.32	1.56	0.16	0.07	0.01	2.36	0.23
4pjt	2.70	0.27	3.63	0.36	2.57	0.26	0.17	0.02	2.54	0.25
4zzz	2.25	0.22	14.11	1.40	12.41	1.23	0.18	0.02	3.52	0.35
5a00	2.82	0.28	10.7	1.00	9.96	0.99	0.19	0.02	3.50	0.35
5ha9	2.14	0.21	9.26	0.92	8.15	0.81	0.29	0.03	3.51	0.35
6ghk	3.04	0.30	6.36	0.63	5.18	0.52	0.11	0.01	3.79	0.38
7kk3	2.36	0.23	3.59	0.36	2.42	0.24	0.13	0.01	2.80	0.28
7kk6	2.49	0.25	11.36	1.13	9.63	0.96	0.10	0.01	3.60	0.36
3gjw	2.77	0.28	8.46	0.84	7.77	0.77	0.09	0.01	3.02	0.30
3gn7	2.26	0.22	16.11	1.60	15.11	1.50	0.15	0.01	3.20	0.32
3l3m	3.01	0.30	9.34	0.93	7.21	0.72	0.09	0.01	3.58	0.36
4l6s	2.63	0.26	9.23	0.92	8.85	0.88	0.13	0.01	2.92	0.29
4rv6	2.98	0.30	5.3-	0.53	3.72	0.37	0.16	0.02	2.78	0.28
4und	2.69	0.28	3.73	0.37	2.68	0.27	0.14	0.01	2.51	0.25
4uxb	2.57	0.26	8.42	0.84	6.74	0.67	0.15	0.02	2.99	0.30
5wry	1.23	0.12	2.84	0.28	1.59	0.16	0.06	0.01	2.33	0.23
5xsr	2.89	0.29	9.70	0.97	6.80	0.68	0.13	0.01	4.75	0.47
5xst	2.63	0.26	12.25	1.22	9.92	0.99	0.14	0.01	3.96	0.39
5xsu	2.74	0.27	9.86	0.98	7.58	0.75	0.11	0.01	3.30	0.33
6vkk	3.66	0.36	31.05	3.09	25.21	2.51	0.31	0.03	8.52	0.85
7aab	3.35	0.33	14.23	1.42	13.32	1.33	0.14	0.01	3.89	0.39
7aac	2.36	0.24	7.95	0.79	6.84	0.68	0.08	0.01	3.10	0.31
7cmw	3.06	0.30	12.41	1.23	10.87	1.08	0.18	0.02	2.63	0.26

sd Standard Deviation; se Standard Error of the Mean. All the energy terms are in Kcal/mol.

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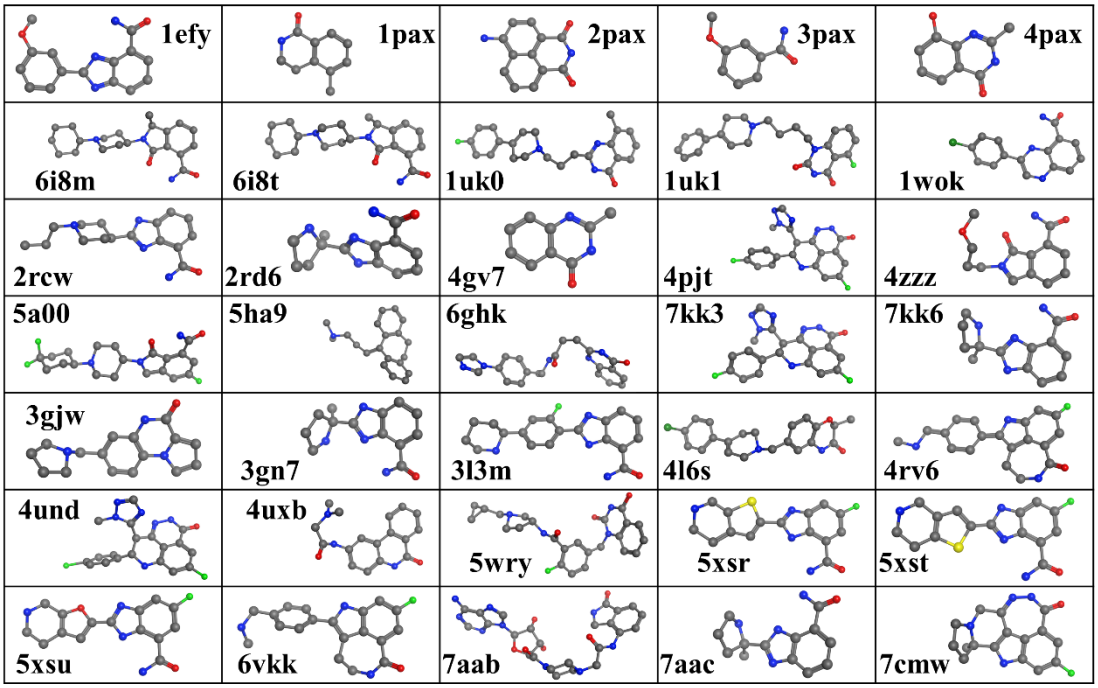

Figure S1. 3D structure of ligands in 35 models.

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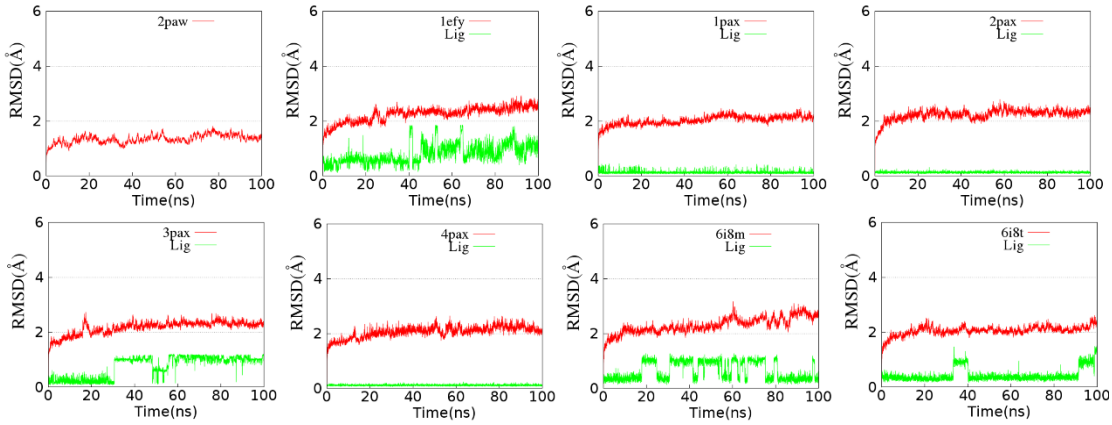

Figure S2. RMSDs of models in Group 1 and Group 2.

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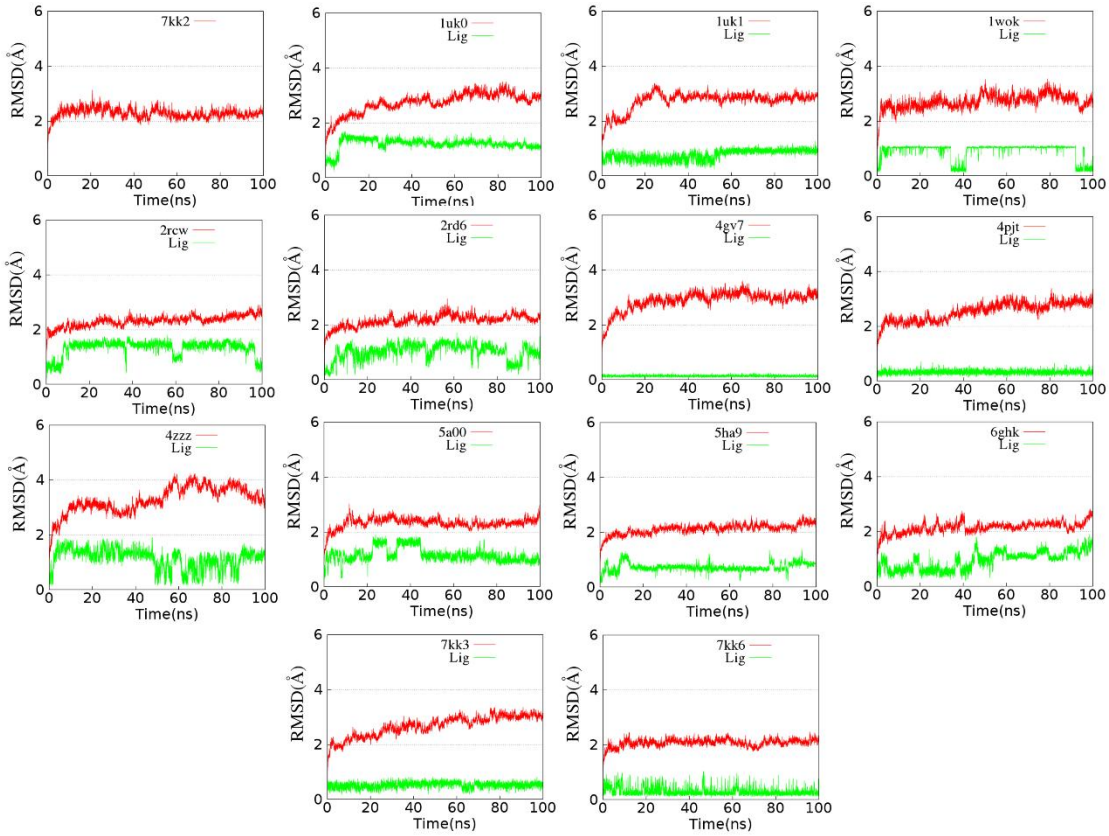

Figure S3. RMSDs of models in Group 3 and Group 4.

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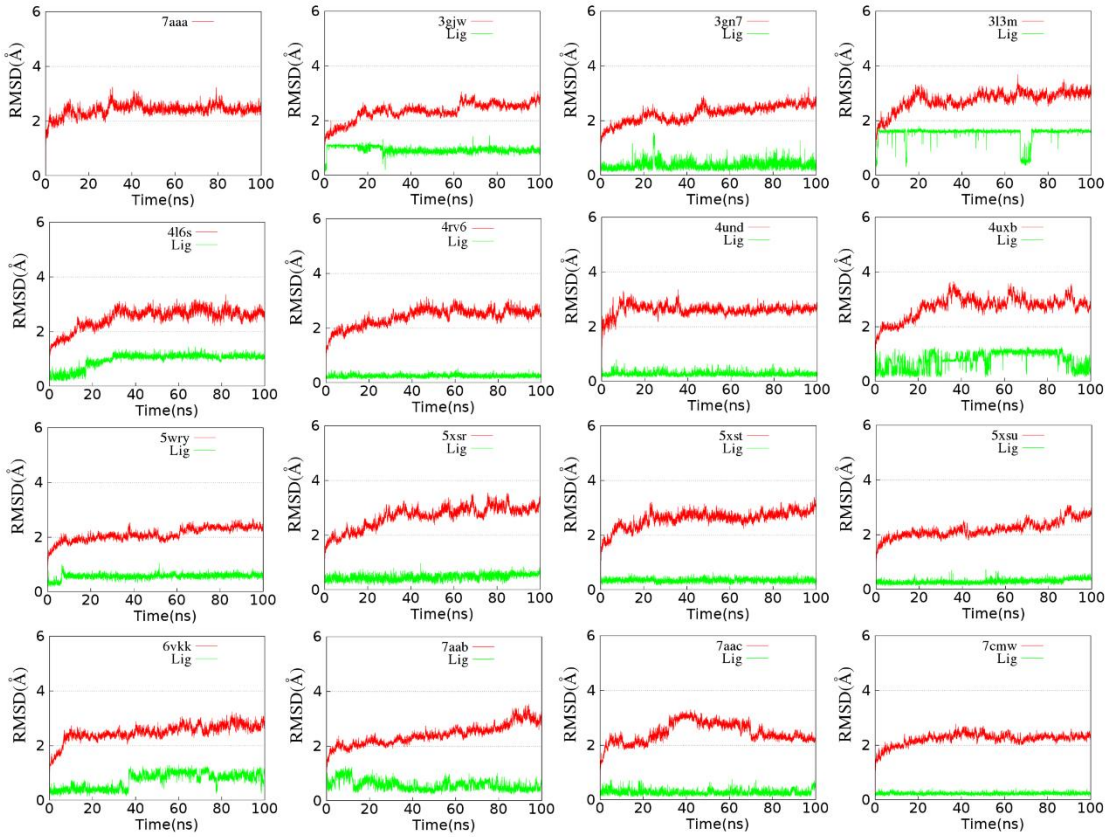

Figure S4. RMSDs of models in Group 5 and Group 6.

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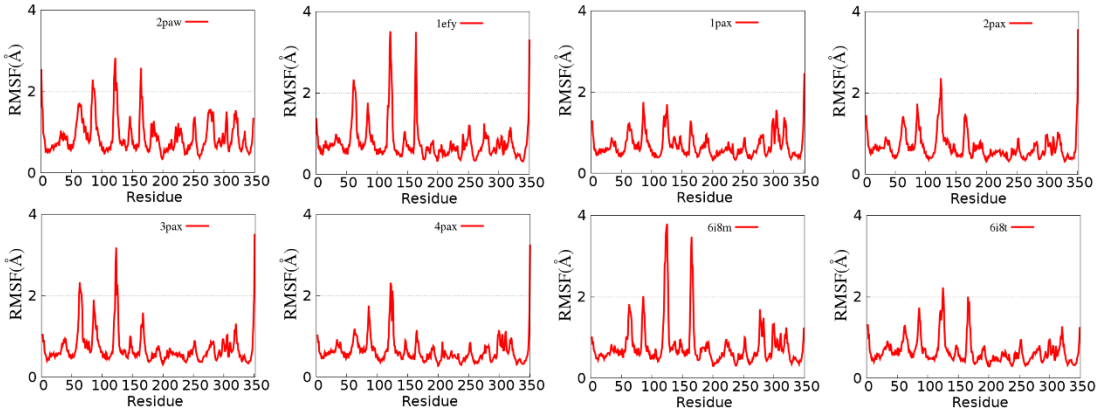

Figure S5. RMSFs of models in Group 1 and Group 2.

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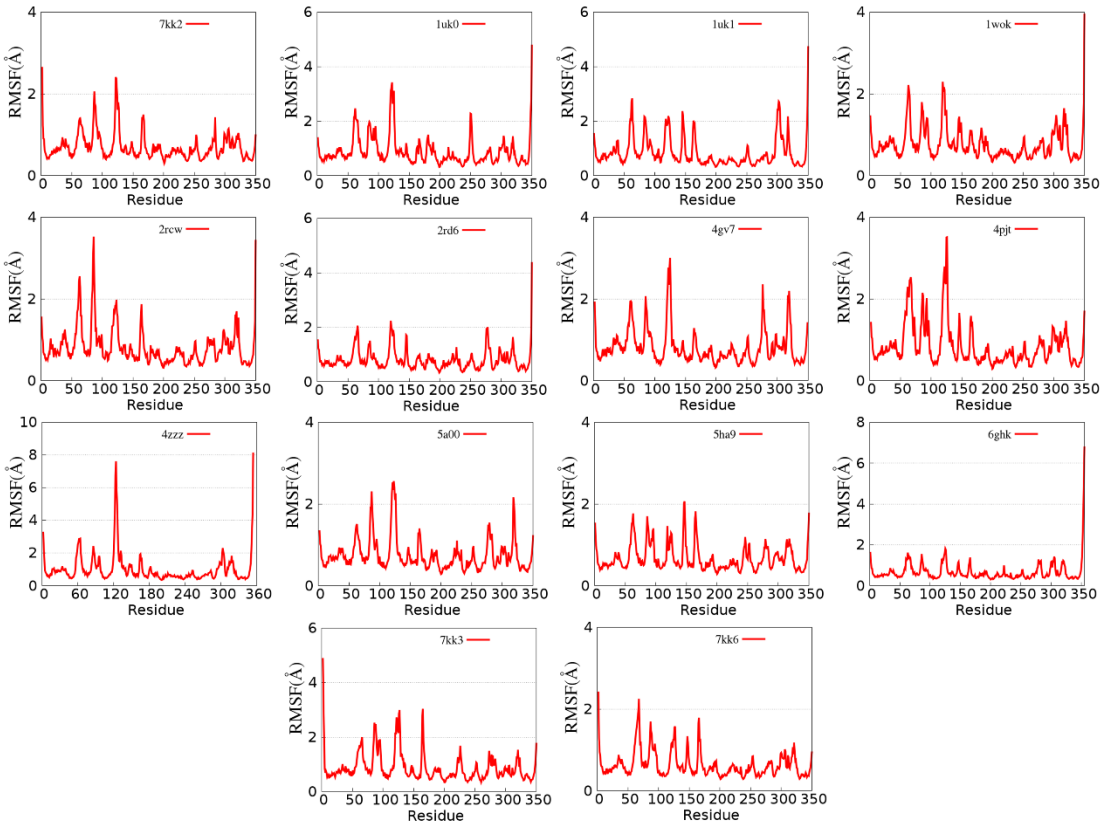

Figure S6. RMSFs of models in Group 3 and Group 4.

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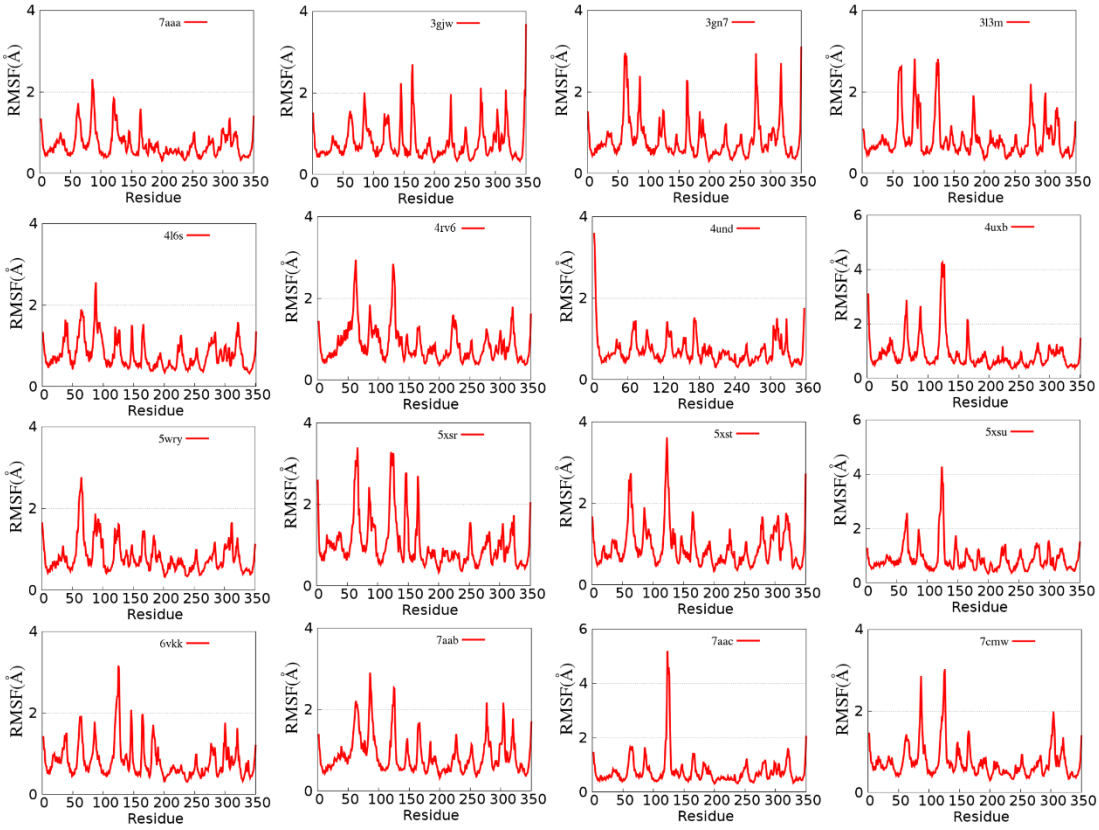

Figure S7. RMSFs of models in Group 5 and Group 6.

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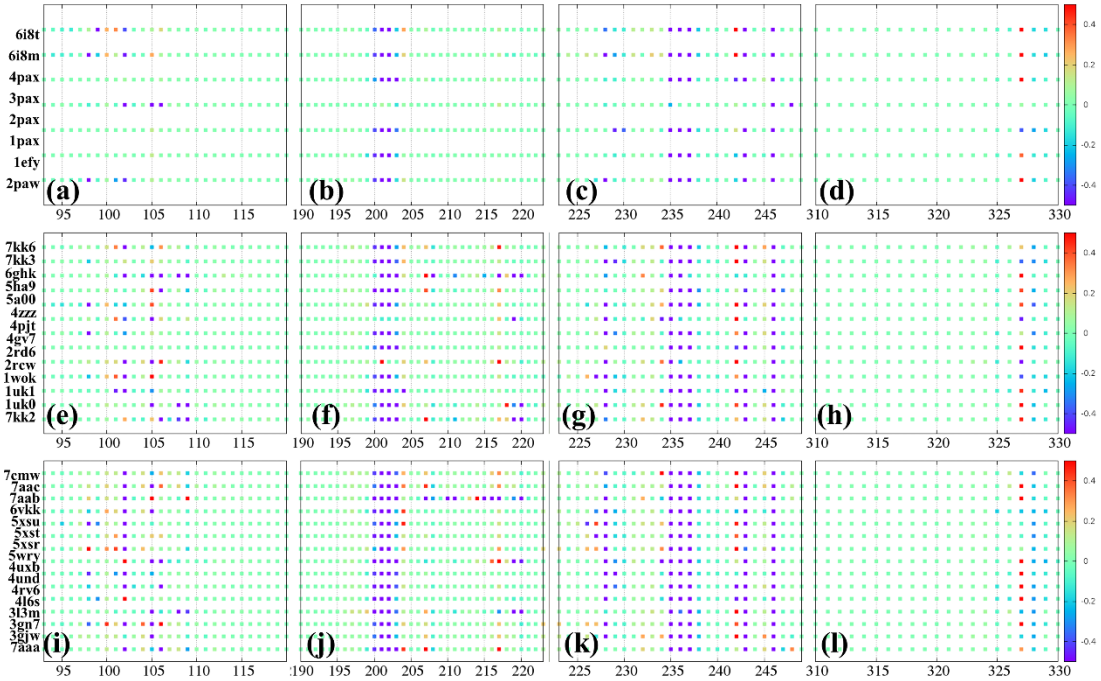

Figure S8. Per-residue energy contribution spectra of 4 regions in CAT on the surface of CAT/inhibitor.

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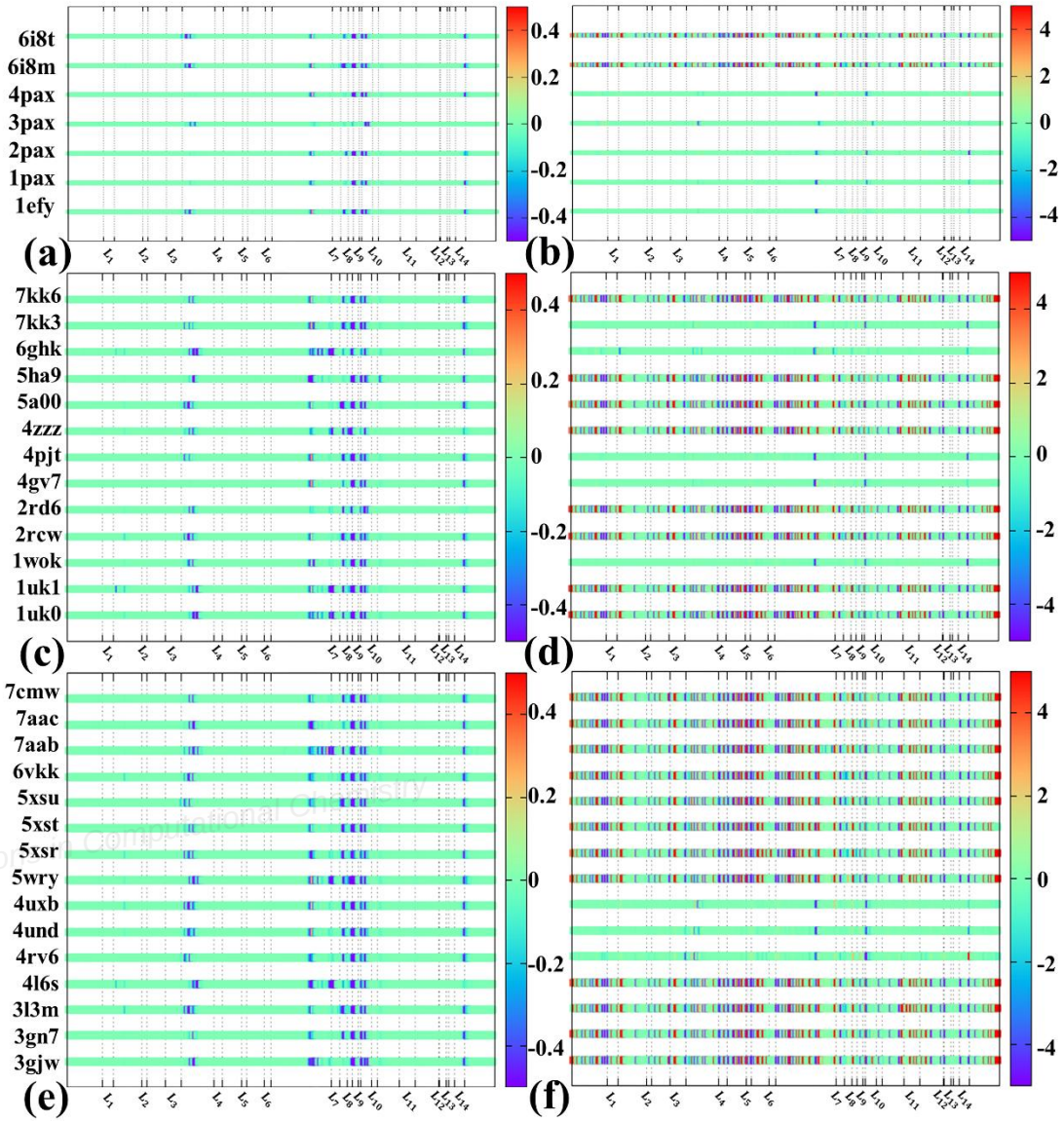

Figure S9. (a, c, e) Per-residue Van der Waals energy contribution spectra of CAT on the surface of CAT/inhibitor. (b, d, f) Per-residue Electrostatic energy contribution spectra of CAT on the surface of CAT/inhibitor.

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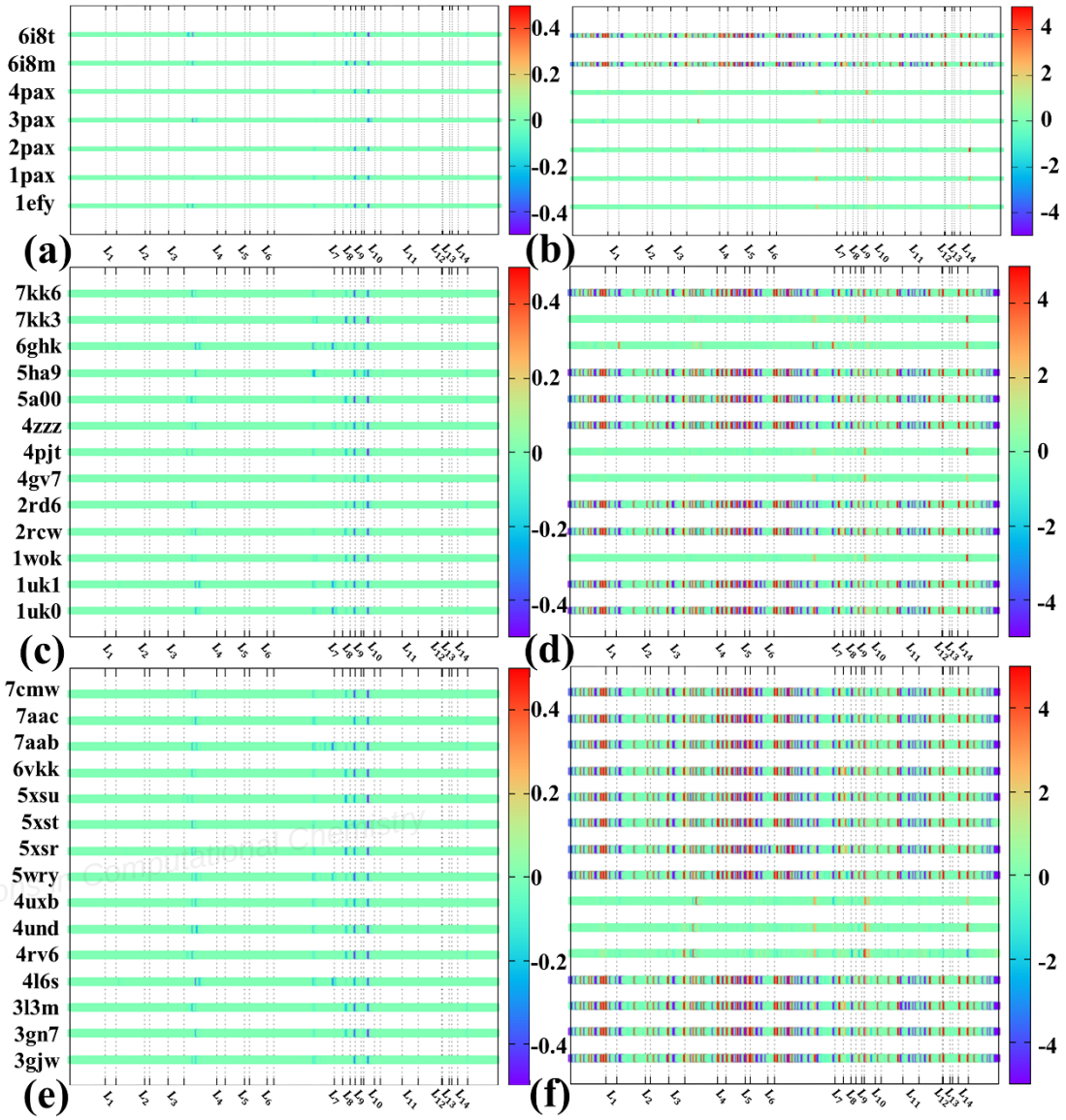

Figure S10. (a, c, e) Per-residue Nonpolar solvation free energy contribution spectra of CAT on the surface of CAT/inhibitor. (b, d, f) Per-residue Polar solvation free energy contribution spectra of CAT on the surface of CAT/inhibitor.

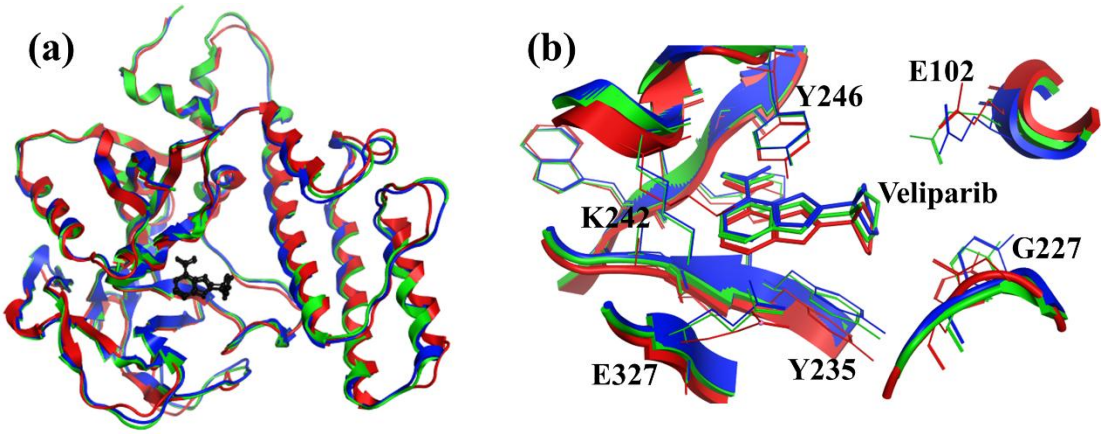

Figure S11. (a) the crystal structure differences among 2rd6 (red), 7kk6 (green) and 7aac (blue). (b) the region of ligand binding sites among 2rd6 (red), 7kk6 (green) and 7aac (blue).

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