Supporting information

SMD-based Interaction-energy Fingerprints Can Predict Accurately the Dissociation Rate Constants of HIV-1 Protease Inhibitors

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Table S1. The 48 residues within the 5Å distance away from the surface of dissociation channel.

Chain A				Chain B †			
Polar		Nonpolar		Polar		Nonpolar	
Arg8	Asp25	Leu10	Leu23	Arg8*	Asp25*	Pro9*	Leu10*
Gly27	Asp29	Ala28	Val32	Gly27*	Asp29*	Leu23*	Ala28*
Asp30	Glu35	Ile47	Ile50	Asp30*	Thr31*	Val32*	Ile47*
Gly48	Gly49	Phe53	Ile54	Gly48*	Gly49*	Ile50*	Phe53*
Gly51	Gly52	Ile76	Pro81	Gly51*	Gly52*	Ile54*	Ile76*
Thr80	Arg87	Val82	Ile84	Thr80*		Pro81*	Val82*
						Ile84*	

† Residues of chain B are marked by asterisk.

Table S2. The molecular docking results of 37 HIV-1 PIs

Classify	PubChem CID	ID*	k_{off}(s^{-1})	-log(k_{off})	Total_Score	Crash	Polar
Non-B268 analogues	505989	B355	0.373	0.428	9.54	-4.48	5.22
	505988	B295	0.436	0.361	11.01	-2.17	5.04
P1/P1' analogues of B268	44398349	A037	0.000365	3.438	9.32	-3.67	4.07
	44398443	A038	0.000487	3.312	8.51	-3.07	4.27
	44398241	B268	0.00367	2.435	8.03	-2.69	2.62
	44398402	B277	0.00485	2.314	7.71	-3.58	4.11
	44398218	B408	0.00169	2.772	8.43	-2.05	2.91
	44398382	B409	0.000432	3.365	10.99	-3.15	5.72
	44398220	B412	0.000817	3.088	7.79	-3.07	6.45
	44398450	B429	0.000373	3.428	8.19	-3.09	4.35
	44398222	B439	0.00163	2.788	9.44	-4.84	3.63
	44398355	B440	0.000303	3.519	9.55	-3.29	5.80
P2/P2' and central hydroxy analogues	44367226	A015	0.938	0.0278	11.24	-5.18	5.59
	44398440	A016	0.0605	1.218	9.15	-5.43	5.71
	44367311	A017	0.179	0.747	10.05	-4.17	5.95
	44367216	A018	0.474	0.324	9.58	-7.30	6.24
	44367286	B249	0.273	0.564	14.65	-3.06	5.91
	44367031	B322	0.0677	1.169	11.30	-3.34	2.86
	44398299	B347	0.027	1.569	8.71	-2.03	3.18
	44366952	B365	0.0309	1.510	8.46	-5.75	4.03
	44398447	B369	0.0133	1.876	8.83	-2.61	3.20
	44398334	B388	0.0227	1.644	7.66	-1.70	2.76
	44398276	B425	0.234	0.631	8.76	-2.27	4.10
	44367110	B435	0.00653	2.185	10.18	-3.17	2.36
Cyclic sulfamide compounds	475876	A021	0.0273	1.564	11.82	-3.66	4.80
	475874	A023	0.139	0.857	10.73	-3.27	4.30
	445758	A024	0.0685	1.164	12.83	-3.47	4.41
	44398441	A030	0.042	1.377	12.69	-4.10	6.92
	486804	A045	0.263	0.580	13.01	-4.85	5.53
	5329	A047	0.0697	1.157	4.8	-0.46	4.21
Clinical	441243	Saq	0.000227	3.644	9.61	-6.91	-4.09
	92727	Lop	0.000654	3.184	12.23	-2.25	3.00
	64143	Nelf	0.000668	3.175	8.39	-4.27	3.12
	5362440	Ind	0.00158	2.801	9.71	-2.65	5.60
	392622	Rit	0.00216	2.666	9.74	-6.25	4.05
	65016	Amp	0.00488	2.312	10.23	-2.82	3.26
	148192	Ataz	0.00069	3.161	10.41	-4.63	4.40

Table S3. The result of 30-times repeating modeling

Model	-log(k_{off})			Model	-log(k_{off})			Model	-log(k_{off})		
	R^2	Q^2	R_{pred}^2		R^2	Q^2	R_{pred}^2		R^2	Q^2	R_{pred}^2
1	0.730	0.730	0.800	11	0.751	0.749	0.833	21	0.729	0.727	0.871
2	0.775	0.774	0.826	12	0.755	0.754	0.798	22	0.731	0.730	0.874
3	0.728	0.722	0.872	13	0.795	0.794	0.684	23	0.743	0.739	0.851
4	0.802	0.801	0.607	14	0.785	0.783	0.685	24	0.736	0.733	0.860
5	0.727	0.725	0.889	15	0.770	0.765	0.786	25	0.749	0.742	0.804
6	0.751	0.750	0.785	16	0.754	0.753	0.759	26	0.748	0.746	0.800
7	0.728	0.727	0.878	17	0.706	0.704	0.914	27	0.733	0.733	0.824
8	0.715	0.712	0.919	18	0.737	0.736	0.805	28	0.787	0.786	0.702
9	0.765	0.760	0.785	19	0.744	0.742	0.804	29	0.749	0.747	0.874
10	0.750	0.748	0.803	20	0.744	0.744	0.870	30	0.818	0.814	0.649

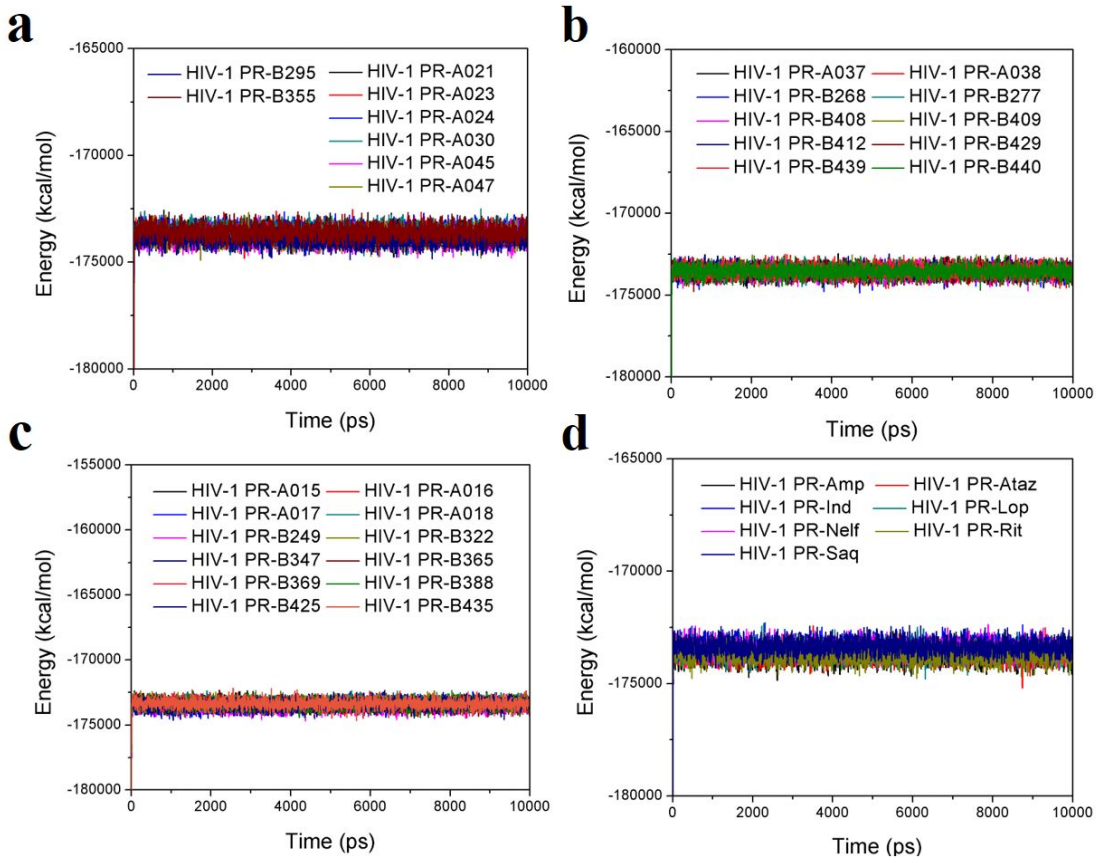

Fig.S1. The energy evolutions in the MD simulations of the 37 HIV-1 PR complexes. (a) non-B268 analogues, cyclic sulfamide compounds; (b) P1/P1' analogues of B268; (c) P2/P2' and central hydroxy analogues; (d) clinical medicines.

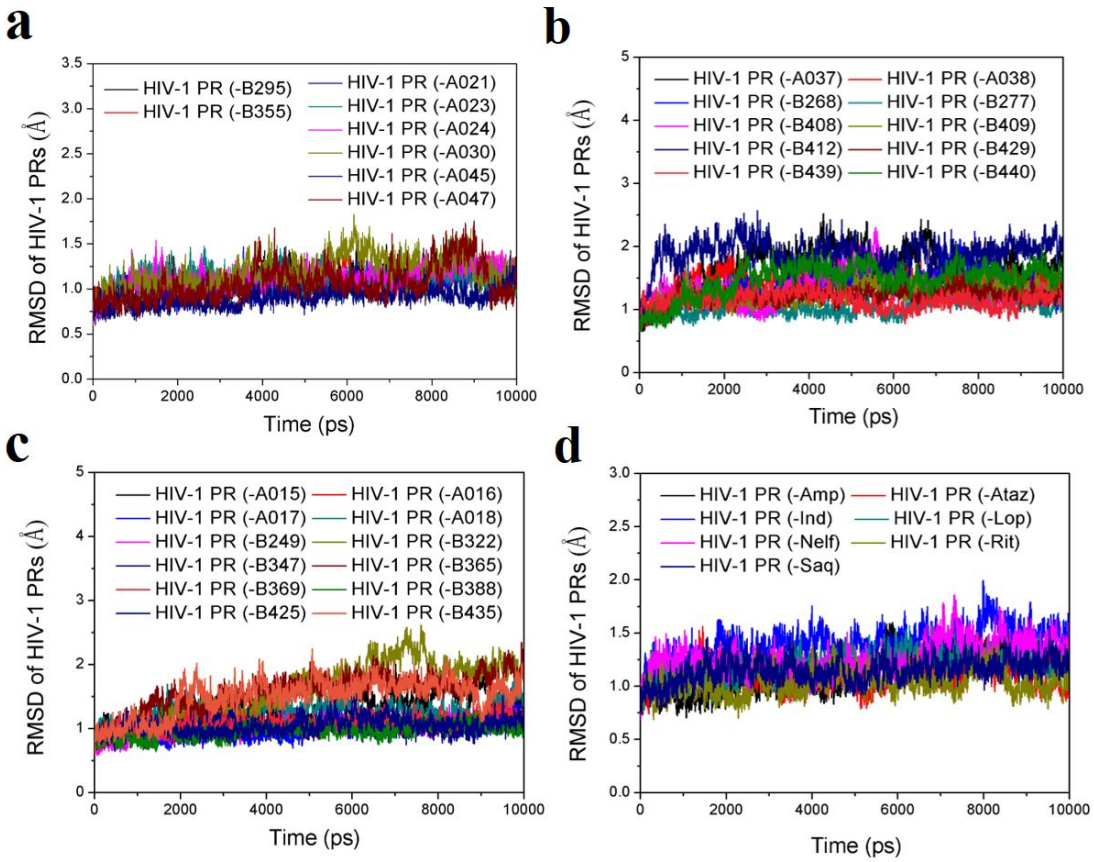

Fig.S2. The RMSDs of the HIV-1 PR backbone. (a) non-B268 analogues, cyclic sulfamide compounds; (b) P1/P1' analogues of B268; (c) P2/P2' and central hydroxy analogues; (d) clinical medicines.

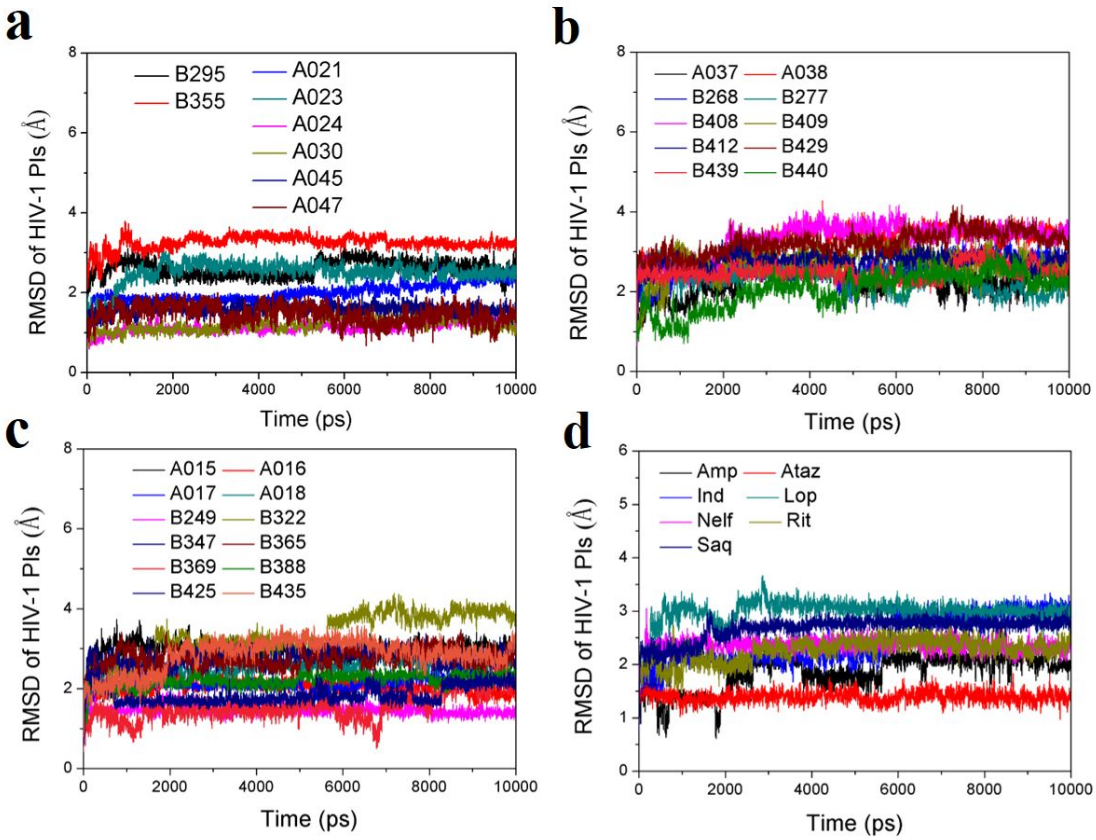

Fig.S3. The RMSDs of the 37 HIV-1 PIs. (a) non-B268 analogues, cyclic sulfamide compounds; (b) P1/P1' analogues of B268; (c) P2/P2' and central hydroxy analogues; (d) clinical medicines.