Table S1. PDB codes of unbound and bound structures, chain length, RMSDs between bound and unbound structures, native peptides or ligands, and peptide sequences for the proteins used in this study.

Protein	PDB Code		Chain Length	RMSD (Å)	Peptide/ Ligand	
	Bound (Holo)	Unbound (Apo)			Name	Sequence of Peptide
PSD-95	1BE9	1BFE	119	0.470	Cript	KQTSV
GRIP	1N7F	1N7E	97	0.422	Liprin	ATVRTYSC
Syntenin	1OBX	1NTE	79	0.383	IL5R-a	DSVF
Syntenin	1OBY	1NTE	79	0.370	Syndecan-4	NEFYA
Syntenin	NA	1NTE	79	-	Merlin	FFEEL
SH3 domain of GRB2	1IO6	1GFD	59	0.856	-	RHYRPLPPLP
SH3 domain of GRB2	NA	1GFD	59	-	VPP	VPPPVPPRRR
Cyclophilin A	2CYH	2CPL	164	0.202	-	AP
Cyclophilin A	1AWQ	2CPL	164	0.453	Peptide	HAGPIA
Methyltransferase	1BC5	1AF7	274	0.429	Pentapeptide	NWETF
Aldose Reductase	2FZB	2ACR	315	0.366	[Tolrestat (TOL)][4]	-
Aldose Reductase	1T40	2ACR	315	0.187	IDD552	-
Carboxypeptidase	2CTC	1M4L	307	0.103	HFA	-
Carboxypeptidase	7CPA	1M4L	307	0.216	FVF	-
TIM	4TIM	3TIM	250 (A,B)	0.303	2-PG	-
TIM	6TIM	3TIM	250 (A,B)	0.317	G3P	-
ABP	1LRH	1LR5	163(A,B,C,D)	0.171	NLA	-
Acetylcholinesterase	1GPK	1EA5	537	0.143	HUP	-
Adenosine Deaminase	1UML	1VFL	356	0.402	FR4	-
Quinone Reductase 2	1SG0	1QR2	230 (A,B)	0.217	STL	-
HIV-Protease	1HBV	2PC0*	198 (A,B)	1.650	SB203238	-
HIV-Protease	1HEG	2PC0*	198 (A,B)	1.614	SKF 107457	-
HIV-Protease	1HIH	2PC0*	198 (A,B)	1.343	CGP-53820	-
HIV-Protease	1HIV	2PC0*	198 (A,B)	1.422	U75875	-
HIV-Protease	1HPS	2PC0*	198 (A,B)	1.606	SB206343	-
HIV-Protease	1HTE	2PC0*	198 (A,B)	1.505	GR123976	-
HIV-Protease	1HTF	2PC0*	198 (A,B)	1.436	GR126045	-
HIV-Protease	1HTG	2PC0*	198 (A,B)	1.405	GR137615	-
HIV-Protease	1HVI	2PC0*	198 (A,B)	1.344	A77003 (R,S)	-
HIV-Protease	1HVJ	2PC0*	198 (A,B)	1.347	A78791 (S,-)	-
HIV-Protease	1HVK	2PC0*	198 (A,B)	1.352	A76928 (S,S)	-
HIV-Protease	1HVL	2PC0*	198 (A,B)	1.347	A76889 (R,R)	-
HIV-Protease	1HVS	2PC0*	198 (A,B)	1.406	A77	-
HIV-Protease	1SBG	2PC0*	198 (A,B)	1.561	IM1	-
HIV-Protease	4HVP	2PC0*	198 (A,B)	1.538	MVT-101	-
HIV-Protease	4PHV	2PC0*	198 (A,B)	1.373	L-700, 417	-
HIV-Protease	5HVP	2PC0*	198 (A,B)	1.427	ACETYL-PEPSTATIN	-
HIV-Protease	9HVP	2PC0*	198 (A,B)	1.512	A-74704	-
HIV-Protease	1A30	2PC0*	198 (A,B)	1.490	Tri-peptide	EDL
HIV-Protease	1KZK	2PC0*	198 (A,B)	1.253	JE-2147	-
Carbonic Anhydrase II	1OQ5	2ILI	259	0.134	Celecoxib	-
Carbonic Anhydrase II	1AVN	2ILI	259	0.254	Histamine	-

Carbonic Anhydrase II	1CIL	2ILI	259	0.239	ETS	-
Carbonic Anhydrase II	1CIM	2ILI	259	0.258	PTS	-
Carbonic Anhydrase II	1CIN	2ILI	259	0.244	MTS	-
Carbonic Anhydrase II	1CNW	2ILI	259	0.231	EG1	-
Carbonic Anhydrase II	1CNX	2ILI	259	0.248	EG2	-
Carbonic Anhydrase II	1CNY	2ILI	259	0.258	EG3	-
Carbonic Anhydrase II	1OKL	2ILI	259	0.255	MNS	-
Alcohol Deydrogenase	1ADB	8ADH	374	1.218	CND	-
Alcohol Deydrogenase	1ADC	8ADH	374	1.219	PAD	-
Alcohol Deydrogenase	1ADF	8ADH	374	0.330	TAD	-
Alcohol Deydrogenase	1BTO	8ADH	374	1.137	SSB	-
Alcohol Deydrogenase	1HLD	8ADH	374	1.135	PFB,NAD	-
Alcohol Deydrogenase	1LDE	8ADH	374	1.148	FPI,NAD	-
Alcohol Deydrogenase	1LDY	8ADH	374	1.152	CXF,NAD	-
Alcohol Deydrogenase	3BTO	8ADH	374	1.160	SSB,NAD	-
Alpha-Thrombin	1A4W	1C5L	274(L,H,I)	0.351	QWE	-
Alpha-Thrombin	1AE8	1C5L	298(L,H,I)	0.331	AZL	-
Alpha-Thrombin	1BMM	1C5L	295(L,H,I)	0.455	BMS-186282	-
Alpha-Thrombin	1BMN	1C5L	292(L,H,I)	0.423	BMS-189090	-
Alpha-Thrombin	1D3D	1C5L	290(L,H,I)	0.352	BZT	-
Alpha-Thrombin	1D3P	1C5L	290(L,H,I)	0.317	BT3	-
Alpha-Thrombin	1D4P	1C5L	290(L,H,I)	0.333	BPP	-
Alpha-Thrombin	1DWB	1C5L	298(L,H,I)	0.386	Benzyldiamine	-
Alpha-Thrombin	1DWC	1C5L	298(L,H,I)	0.386	MD-805 (Argatroban)	-
Alpha-Thrombin	1DWD	1C5L	298(L,H,I)	0.378	NAPAP	-
Alpha-Thrombin	1HDT	1C5L	303(L,H,I)	0.511	BMS-183507	-
Alpha-Thrombin	1UVS	1C5L	268(L,H,I)	0.479	BM51.1011	-
Alpha-Thrombin	1OYT	1C5L	305(L,H,I)	0.387	FSN	-
Cytohchrome C Peroxidase	1AC4	1CCP*	291	0.286	TMT	-
Cytohchrome C Peroxidase	1AC8	1CCP*	291	0.299	TMZ	-
Cytohchrome C Peroxidase	1AEB	1CCP*	291	0.299	3MT	-
Cytohchrome C Peroxidase	1AED	1CCP*	291	0.299	DTI	-
Cytohchrome C Peroxidase	1AEE	1CCP*	291	0.309	ANL	-
Cytohchrome C Peroxidase	1AEF	1CCP*	291	0.299	3AP	-
Cytohchrome C Peroxidase	1AEG	1CCP*	291	0.299	4AP	-
Cytohchrome C Peroxidase	1AEH	1CCP*	291	0.299	24T	-
Cytohchrome C Peroxidase	1AEJ	1CCP*	291	0.299	NVI	-
Cytohchrome C Peroxidase	1AEK	1CCP*	291	0.299	IDM	-
Cytohchrome C Peroxidase	1AEM	1CCP*	291	0.299	MPI	-
Cytohchrome C Peroxidase	1AEN	1CCP*	291	0.286	25T	-
Cytohchrome C Peroxidase	1AEO	1CCP*	291	0.286	2AP	-
Cytohchrome C Peroxidase	1AEQ	1CCP*	291	0.299	2EZ	-
Cytohchrome C Peroxidase	1AES	1CCP*	291	0.310	IMD	-
Cytohchrome C Peroxidase	1AET	1CCP*	291	0.281	1MZ	-
Cytohchrome C Peroxidase	1AEU	1CCP*	291	0.286	2MZ	-
Cytohchrome C Peroxidase	1AEV	1CCP*	291	0.267	AMT	-

- Modeled Unbound structures were used in these cases.

Table S2. RMSD (Å) values between the ligand positions of the lowest energy docked poses obtained from rigid bound, rigid unbound and BP-Dock docking and that of the bound crystal structure. Only heavy atoms of the ligand are taken into account for RMSD calculation.

Protein	Peptide/Ligand	RMSD (Å)		
		Rigid		BP-Dock
		Bound (Holo)	Unbound (Apo)	Unbound (Apo)
HIV-Protease	SB203238	0.25	1.02	1.37
HIV-Protease	SKF 107457	1.05	1.23	1.57
HIV-Protease	CGP-53820	0.36	1.02	0.9
HIV-Protease	U75875	0.34	0.81	2.49
HIV-Protease	SB206343	0.44	1.06	0.8
HIV-Protease	GR123976	0.5	0.9	0.86
HIV-Protease	GR126045	0.3	1.19	0.94
HIV-Protease	GR137615	0.21	0.69	0.77
HIV-Protease	A77003 (R,S)	0.45	1.00	0.82
HIV-Protease	A78791 (S,-)	0.24	0.84	0.79
HIV-Protease	A76928 (S,S)	0.26	1.02	1.57
HIV-Protease	A76889 (R,R)	0.47	0.75	1.22
HIV-Protease	A77	0.24	0.88	1.02
HIV-Protease	IM1	0.21	0.72	1.93
HIV-Protease	MVT-101	0.23	0.91	1.2
HIV-Protease	L-700, 417	0.35	0.56	0.72
HIV-Protease	ACETYL-PEPSTATIN	0.36	1.12	1.5
HIV-Protease	A-74704	0.27	1.13	1.33
HIV-Protease	Tri-peptide	0.3	0.82	1.33
HIV-Protease	JE-2147	0.27	0.89	1.01
Carbonic Anhydrase II	Celecoxib	0.38	0.79	0.73
Carbonic Anhydrase II	Histamine	3.8	3.06	3.17
Carbonic Anhydrase II	ETS	0.23	1.22	0.41
Carbonic Anhydrase II	PTS	0.33	1.27	0.41
Carbonic Anhydrase II	MTS	0.23	1.3	0.76
Carbonic Anhydrase II	EG1	0.94	1.02	0.79
Carbonic Anhydrase II	EG2	0.55	0.34	0.23
Carbonic Anhydrase II	EG3	0.42	0.69	0.24
Carbonic Anhydrase II	MNS	0.78	0.8	0.74
Alcohol Deydrogenase	CND	0.33	0.94	0.54
Alcohol Deydrogenase	PAD	0.32	0.68	0.86
Alcohol Deydrogenase	TAD	0.28	0.91	1.08
Alcohol Deydrogenase	SSB	0.22	1.21	0.86
Alcohol Deydrogenase	PFB,NAD	0.25	1.24	0.82
Alcohol Deydrogenase	FPI,NAD	0.3	1.03	0.79
Alcohol Deydrogenase	CXF,NAD	0.19	0.77	0.87
Alcohol Deydrogenase	SSB,NAD	0.27	0.94	1
Alpha-Thrombin	QWE	0.47	0.46	0.44
Alpha-Thrombin	AZL	0.23	0.48	0.28
Alpha-Thrombin	BMS-186282	0.35	0.46	0.31
Alpha-Thrombin	BMS-189090	0.25	0.56	0.69
Alpha-Thrombin	BZT	0.34	1.36	0.87
Alpha-Thrombin	BT3	0.25	0.75	0.75
Alpha-Thrombin	BPP	0.31	0.4	0.36
Alpha-Thrombin	Benzyldiamine	0.3	0.36	0.32
Alpha-Thrombin	MD-805 (Argatroban)	0.9	1.31	0.65
Alpha-Thrombin	NAPAP	0.34	0.52	0.44
Alpha-Thrombin	BMS-183507	0.38	0.39	0.32
Alpha-Thrombin	BM51.1011	0.56	0.32	0.14
Alpha-Thrombin	FSN	0.26	1.13	0.69
Cytohchrome C Peroxidase	TMT	1.33	1.39	1.31
Cytohchrome C Peroxidase	TMZ	0.56	1.11	1.11
Cytohchrome C Peroxidase	3MT	0.2	0.97	0.82
Cytohchrome C Peroxidase	DTI	0.57	0.83	0.71

Cytohchrome C Peroxidase	ANL	0.28	0.66	0.49
Cytohchrome C Peroxidase	3AP	0.25	1.5	1.38
Cytohchrome C Peroxidase	4AP	0.95	1.7	1.49
Cytohchrome C Peroxidase	24T	0.48	0.58	0.52
Cytohchrome C Peroxidase	NVI	0.56	0.72	0.56
Cytohchrome C Peroxidase	IDM	1.06	1.45	1.12
Cytohchrome C Peroxidase	MPI	0.75	0.96	0.86
Cytohchrome C Peroxidase	25T	0.84	1.67	1.56
Cytohchrome C Peroxidase	2AP	0.7	0.32	0.27
Cytohchrome C Peroxidase	2EZ	0.74	1.34	1.44
Cytohchrome C Peroxidase	IMD	0.24	1.35	1.27
Cytohchrome C Peroxidase	1MZ	0.19	0.21	0.2
Cytohchrome C Peroxidase	2MZ	2.03	1.65	1.67
Cytohchrome C Peroxidase	AMT	0.46	1.01	0.37
PSD-95	Cript	0.4	0.44	0.32
GRIP	Liprin	0.19	0.62	0.39
Syntenin	IL5R-a	0.56	0.85	0.85
Syntenin	Syndecan-4	0.17	0.8	0.46
Syntenin	Merlin	0.62	0.89	0.64
SH3 domain of GRB2	RHYRPLPPLP	1.42	0.97	0.82
SH3 domain of GRB2	VPPPVPPRRR	0.44	0.63	0.3
Cyclophilin A	AP	0.48	0.28	0.63
Cyclophilin A	HAGPIA	0.1	0.26	0.23
Methyltransferase	NWETF	0.59	0.43	0.26
Aldose Reductase	Tolrestat (TOL)	0.2	0.65	0.5
Aldose Reductase	IDD552	0.2	7.55	1.04
Carboxypeptidase	HFA	0.22	0.33	0.5
Carboxypeptidase	FVF	0.36	0.44	0.67
TIM	2-PG	0.54	0.51	0.5
TIM	G3P	0.3	0.53	0.37
ABP	NLA	0.3	0.64	0.53
Acetylcholinesterase	Huperzine A (HUP)	0.34	0.63	0.31
Adenosine deaminase	FR233624 (FR4)	0.36	0.38	0.34
Quinone reductase 2	Resveratrol (STL)	0.27	1.31	0.69

Table S3. RMSD (Å) values between the ligand positions of the lowest energy docked poses obtained from rigid and flexible BP-Dock docking of homologue CIPP and that of the bound crystal structure.

Homologue protein	Peptide	RMSD (Å)	
		Rigid	BP-Dock
CIPP	KQTSV	0.49	0.51
	DSVF	2.21	1.07
	NEFYA	0.72	0.56
	EYLGLDVPV	0.71	0.31

Table S4. RMSD (Å) values between the ligand positions of the lowest energy docked poses obtained from rigid bound, BP-Dock unbound and Backrub unbound docking of PDZ domain proteins and that of the holo crystal structure.

Protein	Peptide	RMSD (Å)		
		Rigid_Bound	BP-Dock_Unbound	Backrub_Unbound
PSD-95	KQTSV	0.4	0.32	1.25
PSD-95	ATVRTYSC	NA	1.35	1.29
GRIP	ATVRTYSC	0.19	0.39	0.59
GRIP	KQTSV	NA	0.52	0.54
Syntenin	DSVF	0.56	0.85	0.91
Syntenin	NEFYA	0.17	0.46	1.05
CIPP	KQTSV	NA	0.51	0.65
CIPP	EYLGLDVPV	NA	0.31	1.39

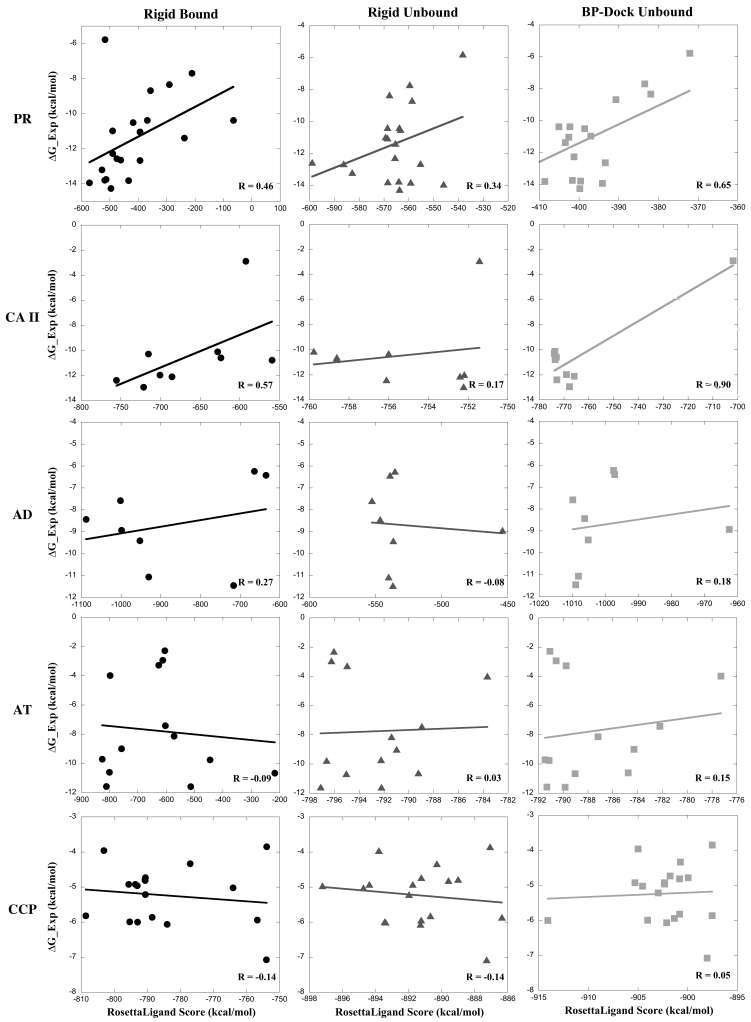

Figure S1. Correlation plots of RosettaLigand energy scores vs. experimental binding energies for HIV-1 protease (PR), carbonic anhydrase II (CA II), alcohol dehydrogenase (AD), alpha-thrombin (AT) and cytochrome C peroxidase (CCP).