Supplementary Materials

Exploring the binding mode of HIV-1 Vif inhibitors by blind docking, molecular dynamics and MM/GBSA

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Binding free energies and individual energy terms of five compounds are listed in Table S1. The correlation between the experimental and the calculated pIC_{50} of eleven binding modes are shown in Figure S1.

Compound 1								
Residue	$\Delta G_{ m vdw}$	$\Delta G_{ m ele}$	$\Delta G_{ m GB}$	$\Delta G_{ m SA}$	$\Delta G_{ m residue-inhibitor}$			
GLN 136	-1.10	-0.17	-0.20	-0.26	-1.72			
ALA 137	-0.21	-0.12	0.06	-0.05	-0.31			
GLY 138	-0.39	-0.03	-0.02	-0.09	-0.52			
HIS 139	-2.06	-0.01	-0.09	-0.33	-2.48			
SER 144	-0.70	-0.35	0.15	-0.19	-1.08			
TYR 147	-1.08	0.51	-0.37	-0.19	-1.13			
LEU 148	-0.42	0.01	-0.01	-0.11	-0.53			
LEU 150	-0.98	-0.29	-0.09	-0.16	-1.51			
ALA 151	-1.77	0.38	-0.36	-0.23	-1.98			
ILE 154	-0.76	-0.14	0.05	-0.17	-1.02			
THR 155	-1.55	-0.07	0.01	-0.28	-1.89			
LYS 176	-0.64	-1.86	1.50	-0.14	-1.13			
PRO 177	-1.11	0.57	-0.50	-0.19	-1.22			
		Comp	pound 2					
Residue	$\Delta G_{ m vdw}$	$\Delta G_{ m ele}$	$\Delta G_{ m GB}$	$\Delta G_{ m SA}$	$\Delta G_{ m residue-inhibitor}$			
GLN 136	-0.70	-0.24	-0.48	-0.16	-1.57			
GLY 138	-1.70	-0.66	-0.15	-0.26	-2.78			
HIS 139	-1.55	-0.74	0.53	-0.24	-2.00			
ASN 140	-1.51	-0.02	-0.2	-0.28	-2.00			
TYR 147	-2.63	0.17	-0.18	-0.36	-3.00			
LEU 148	-0.77	0.11	-0.09	-0.24	-0.99			
LEU 150	-0.81	0.06	-0.18	-0.15	-1.08			
ALA 151	-1.53	0.35	-0.39	-0.24	-1.81			
ILE 154	-0.50	-0.15	0.08	-0.11	-0.67			
THR 155	-1.22	-0.49	0.35	-0.30	-1.65			
ILE 159	-0.60	-0.20	0.18	-0.14	-0.72			
ARG 173	-0.45	-2.40	2.21	-0.09	-0.74			
PRO 177	-1.11	-3.24	2.60	-0.20	-1.95			
		Comp	bound 3					
Residue	$\Delta G_{ m vdw}$	$\Delta G_{ m ele}$	$\Delta G_{ m GB}$	$\Delta G_{ m SA}$	$\Delta G_{ m residue-inhibitor}$			
GLN 136	-1.89	-1.80	0.46	-0.43	-3.66			
ALA 137	-1.49	-1.07	0.42	-0.19	-2.33			
GLY 138	-1.65	-1.15	0.45	-0.20	-2.55			
HIS 139	-2.53	-1.60	0.06	-0.31	-4.37			
ASN 140	-0.68	-0.89	0.39	-0.70	-1.28			
LYS 141	-1.08	-1.26	0.47	-0.20	-2.07			
VAL 142	-0.37	0.24	-0.21	-0.07	-0.41			
TYR 147	-1.90	-0.20	0.04	-0.25	-2.31			
LEU 148	-1.37	0.31	-0.35	-0.32	-1.73			
LEU 150	-1.25	0.95	-0.82	-0.20	-1.31			
ALA 151	-2.39	0.59	-0.59	-0.25	-2.64			

Table S1. Binding free energies and individual energy terms of five compounds.

ILE 154	-0.78	-0.55	0.24	-0.20	-1.29			
Compound 4								
Residue	$\Delta G_{ m vdw}$	$\Delta G_{ m ele}$	$\Delta G_{ m GB}$	$\Delta G_{ m SA}$	$\Delta G_{ m residue-inhibitor}$			
GLN 136	-0.53	-0.24	0.16	-0.16	-0.77			
HIS 139	-0.49	-0.25	0.20	-0.07	-0.61			
ASN 140	-1.97	-0.78	0.04	-0.35	-3.06			
LYS 141	-1.03	-1.94	1.60	-0.16	-1.52			
VAL 142	-0.57	0.19	-0.20	-0.19	-0.77			
TYR 147	-1.50	-0.06	-0.17	-0.24	-1.97			
LEU 148	-1.68	0.13	-0.13	-0.33	-2.01			
LEU 150	-1.09	-0.52	0.12	-0.20	-1.66			
ALA 151	-2.29	-0.15	0.05	-0.28	-2.67			
ALA 152	-0.57	-0.02	0.11	-0.13	-0.62			
ILE 154	-0.48	-0.19	0.10	-0.13	-0.70			
THR 155	-0.41	0.07	-0.08	-0.13	-0.55			
LYS 176	-0.27	-2.01	1.81	-0.09	-0.57			
Compound 5								
Residue	$\Delta G_{ m vdw}$	$\Delta G_{ m ele}$	$\Delta G_{ m GB}$	$\Delta G_{ m SA}$	$\Delta G_{ m residue-inhibitor}$			
Residue GLU 134	$\Delta G_{\rm vdw}$ -0.42	$\Delta G_{\rm ele}$ -1.26	$\frac{\Delta G_{\rm GB}}{1.12}$	$\Delta G_{\rm SA}$ -0.17	$\Delta G_{\text{residue-inhibitor}}$ -0.74			
GLU 134 GLN 136	$\frac{\Delta G_{\rm vdw}}{-0.42}$ -2.42	$\Delta G_{\rm ele}$ -1.26 -1.00	$\frac{\Delta G_{\rm GB}}{1.12}$ 0.58	$\Delta G_{\rm SA}$ -0.17 -0.35	$\Delta G_{\text{residue-inhibitor}}$ -0.74 -3.19			
ResidueGLU 134GLN 136ALA 137	$\Delta G_{\rm vdw}$ -0.42 -2.42 -1.11	$\Delta G_{\rm ele}$ -1.26 -1.00 0.01	$\Delta G_{\rm GB}$ 1.12 0.58 -0.02	$\Delta G_{\rm SA}$ -0.17 -0.35 -0.19	$\frac{\Delta G_{\text{residue-inhibitor}}}{-0.74}$ -3.19 -1.30			
Residue GLU 134 GLN 136 ALA 137 GLY 138	$\begin{array}{c} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \end{array}$	$ \Delta G_{ele} -1.26 -1.00 0.01 0.26 $	$ \Delta G_{\rm GB} 1.12 0.58 -0.02 -0.05 $	$ \Delta G_{SA} -0.17 -0.35 -0.19 -0.16 $	$\begin{array}{r} \Delta G_{\text{residue-inhibitor}} \\ -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \end{array}$	$\begin{array}{c c} \Delta G_{\rm ele} \\ \hline -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \end{array}$	$\begin{array}{c} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \end{array}$	$ \Delta G_{SA} -0.17 -0.35 -0.19 -0.16 -0.06 $	$\Delta G_{\text{residue-inhibitor}}$ -0.74 -3.19 -1.30 -1.07 -0.44			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \end{array}$	$\begin{tabular}{c} \Delta G_{\rm ele} \\ -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \end{tabular}$	$\begin{array}{c} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \end{array}$	$\begin{array}{r} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \end{array}$	$\Delta G_{\text{residue-inhibitor}}$ -0.74 -3.19 -1.30 -1.07 -0.44 -0.48			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \end{array}$	$\begin{array}{c c} \Delta G_{\rm ele} \\ \hline -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \end{array}$	$\begin{array}{c} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \end{array}$	$\begin{array}{r} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \end{array}$	$\begin{array}{r} \Delta G_{\rm residue-inhibitor} \\ -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143 SER 144	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \\ -0.32 \end{array}$	$\begin{array}{c c} \Delta G_{\rm ele} \\ \hline -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \\ -0.80 \end{array}$	$\begin{array}{c} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \\ 0.59 \end{array}$	$\begin{array}{r} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \\ -0.06 \end{array}$	$\begin{array}{r} \Delta G_{\rm residue-inhibitor} \\ -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \\ -0.60 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143 SER 144 TYR 147	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \\ -0.32 \\ -3.07 \end{array}$	$\begin{array}{c c} \Delta G_{\rm ele} \\ \hline -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \\ -0.80 \\ -0.83 \end{array}$	$\begin{array}{c} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \\ 0.59 \\ 0.65 \end{array}$	$\begin{array}{r} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \\ -0.06 \\ -0.45 \end{array}$	$\begin{array}{r} \Delta G_{\rm residue-inhibitor} \\ -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \\ -0.60 \\ -3.71 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143 SER 144 TYR 147 LEU 148	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \\ -0.32 \\ -3.07 \\ -1.32 \end{array}$	$\begin{array}{c c} \Delta G_{\rm ele} \\ \hline -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \\ -0.80 \\ -0.83 \\ 0.33 \end{array}$	$\begin{array}{r} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \\ 0.59 \\ 0.65 \\ -0.35 \end{array}$	$\begin{array}{r} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \\ -0.06 \\ -0.45 \\ -0.32 \end{array}$	$\begin{array}{r} \Delta G_{\rm residue-inhibitor} \\ -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \\ -0.60 \\ -3.71 \\ -1.66 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143 SER 144 TYR 147 LEU 148 LEU 150	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \\ -0.32 \\ -3.07 \\ -1.32 \\ -0.97 \end{array}$	$\begin{array}{c c} \Delta G_{\rm ele} \\ \hline -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \\ -0.80 \\ -0.83 \\ 0.33 \\ 0.34 \end{array}$	$\begin{array}{c} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \\ 0.59 \\ 0.65 \\ -0.35 \\ -0.42 \end{array}$	$\begin{array}{r} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \\ -0.06 \\ -0.45 \\ -0.32 \\ -0.20 \end{array}$	$\begin{array}{r} \Delta G_{\rm residue-inhibitor} \\ -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \\ -0.60 \\ -3.71 \\ -1.66 \\ -1.23 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143 SER 144 TYR 147 LEU 148 LEU 150 ALA 151	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \\ -0.32 \\ -3.07 \\ -1.32 \\ -0.97 \\ -2.29 \end{array}$	$\begin{array}{c c} \Delta G_{\rm ele} \\ \hline -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \\ -0.80 \\ -0.83 \\ 0.33 \\ 0.34 \\ 0.07 \end{array}$	$\begin{array}{c} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \\ 0.59 \\ 0.65 \\ -0.35 \\ -0.42 \\ -0.22 \end{array}$	$\begin{array}{r} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \\ -0.06 \\ -0.45 \\ -0.32 \\ -0.20 \\ -0.25 \end{array}$	$\begin{array}{r} \Delta G_{\rm residue-inhibitor} \\ \hline -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \\ -0.60 \\ -3.71 \\ -1.66 \\ -1.23 \\ -2.70 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143 SER 144 TYR 147 LEU 148 LEU 150 ALA 151 ILE 154	$\begin{array}{r} \Delta G_{\rm vdw} \\ \hline -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \\ -0.32 \\ -3.07 \\ -1.32 \\ -0.97 \\ -2.29 \\ -1.14 \end{array}$	$\begin{array}{c} \Delta G_{\rm ele} \\ -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \\ -0.80 \\ -0.83 \\ 0.33 \\ 0.34 \\ 0.07 \\ -0.13 \end{array}$	$\begin{array}{c} \Delta G_{\rm GB} \\ 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \\ 0.59 \\ 0.65 \\ -0.35 \\ -0.42 \\ -0.22 \\ 0.15 \end{array}$	$\begin{array}{r} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \\ -0.06 \\ -0.45 \\ -0.32 \\ -0.20 \\ -0.25 \\ -0.23 \end{array}$	$\begin{array}{r} \Delta G_{\rm residue-inhibitor} \\ \hline -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \\ -0.60 \\ -3.71 \\ -1.66 \\ -1.23 \\ -2.70 \\ -1.35 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143 SER 144 TYR 147 LEU 148 LEU 150 ALA 151 ILE 154 THR 155	$\begin{array}{r} \Delta G_{\rm vdw} \\ -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \\ -0.32 \\ -3.07 \\ -1.32 \\ -0.97 \\ -2.29 \\ -1.14 \\ -0.84 \end{array}$	$\begin{array}{c} \Delta G_{\rm ele} \\ -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \\ -0.80 \\ -0.83 \\ 0.33 \\ 0.34 \\ 0.07 \\ -0.13 \\ -0.27 \end{array}$	$\begin{array}{r c} \Delta G_{\rm GB} \\ \hline 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \\ 0.59 \\ 0.65 \\ -0.35 \\ -0.42 \\ -0.22 \\ 0.15 \\ 0.28 \end{array}$	$\begin{array}{c c} \Delta G_{\rm SA} \\ \hline -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \\ -0.06 \\ -0.45 \\ -0.32 \\ -0.20 \\ -0.25 \\ -0.23 \\ -0.23 \\ -0.23 \end{array}$	$\begin{array}{r c} \Delta G_{\text{residue-inhibitor}} \\ \hline -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \\ -0.60 \\ -3.71 \\ -1.66 \\ -1.23 \\ -2.70 \\ -1.35 \\ -1.07 \end{array}$			
Residue GLU 134 GLN 136 ALA 137 GLY 138 HIS 139 LYS 141 GLY 143 SER 144 TYR 147 LEU 148 LEU 150 ALA 151 ILE 154 THR 155 LYS 176	$\begin{tabular}{ c c c c } \hline \Delta G_{\rm vdw} \\ \hline -0.42 \\ -2.42 \\ -1.11 \\ -1.12 \\ -0.39 \\ -0.35 \\ -0.44 \\ -0.32 \\ -3.07 \\ -1.32 \\ -0.97 \\ -2.29 \\ -1.14 \\ -0.84 \\ -0.97 \end{tabular}$	$\begin{array}{c c} \Delta G_{\rm ele} \\ \hline -1.26 \\ -1.00 \\ 0.01 \\ 0.26 \\ -0.01 \\ 0.15 \\ 0.13 \\ -0.80 \\ -0.83 \\ 0.33 \\ 0.34 \\ 0.07 \\ -0.13 \\ -0.27 \\ -0.24 \end{array}$	$\begin{array}{c} \Delta G_{\rm GB} \\ \hline 1.12 \\ 0.58 \\ -0.02 \\ -0.05 \\ 0.02 \\ -0.17 \\ -0.04 \\ 0.59 \\ 0.65 \\ -0.35 \\ -0.42 \\ -0.22 \\ 0.15 \\ 0.28 \\ 0.15 \end{array}$	$\begin{array}{c} \Delta G_{\rm SA} \\ -0.17 \\ -0.35 \\ -0.19 \\ -0.16 \\ -0.06 \\ -0.10 \\ -0.16 \\ -0.06 \\ -0.45 \\ -0.32 \\ -0.20 \\ -0.25 \\ -0.23 \\ -0.23 \\ -0.23 \\ -0.17 \end{array}$	$\begin{array}{r} \Delta G_{\text{residue-inhibitor}} \\ \hline -0.74 \\ -3.19 \\ -1.30 \\ -1.07 \\ -0.44 \\ -0.48 \\ -0.52 \\ -0.60 \\ -3.71 \\ -1.66 \\ -1.23 \\ -2.70 \\ -1.35 \\ -1.07 \\ -1.23 \end{array}$			







Figure S1. The correlation between the experimental and the calculated plC_{50} of fifteen binding modes.