Supporting Information

Deciphering complex mechanisms of resistance and loss of potency through coupled molecular dynamics and machine learning.

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***Table S1**. Dataset information: HIV-1 protease variants with their experimental inhibition constants (K_i) and PDB accession codes for available structures.*

Name	K_i (nM)	ΔG (kcal/mol)	Set	Cluster	Reference	PDB ID
NL4-3 (WT)	0.005	-15.5	Train	2	(1)	6dgx
Var1-1Mut	0.026	-14.5	Train	2	(1)	6dh0
Var2-2Mut	0.23	-13.2	Train	2	(2)	6opt
Var3-2Mut	0.075	-13.9	Train	2	(1)	-
Var4-5Mut	0.045	-14.2	Train	2	(3)	4q1y
Var5-4Mut	0.42	-12.9	Train	2	(2)	6opu
Var6-8Mut	12.8	-10.8	Train	3	(2)	6opv
Var7-10Mut	156.4	-9.3	Train	3	(2)	6opy
Var8-11Mut	759.2	-8.4	Train	3	(2)	6opz
Var9-9Mut	77.6	-9.8	Train	3	(4)	-
Var10-7Mut	12.1	-10.9	Train	3	(4)	-
Var11-10Mut	57.6	-9.9	Train	3	(4)	-
Var12-6Mut	3.9	-11.5	Train	3	(4)	-
Var13-10Mut	26.0	-10.4	Train	3	(4)	-
Var14-12Mut	12.1	-10.9	Train	3	(4)	-
Var15-12Mut	58.3	-9.9	Train	3	(4)	-
Var16-10Mut	57.0	-9.9	Train	3	(4)	-
Var17-14Mut	11.7	-10.9	Train	3	(4)	-
Var18-20Mut	0.75	-12.5	Test	1	(5)	3ttp
Var19-20Mut	15.0	-10.7	Test	1	(6)	3u7s
Var20-7Mut	0.026	-14.5	Test	2	(7)	3ekt
Var21-24Mut	6.95	-11.2	Test	1	(8)	-
Var22-4Mut (SF2)	0.014	-14.9	Test	2	(9)	1t3r
Var23-6Mut	6.6	-11.2	Test	2	(10)	2f80
Var24-6Mut	17.0	-10.7	Test	2	(11)	3cyw
Var25-20Mut	31.0	-10.3	Test	1	(12)	3ucb
Var26-6Mut	0.51	-12.8	Test	2	(13)	5kqy
Var27-6Mut	1.6	-12.1	Test	2	(11)	3d1z

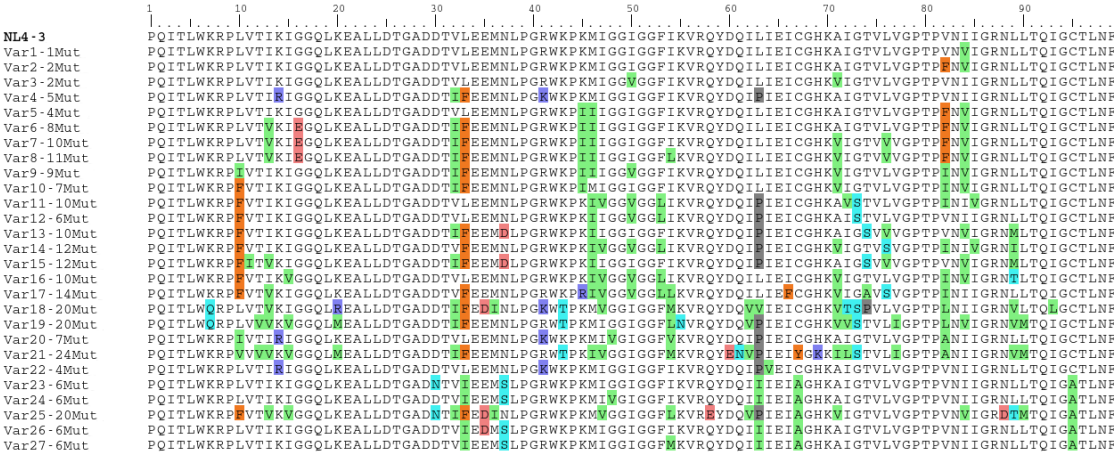

Figure S1. *Amino acid sequence alignment of HIV-1 protease variants in the dataset. Mutations relative to the reference wild type (NL4-3) are colored according to residue type. (Green: Hydrophobic; Orange: Aromatic, Red: Negative Charge; Blue: Positive Charge; Cyan: Polar; Gray: Small)*

References

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