

Supplementary Material

Atazanavir inhibits SARS-CoV-2 replication and pro-inflammatory cytokine production

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Additional Results *in silico*

Molecular Dynamics

The enzyme-LPV complex was stable with a RMSD value not exceeding 3 Å, but when considering LPV alone, its RMSD exceeded 4 Å over the entire simulation (Figure S1A). By contrast, when complexed with ATV, the RMSD of SCV2-MP reached as much as 4 Å in the last 20 ns of the simulation, while the RMSD of ATV alone did not exceed 3 Å over the 100 ns (Figure S1B). After the step of energy minimization, at the beginning of the molecular dynamics, LPV presented 4 hydrogen bonds with the amino acids Thr25, Ser46, Gly143, and Gln189 (Figures S2A and S3A). After 100 ns of molecular dynamics, LPV interacted with Ser46 HIS41 (Figures 3A and 4A).

ATV's interaction, after energy minimization, occurred with residue Gln189 (Figure S2B and S3B), but after 100 ns of molecular dynamics, Glu166 acted as a hydrogen acceptor and His164 as a hydrogen donor (Figure 3B and 4B).

Tables

Table S1. Interactions from Atazanavir (ATV) with the residues from the active site.

Docking Interactions of ATA		
Ligand	Residues	Distance, Å
ATV:H32	ASN142:OD1	1.91
ATV:H32	HIS164:O	2.64
ATV:H8	GLU166:OE1	2.44

Table S2. Interactions from Lopinavir (LPV) with the residues from the active site before (*) and after MD.

Molecular Dynamics Interactions of LPV		
Ligand	Residues	Distance, Å
LPV:O1	THR25:HG1	1.99*
LPV:O2	SER45:HG	1.75*
LPV:O	GLY143:H	2.31*
LPV:O2	GLN189:HE21	1.95*
LPV:O2	SER46:HD	1.70
LPV:O1	HIS41:HE2	2.03

Table S3. Interactions from Atazanavir (ATV) with residues from the active site before (*) and after MD.

Molecular Dynamics Interactions of ATV		
Ligand	Residues	Distance, Å
ATV:H28	GLN189:OE1	2.04*
ATV:H31	HIE167:O	1.87
ATV:H2	GLU166:O	2.51

Legend for the Figures

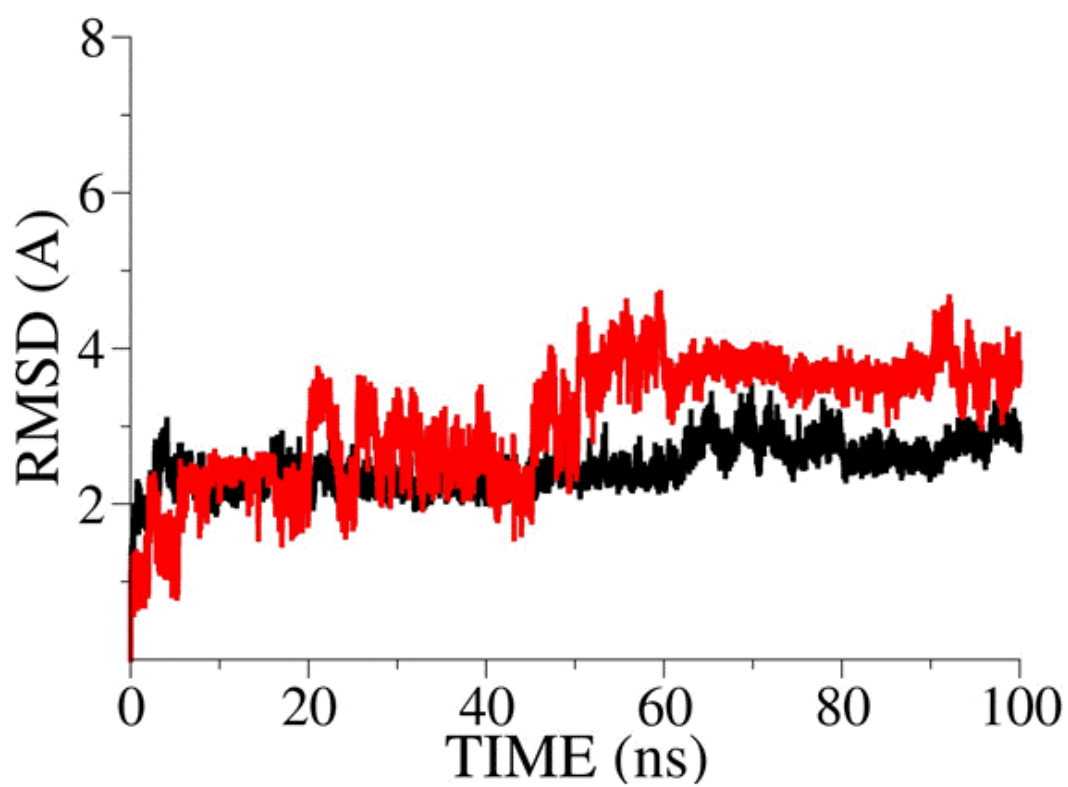
Figure S1. Root Mean Square Deviation (RMSD) along 100 ns of MD simulation of the Mpro (black) when complexed with A) LPV (red) and B) ATV(red). (A) LPV (red) is rather unstable while Mpro (black) remains stable. In (B), it is Mpro (black) that is destabilized while ATV (red) remains stable along the MD simulation.

Figure S2. Representative images of the Root Mean Square Deviation (RMSD) along 100 ns of molecular dynamics (MD) simulation. LPV (A) and ATV (B) are positioned in the Mpro active site at the beginning of 100 ns simulation.

Figure S3. Two-dimensional (2D) representation of the interactions of LPV (A) and ATV (B) into Mpro's active site at the beginning of 100 ns RMSD.

Figure S1

A



B

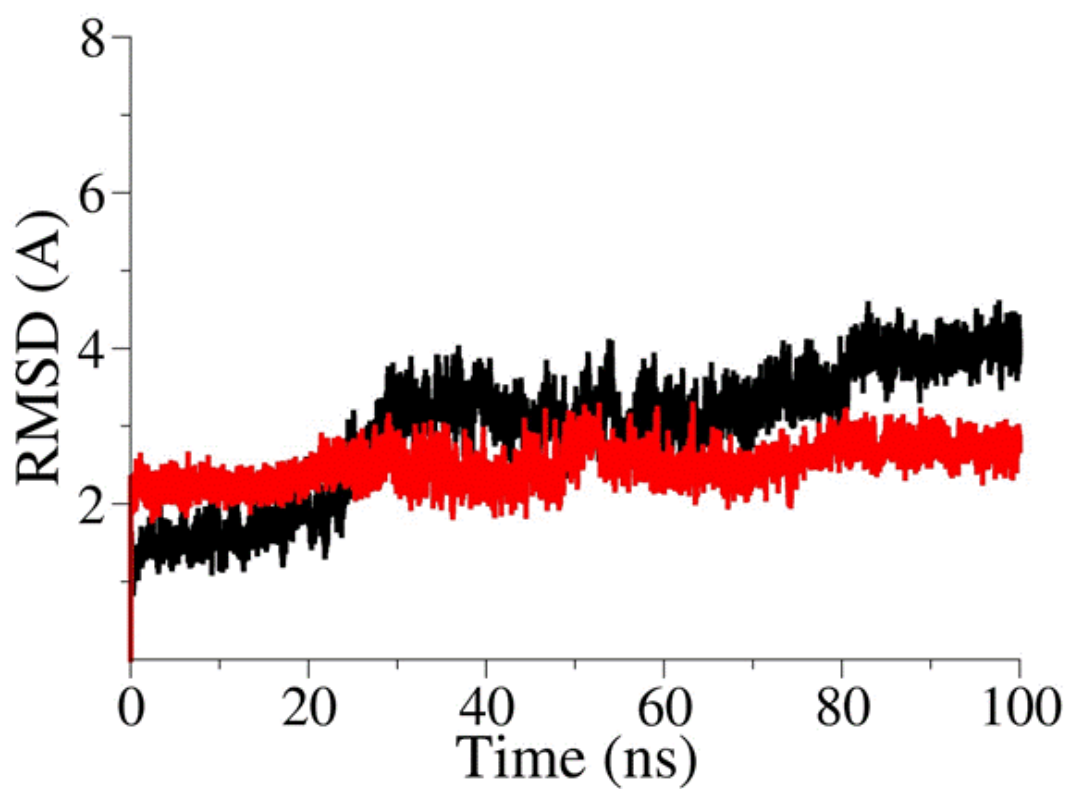
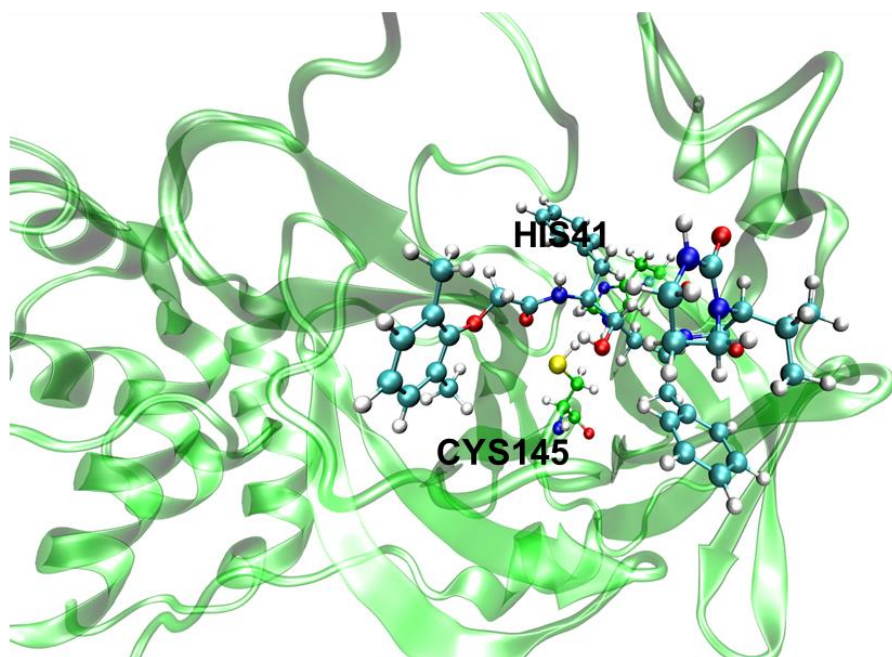


Figure S2

A



B

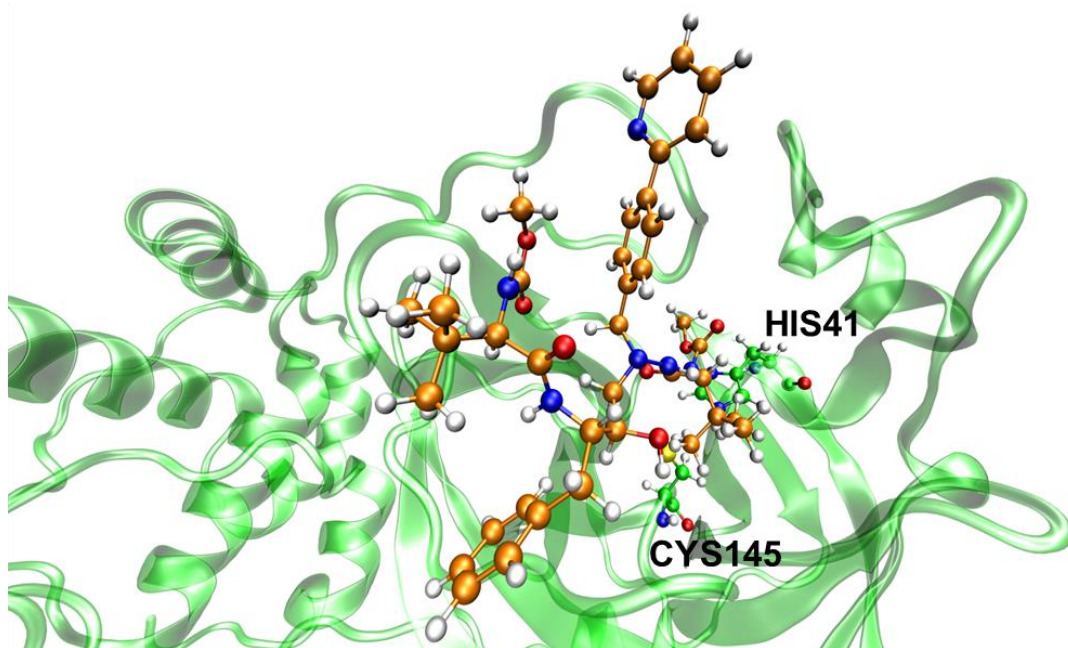
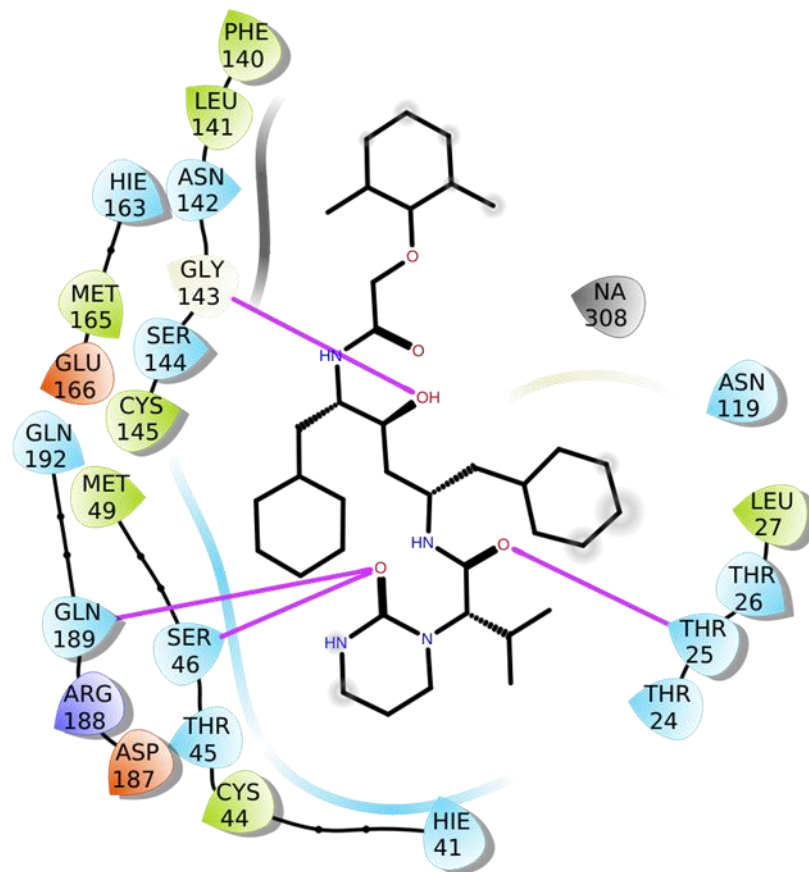


Figure S3

A



B

