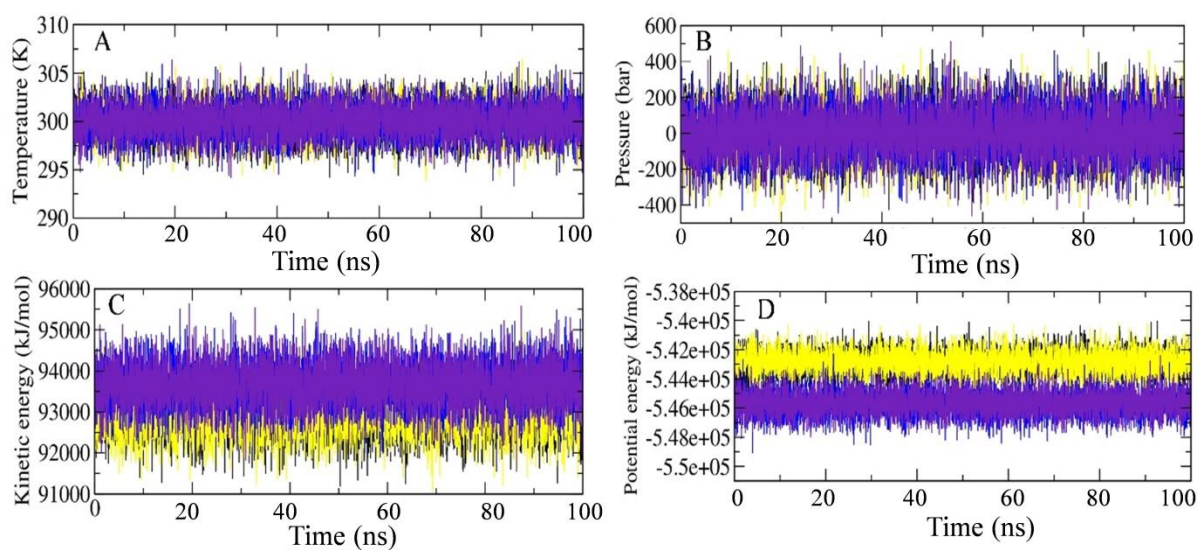


Supplementary Table S1: Distance between amino acid residues at specific time interval of the 100 ns molecular dynamics simulation period (individual and averaged). Additionally average value during the entire period is also tabulated.

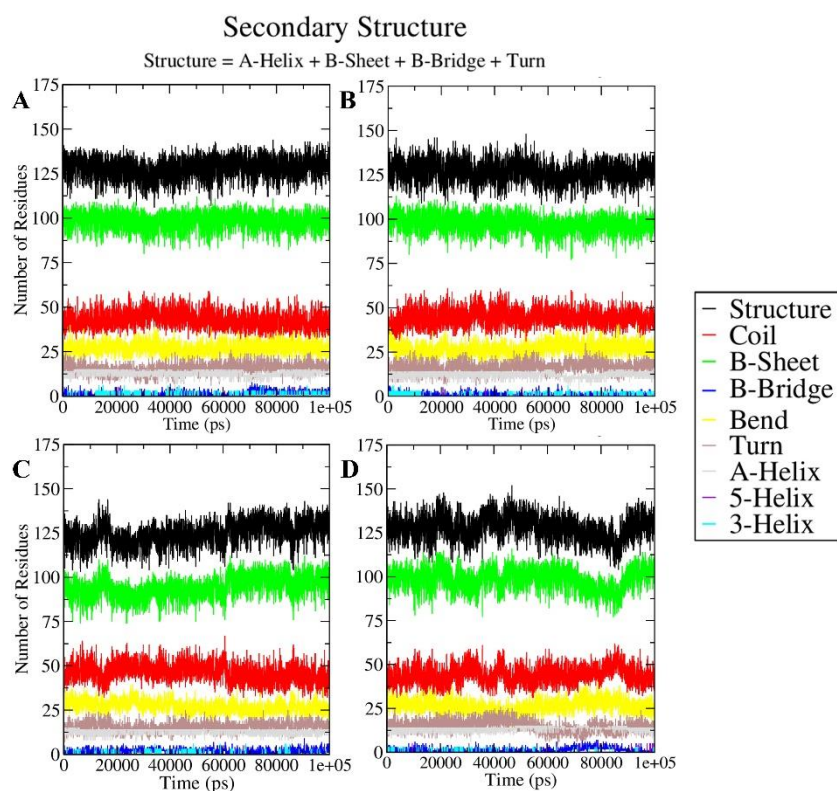
Time (ns)	Asp25-Asp124 (nm)	Asp25-Ile50 (nm)	Asp25-Ile149 (nm)
Unbound wild type protease (WT)			
1	0.69	1.35	1.16
20	0.70	1.38	1.25
40	0.67	1.36	1.15
60	0.68	1.82	1.33
80	0.65	13.6	1.42
100	0.64	1.12	1.32
Average	0.67	1.39	1.27
1-100 ns MD Average Distances	0.6529±0.02235	1.4359±0.1914	1.3359±0.1837
Unbound M46I mutation carrying protease (MI)			
1	0.7	1.47	1.29
20	0.64	1.64	2.15
40	0.67	1.73	2.23
60	0.72	1.79	2.16
80	0.71	1.58	2.42
100	0.65	1.61	2.18
Average	0.68	1.63	2.071
1-100 ns MD Average Distances	0.6838±0.0338	1.7026±0.2291	2.0923±0.2797
Saquinavir bound wild type protease (SQ-WT)			
1	0.73	1.50	1.28
20	0.68	1.24	1.48
40	0.65	1.52	1.63
60	0.71	1.45	1.93
80	0.66	1.41	1.82
100	0.67	1.58	1.70
Average	0.68	1.45	1.64
1-100 ns MD Average Distances	0.6659±0.0215	1.5600±0.1306	1.7312±0.1398
Saquinavir bound M46I protease (SQ-MI)			
1	0.72	1.45	1.28
20	0.70	1.79	2.21
40	0.80	2.16	2.01
60	0.90	1.71	2.18
80	0.87	1.71	2.20
100	0.76	2.29	2.20
Average	0.79	1.85	2.013
1-100 ns MD Average Distances	0.7843±0.0715	1.8856±0.2939	2.0348±0.3014

Supplementary Figure S1



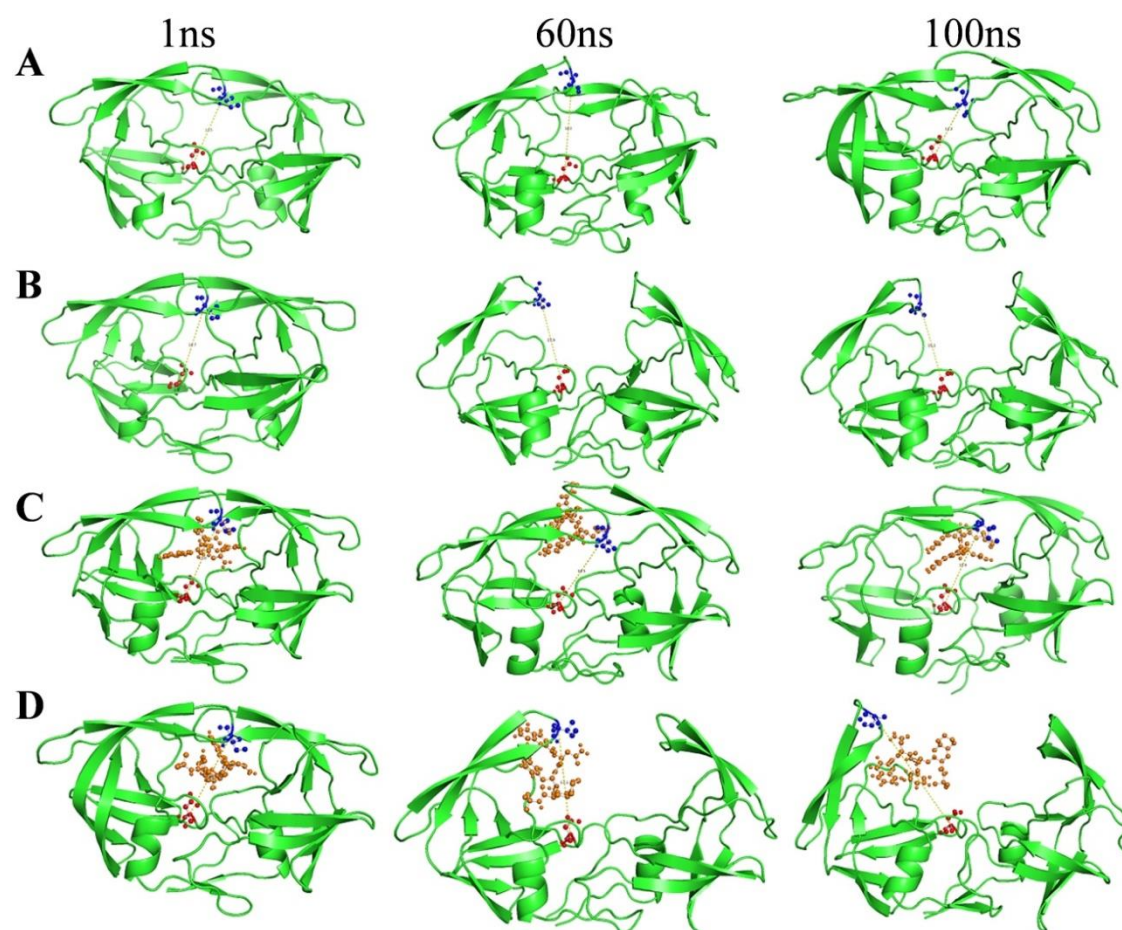
Supplementary Figure S1: Temperature (A), pressure (B), Kinetic energy (C), and potential energy (D) of WT (Black), MI (Yellow), SQ-WT (Blue), and SQ-MI (Purple) simulation systems. WT- Wild type, SQ-WT- Saquinavir bound wild type, MI- M46I mutation carrying protease, and SQ-MI- Saquinavir bound mutation carrying protease.

Supplementary Figure S2



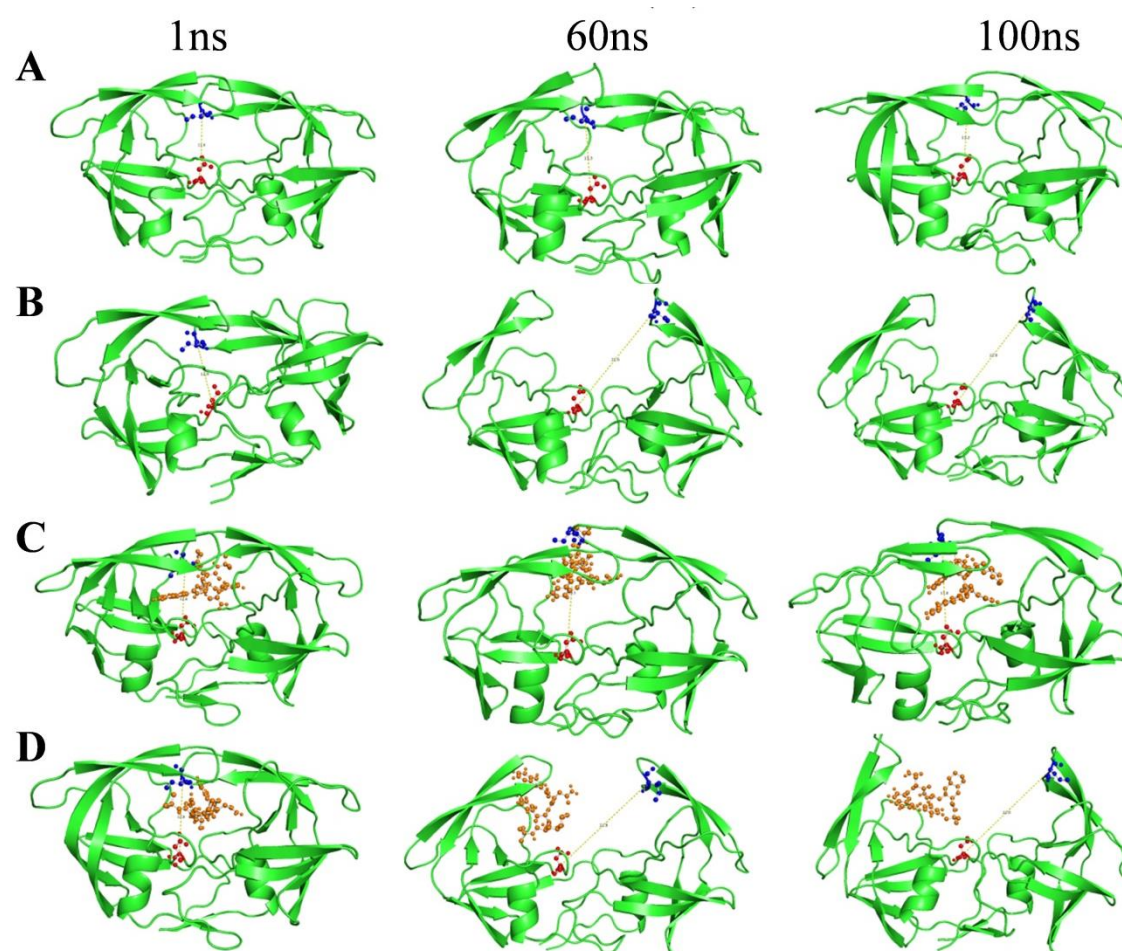
Supplementary Figure S2: Evolution of secondary structure during 100 ns MD simulation for WT (A), MI (B), SQ-WT (C), and SQ-MI (D). WT- Wild type, SQ-WT- Saquinavir bound wild type, MI- M46I mutation carrying protease, and SQ-MI- Saquinavir bound mutation carrying protease.

Supplementary Figure S3



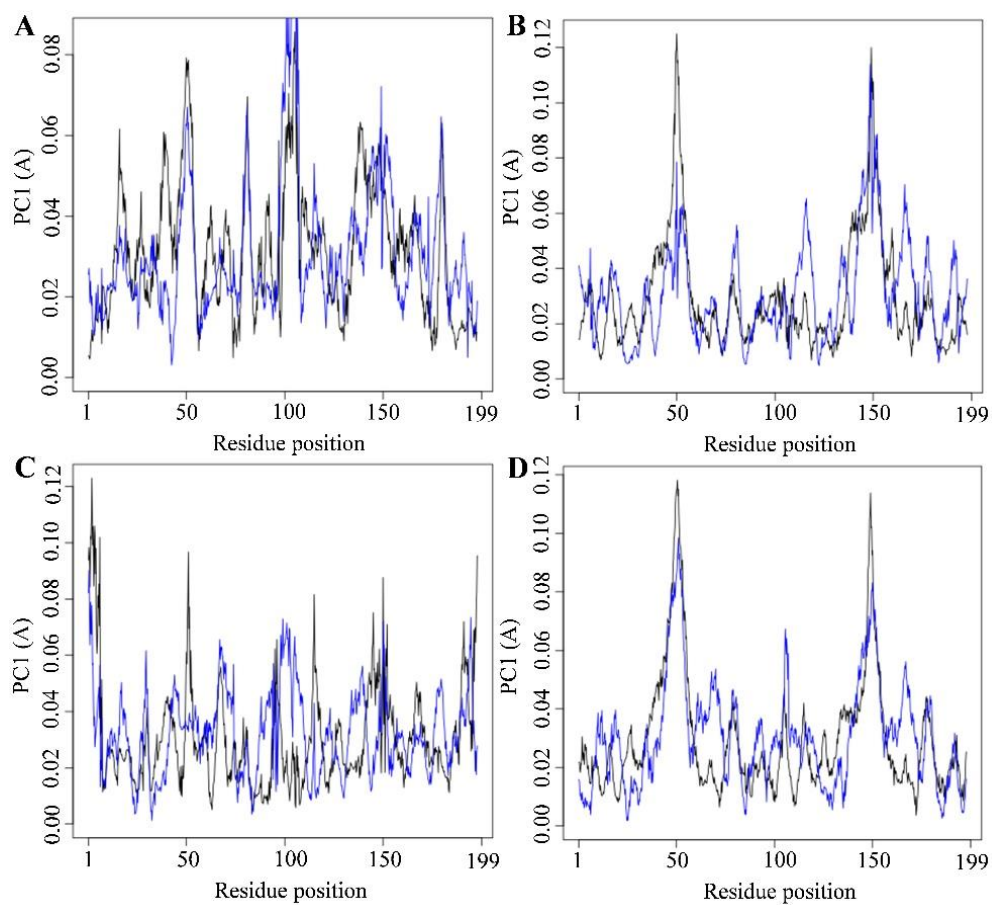
Supplementary Figure S3: Distance between Asp25-Ile50 amino acid residues in (A) WT, (B) MI (C) SQ-WT and (D) SQ-MI systems at 1, 60 and 100 ns simulation period. WT- Wild type, SQ-WT- Saquinavir bound wild type, MI- M46I mutation carrying protease, and SQ-MI- Saquinavir bound mutation carrying protease.

Supplementary Figure S4



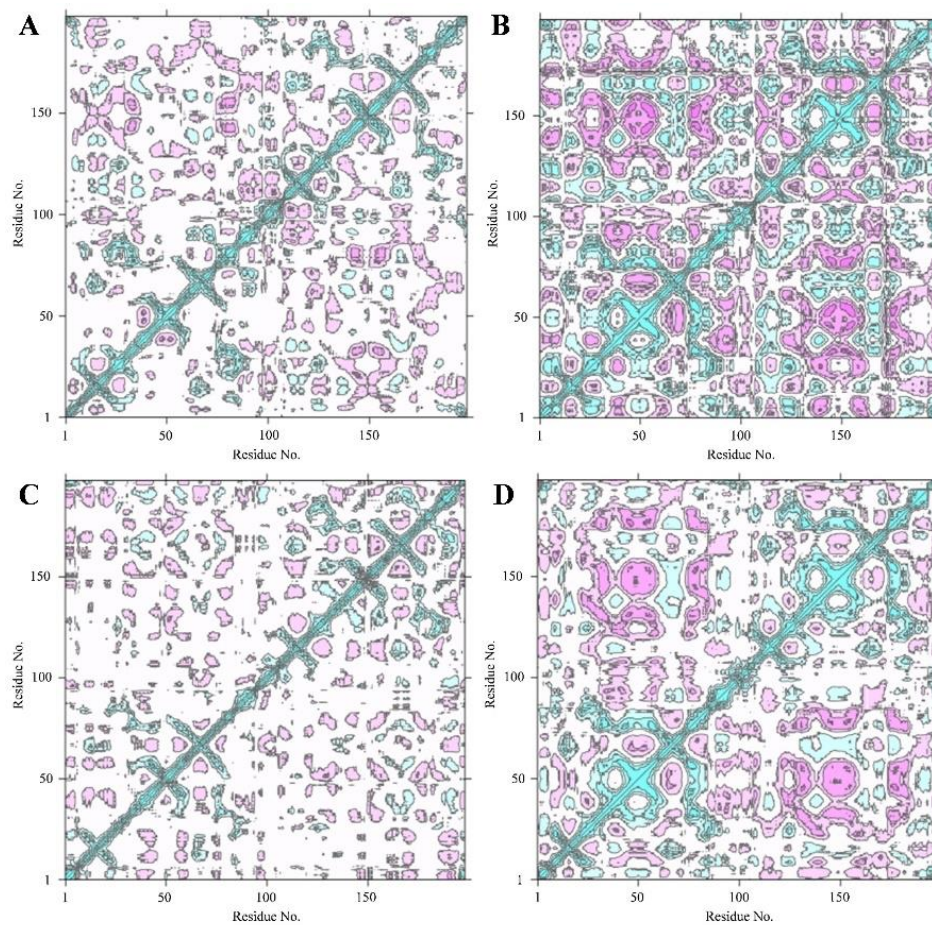
Supplementary Figure S4: Distance between Asp25-Ile149 amino acid residues in (A) WT, (B) MI (C) SQ-WT and (D) SQ-MI systems at 1, 60 and 100 ns simulation period. WT- Wild type, SQ-WT- Saquinavir bound wild type, MI- M46I mutation carrying protease, and SQ-MI- Saquinavir bound mutation carrying protease.

Supplementary Figure S5



Supplementary Figure S5: Projection of PC1 (Blue) on RMSF (Black) during 100 ns MD simulation for WT (A), MI (B), SQ-WT (C), and SQ-MI (D). WT- Wild type, SQ-WT- Saquinavir bound wild type, MI- M46I mutation carrying protease, and SQ-MI- Saquinavir bound mutation carrying protease.

Supplementary Figure S6



Supplementary Figure S6: Dynamic cross correlation matrix (DCCM) of test systems during 100 ns MD simulation for WT (A), MI (B), SQ-WT (C), and SQ-MI (D). WT- Wild type, SQ-WT- Saquinavir bound wild type, MI- M46I mutation carrying protease, and SQ-MI- Saquinavir bound mutation carrying protease.