Electronic Supplementary Material (ESI) for Molecular BioSystems.

Supporting information

Molecular insight on the binding of NNRTI to K103N mutated HIV-1 RT: Molecular dynamics simulations and dynamic pharmacophore analysis

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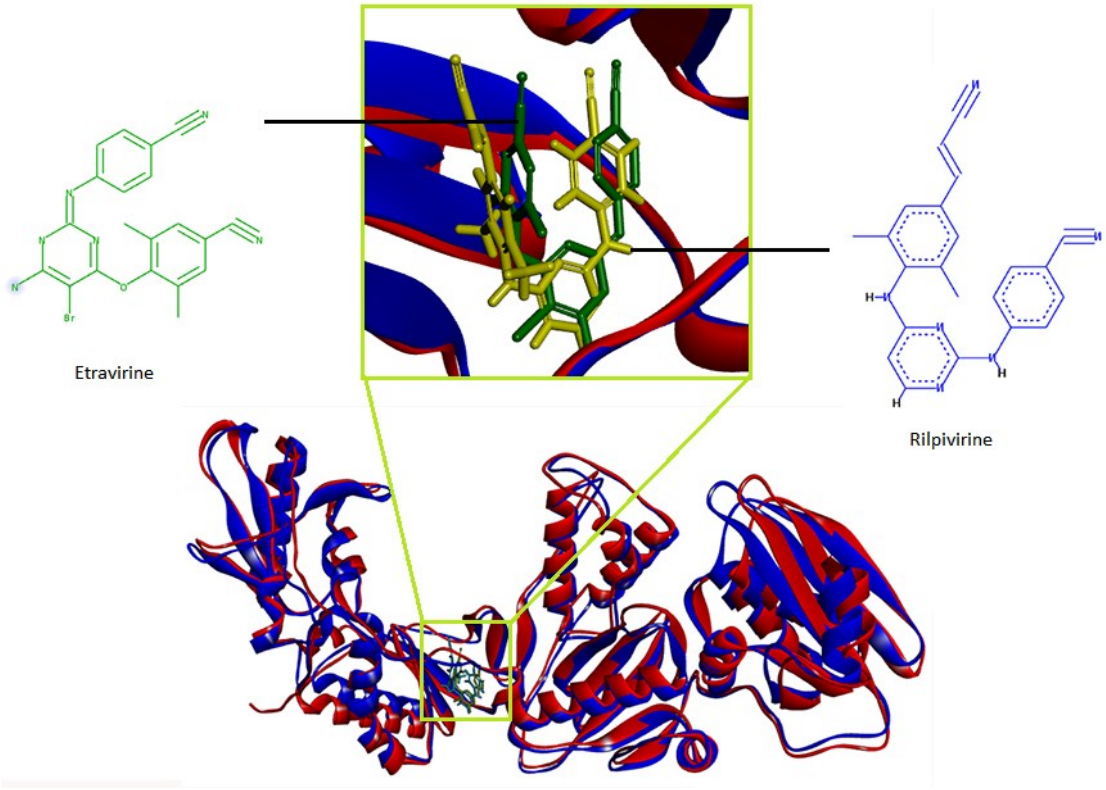
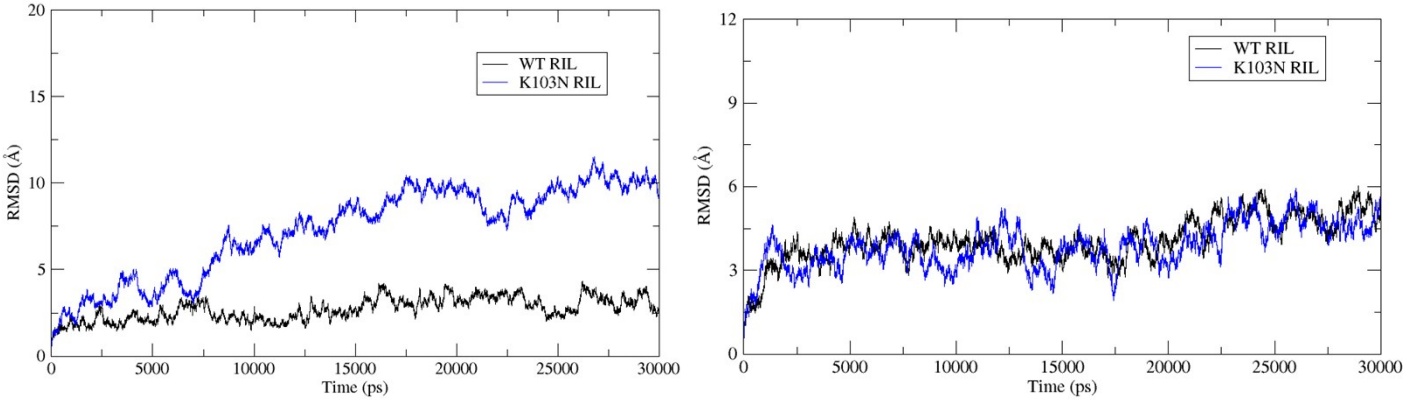
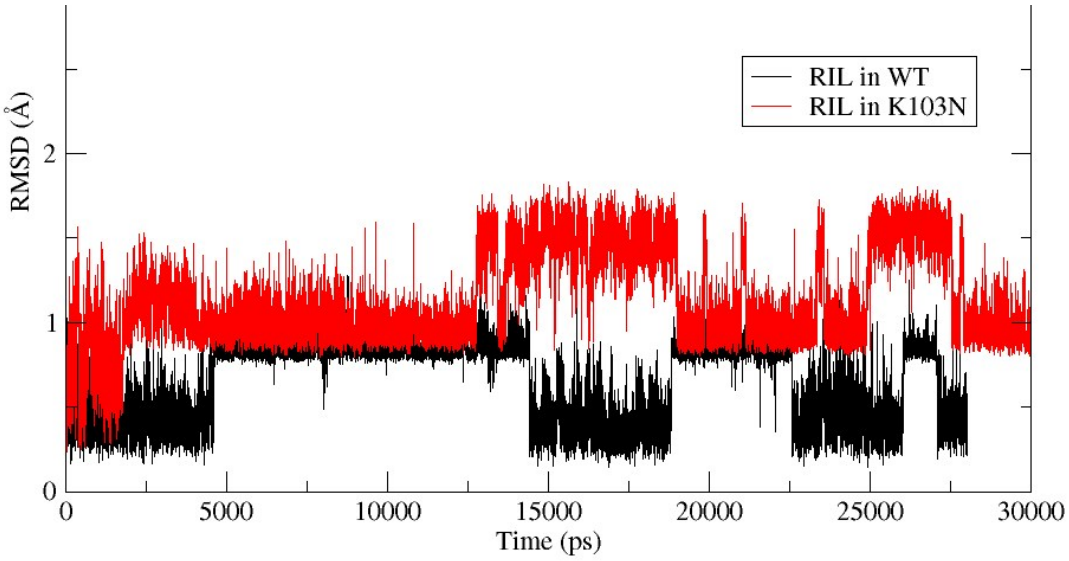


Figure S1. Superimposed structures of 3MED (blue) and 4G1Q (red). Superimposed structure of etravirine and rilpivirine inside the NNRTI binding pocket in their respective PDB is also shown in box.

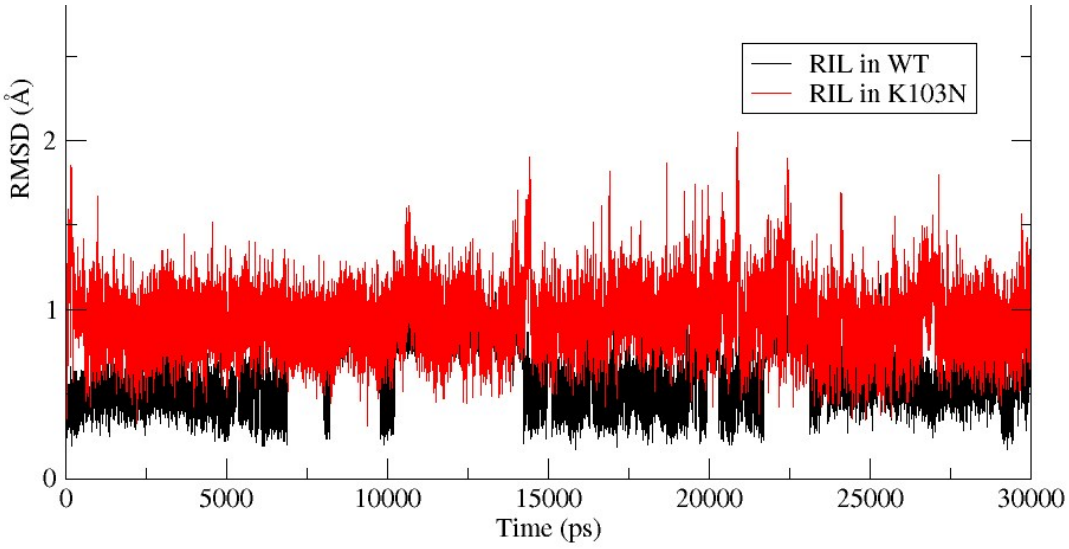


A B

Figure S2. RMSD plot of backbone atoms of HIV-1 RT over two 30 ns MD trajectories



A



B

Figure S3. RMSD of rilpivirine inside the NNIBP of WT RT and K103N RT over two MD run of 30ns

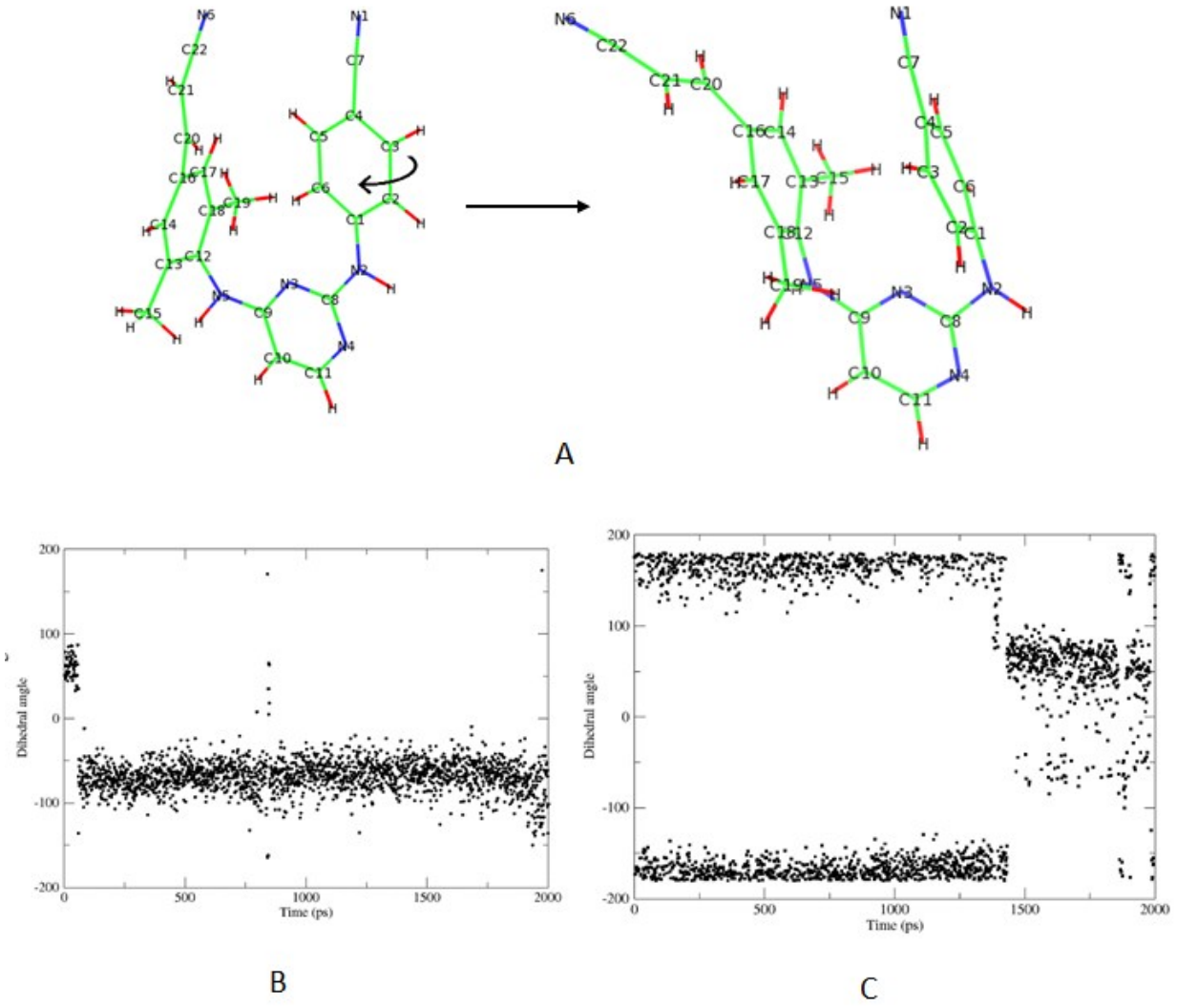


Figure S4. (A) rotation of benzonitrile ring in rilpivirine during the course of simulation (B) plot of rotation angle of rilpivirine in WT-RT (C) in K103N RT

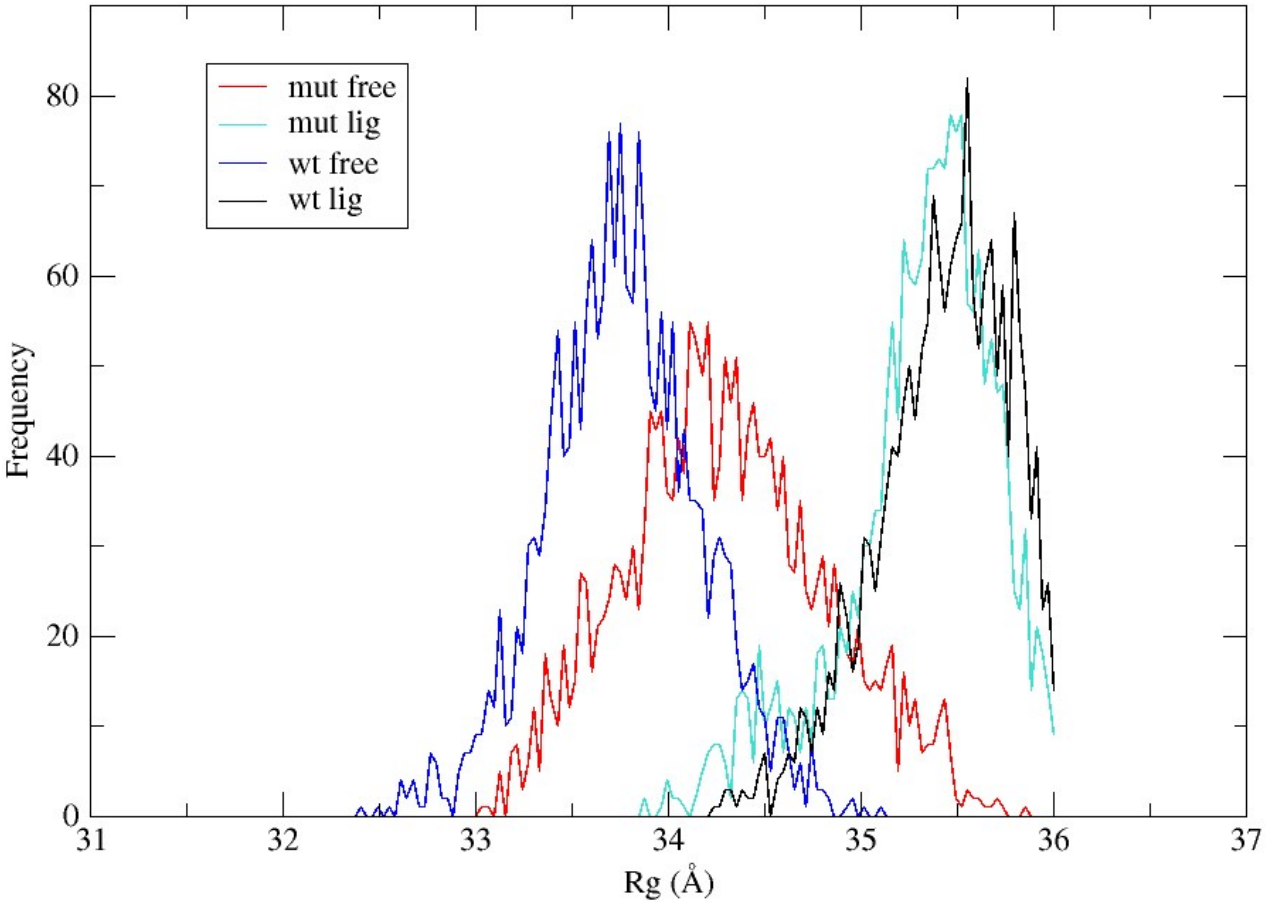


Figure S5. Frequency histogram of Rg (Å) calculated for HIV RT over 30 ns MD simulation.

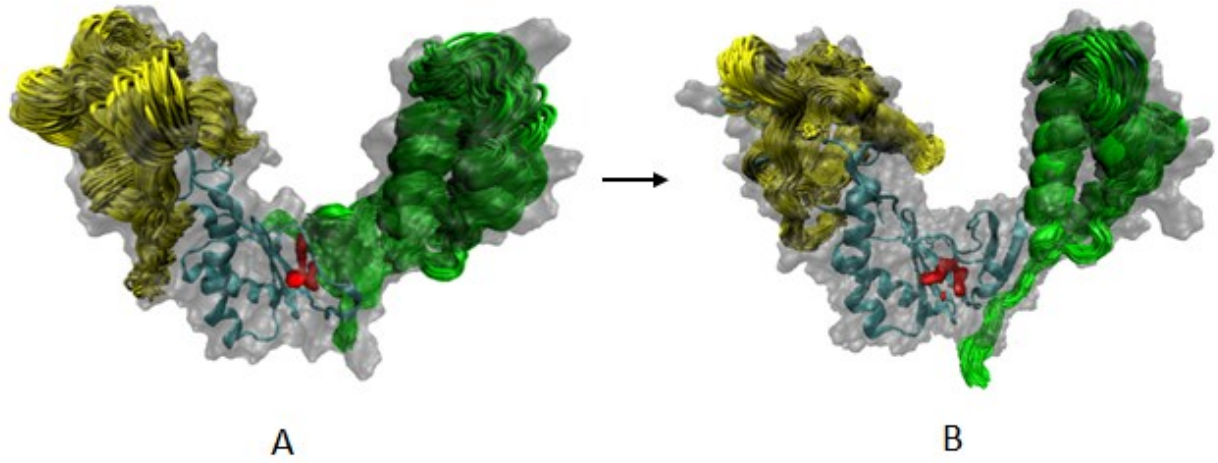


Figure S6. A view of NNRTI binding pocket (red surface) inside the ensemble of (A) WT HIV-1 RT and (B) K103N RT, along with transparent grey external molecular surface, thumb is shown in green and fingers in yellow. The figure is generated from 20 ns MD trajectory. Binding cavity surface is shown at isovalue of 8 in VMD. The unit of isovalue can be expressed as number of alpha sphere centers in an 8 $Å^3$ cube around each grid point per snapshot. The more a cavity is conserved (or dense) the higher this value.

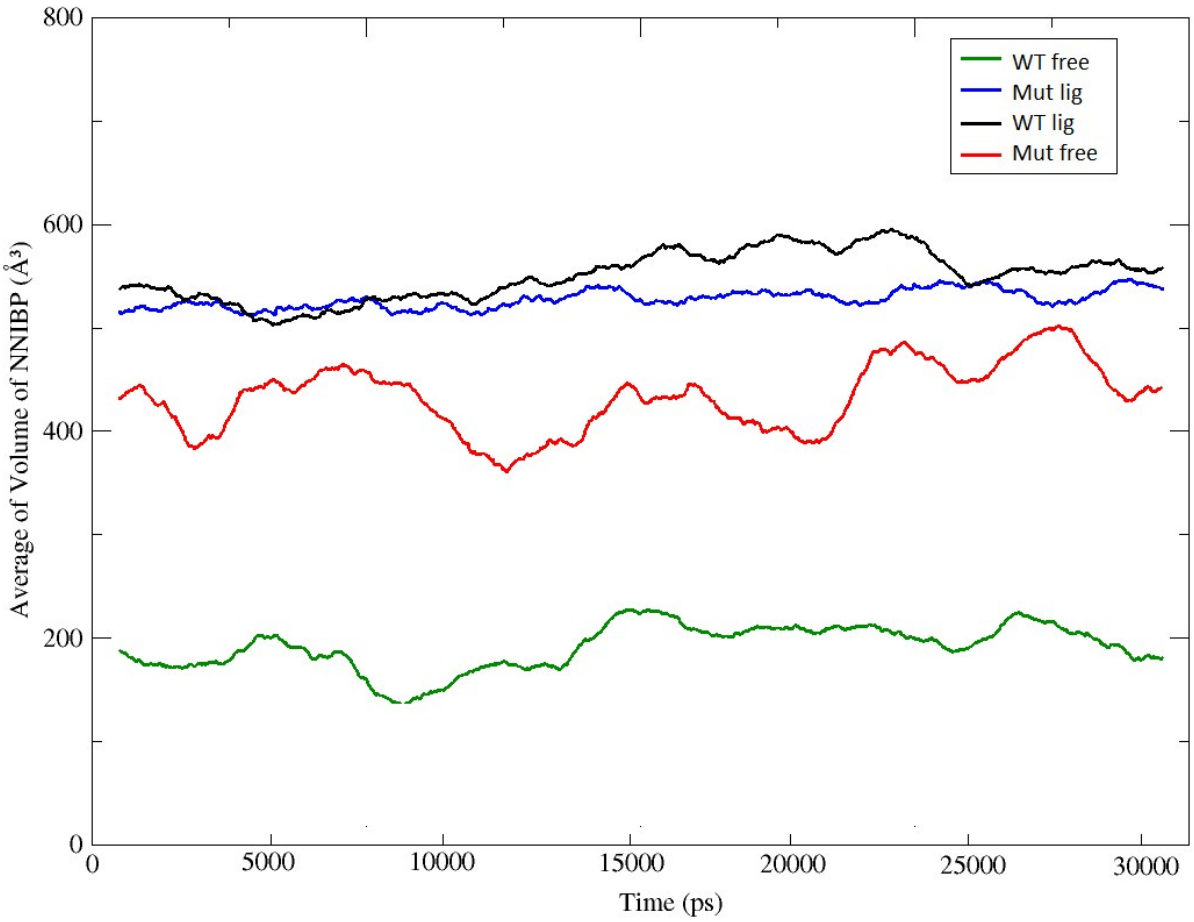


Figure S7. Plot of cumulative average of NNIBP pocket volume (Å) calculated from 30000 snapshots for RT, RT-RIL, K103N RT and K103N RT-RIL. Sliding window of 200 was used to calculate the running average and is plotted against time (ps).

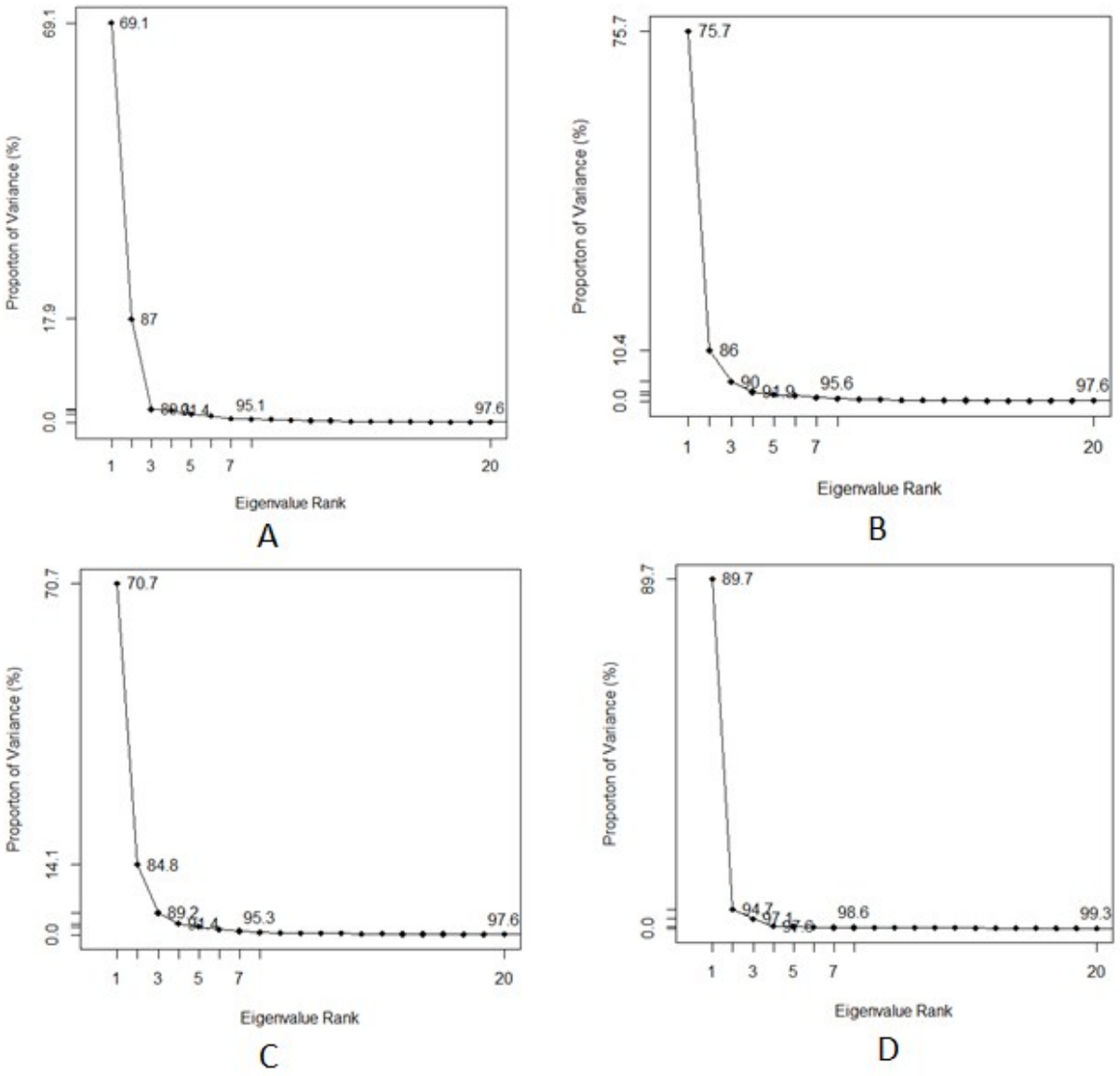
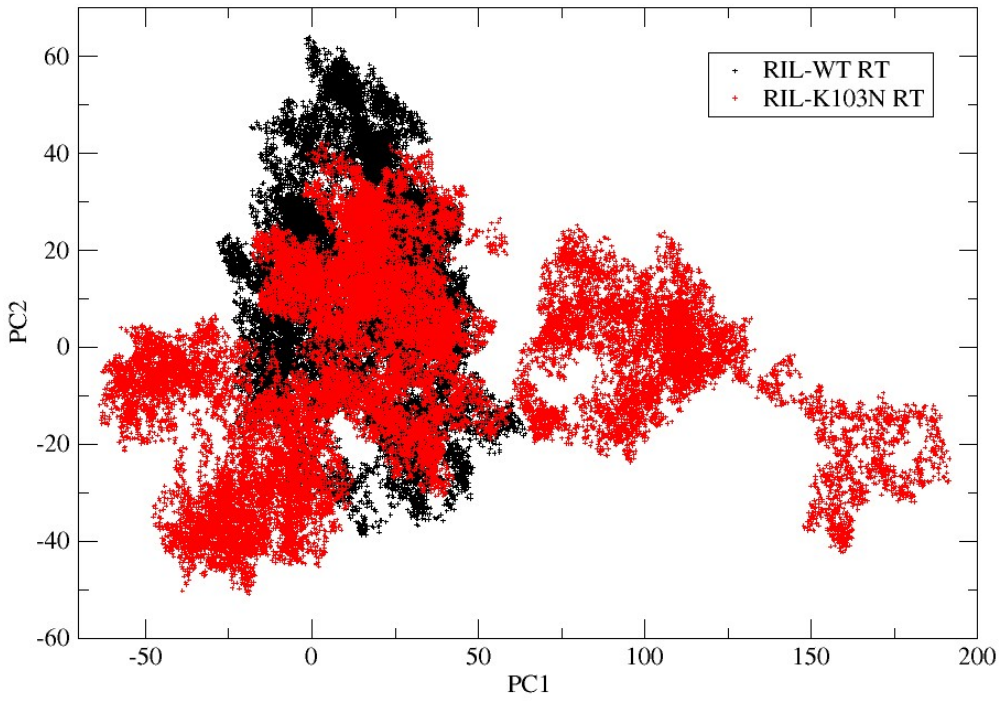
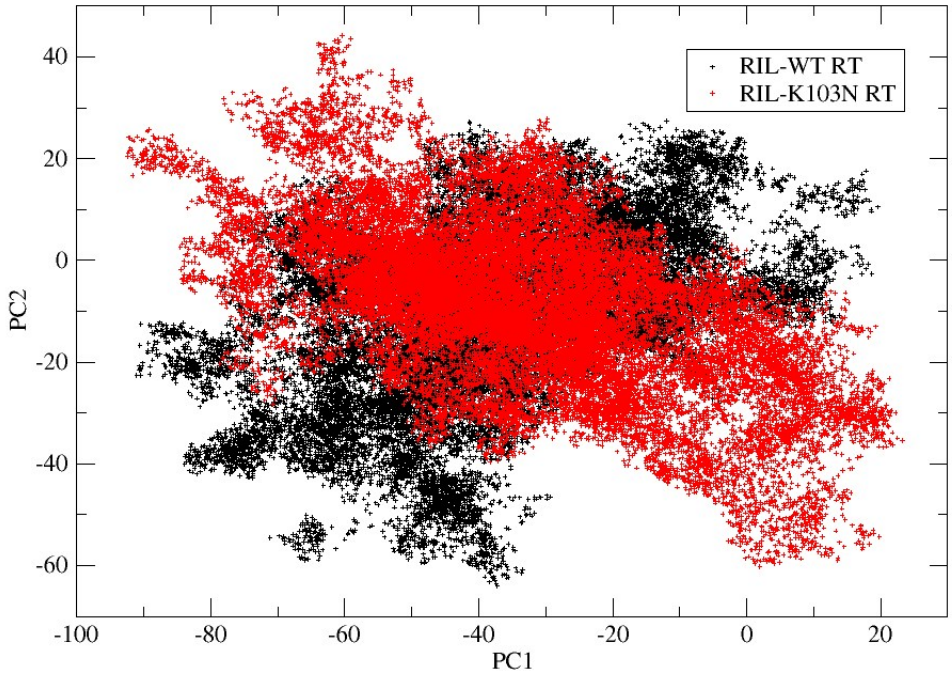


Figure S8. Proportion of variation explained by each PC. Values along the points in plot are cumulative variance**.** (A) K103N free HIV-1 RT, (B) WT free (C) WT-RIL (D) K103N-RIL



(A)



(B)

Figure S9. Projection of MD trajectories on the first two PCs (**A**) MD simulation 1 (**B**) MD simulation 2