CD4-dependent and CD4-independent HIV-1 gp120 molecular mechanisms

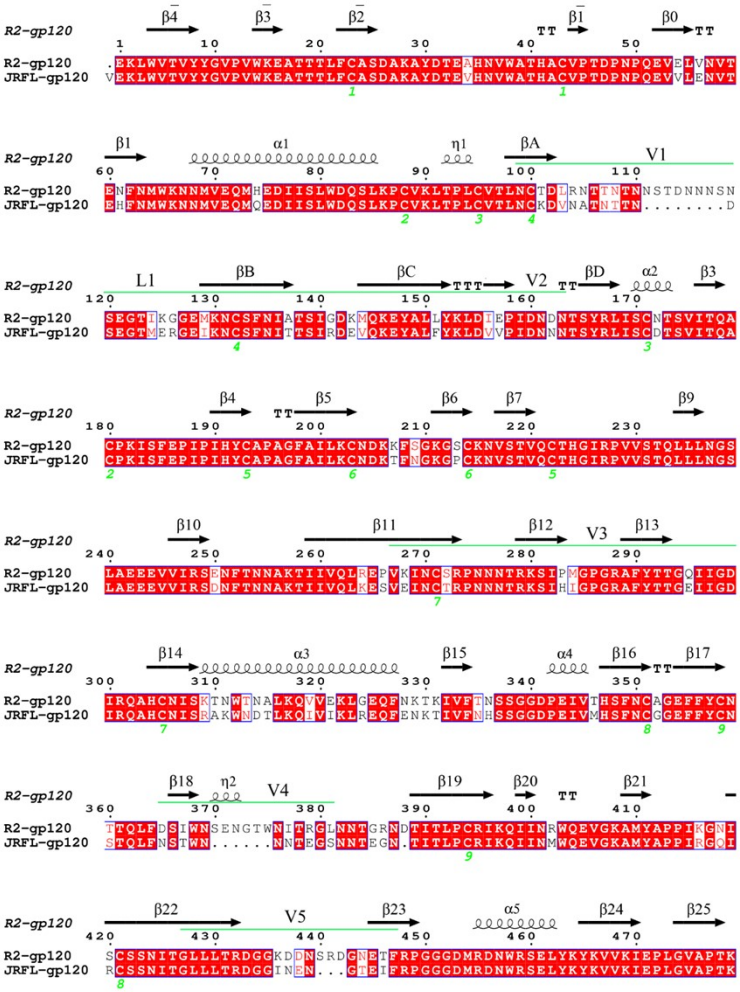

Figure S1. Target and template sequence alignments. R2 gp120 was used as the template sequence with known crystal structure. Residues are numbered according to the template sequence. Conserved residues are shaded in light red. Regular secondary structural elements are numbered according to the HXBc2 crystal structures (PDB IDs:1G9M and 3JWD), with black arrows and black spirals representing β-strands and α-helices (or 3/10 helices), respectively.

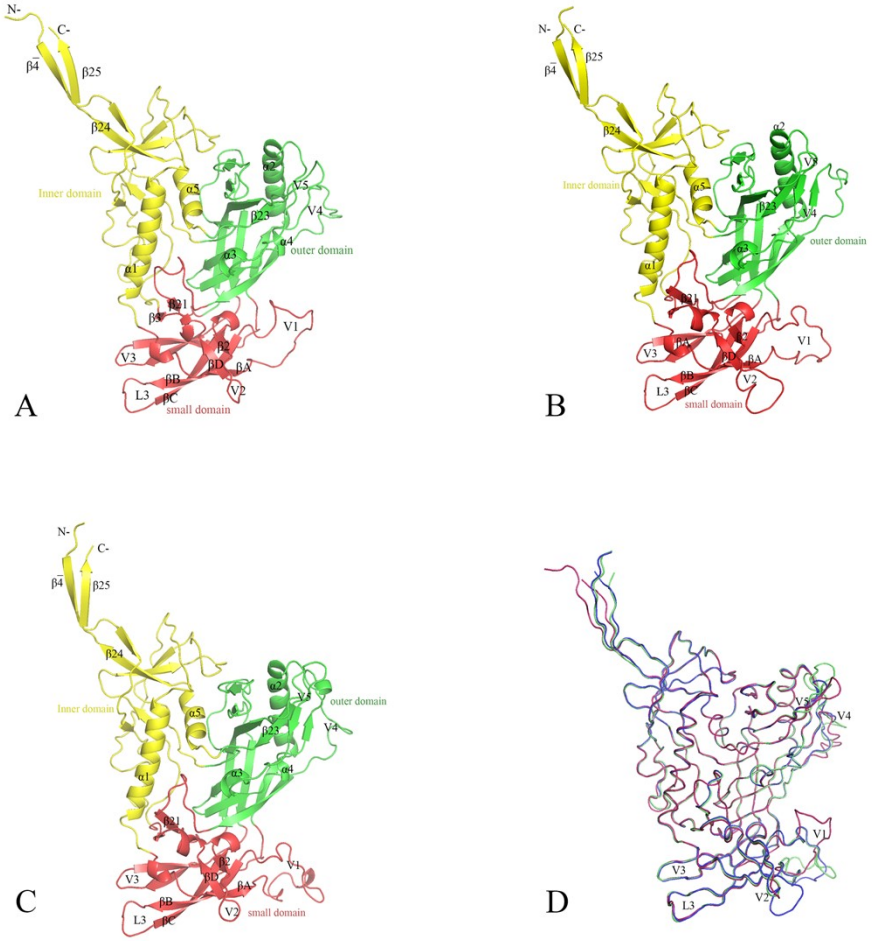

Figure S2. Structural models of the two near full-length gp120s in the unliganded state. These models served as the simulation system starting structures. (A) JR-FL gp120 model ribbon representation. (B) H061.14 gp120 model ribbon representation. (C) R2 gp120 model ribbon representation. (C) Backbone superposition of R2 gp120 (green), H061.14 gp120(blue) and JR-FL gp120 (red) models.

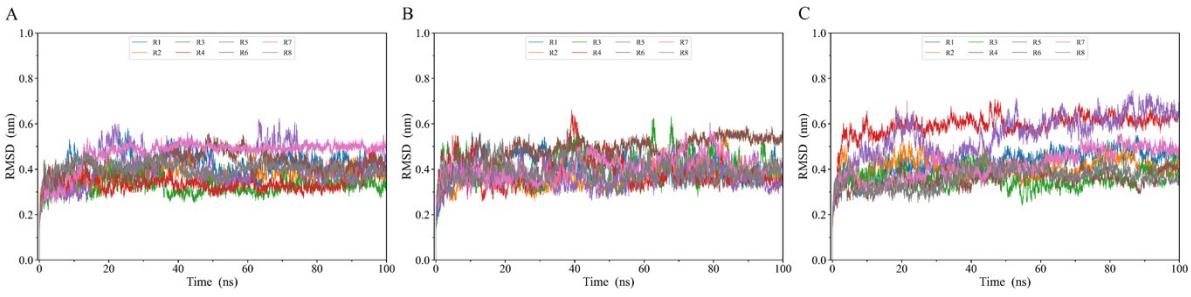

Figure S3. Temporal evolution of gp120 backbone RMSD values for (A) H061.14 gp120, (B) JR-FL gp120 and (C) R2 gp120 relative to their respective starting structures calculated from 8 MD simulation replicas (R1 to R8).

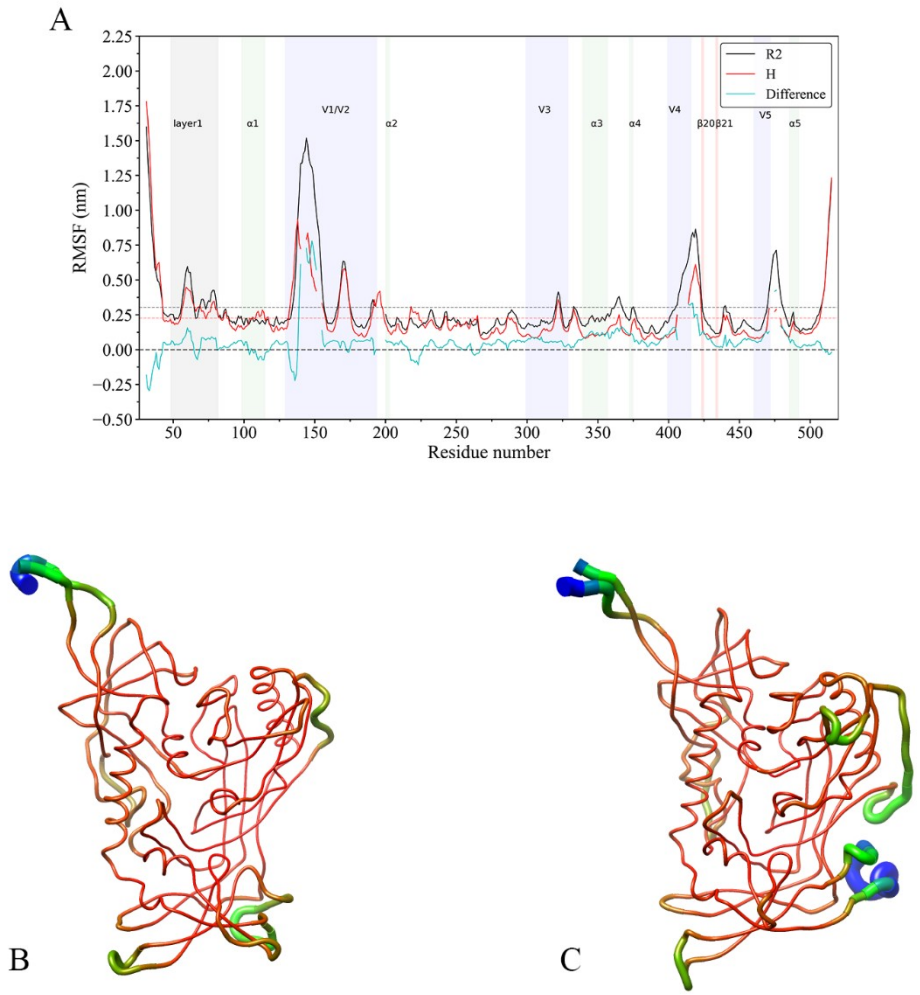

Figure S4. H061.14 gp120 and R2 gp120 structural flexibility comparison. (A) Per-residue average backbone RMSF profiles calculated from R2 gp120 (black line) and H061.14 gp120 (red line) MD trajectories. (B) H061.14 gp120 and (C) R2 gp120 3D backbone representation structures mapped with per-residue average backbone RMSF values. The backbone color ranges from red to blue, which correspond to line thickness and denote backbone RMSF values varying from lowest to highest.

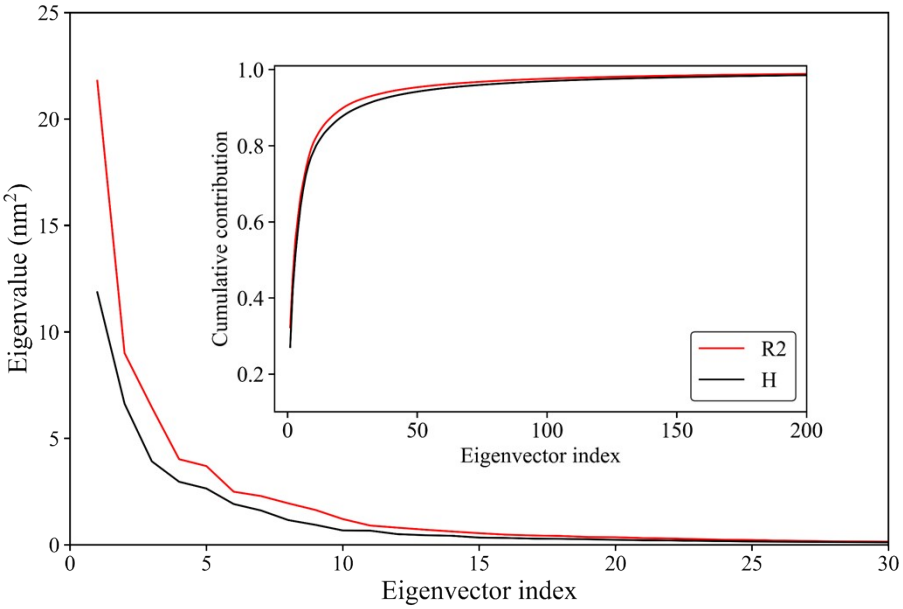

Figure S5. Eigenvalues of the first 30 eigenvectors (main plot) and cumulative contribution of all eigenvectors to the total mean square fluctuations (inset plot) for H061.14 gp120 (black line) and R2 gp120 (red line)

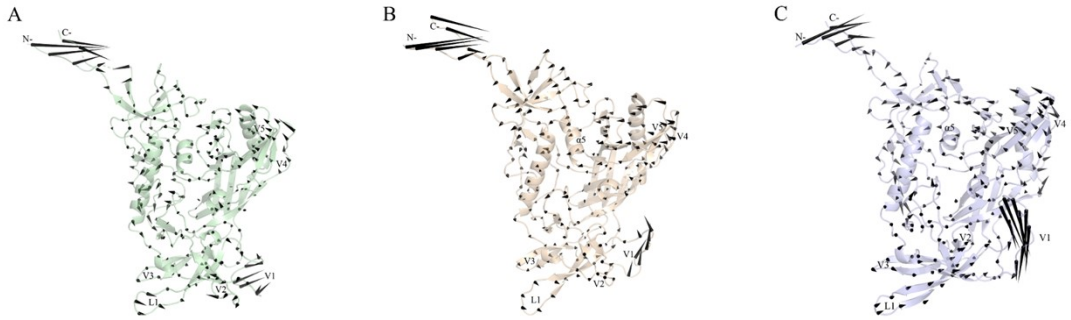

Figure S6. Porcupine plots showing the three gp120 structural models' largest-amplitude collective motions. (A) H061.14 gp120 collective motion patterns, along the eigenvector 1direction. (B) JR-FL gp120 collective motion patterns, along the eigenvector 1direction. (C) R2 gp120 collective motion patterns, along the eigenvector 1direction. The direction and length of the cones drawn on the C_α atoms represent the atom's fluctuation direction and amplitude, respectively.

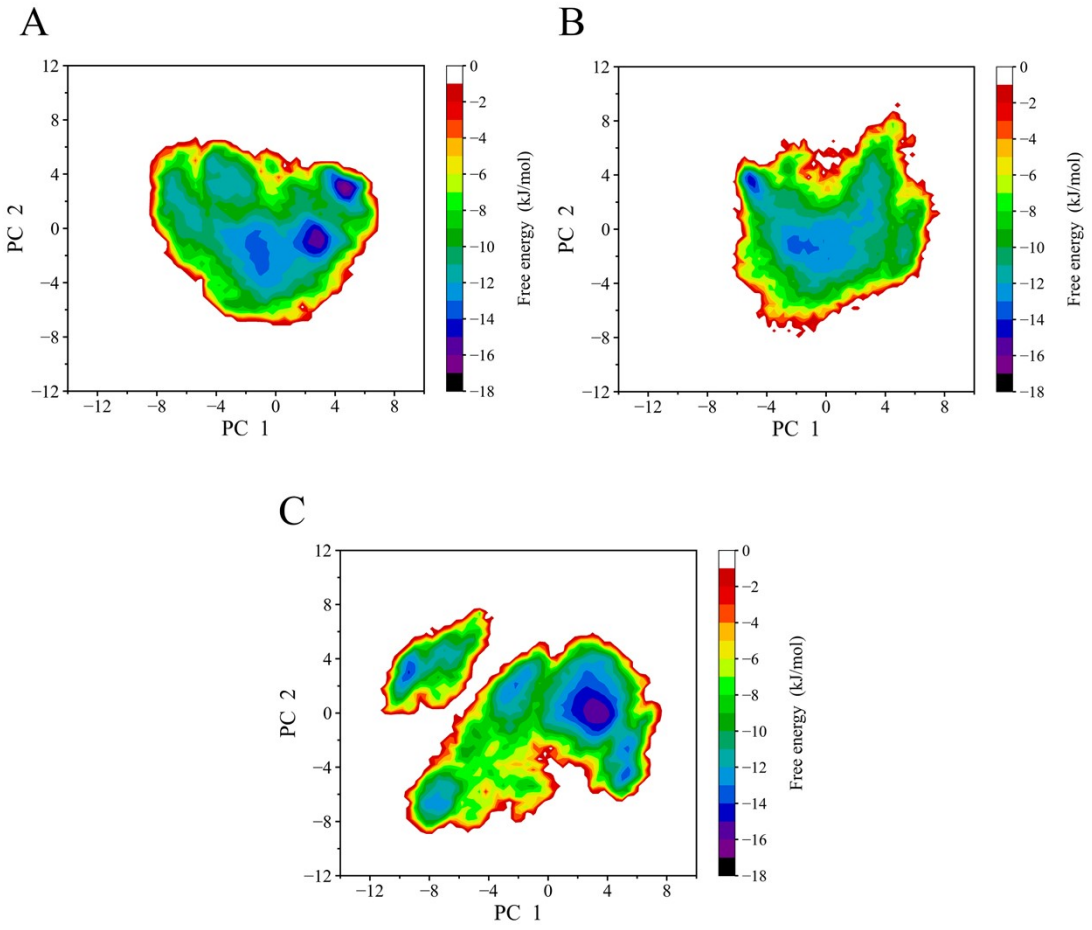

Figure S7. Constructed free energy landscapes (FELs) of (A) H061.14 gp120, (B) JR-FL gp120 and (C) R2 gp120 FEL using eigenvector 1 and 2 projections as the reaction coordinates. The color bar denotes the relative free-energy level in kJ mol-1.

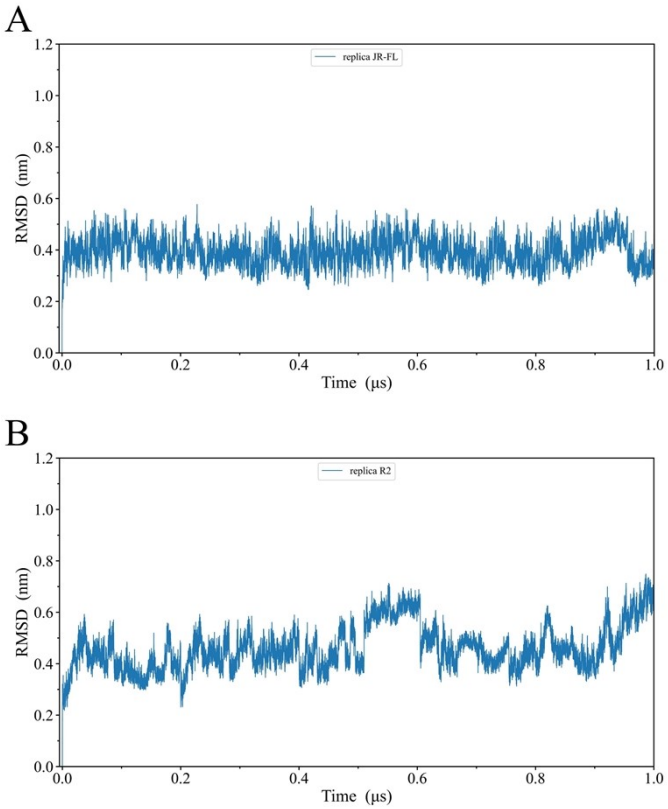

Figure S8. Time evolutions of the backbone RMSD values of the two gp120 forms with respect to their respective starting structures calculated from the MD simulation. (A) JR-FL gp120, (B) R2 gp120.

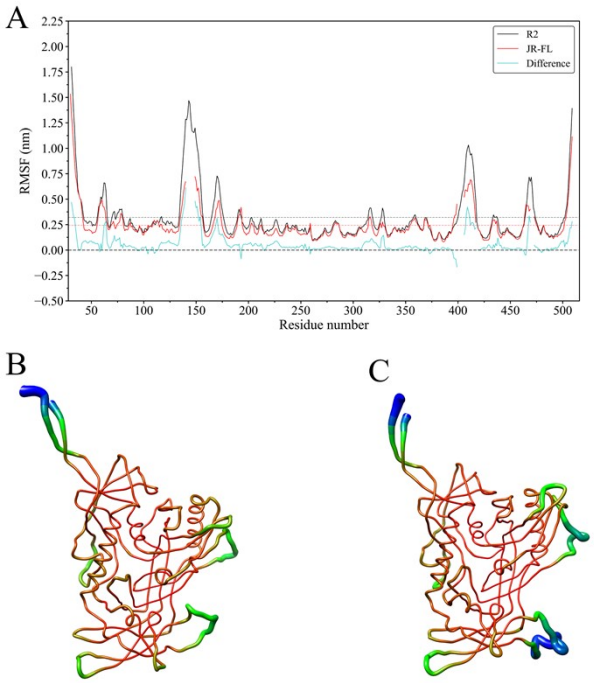

Figure S9. JR-FL gp120 and R2 gp120 structural flexibility comparison. (A) Per-residue average backbone RMSF profiles calculated from R2 gp120 (black line) and JR-FL gp120 (red line) MD trajectories. (B) JR-FL gp120 and (C) R2 gp120 3D backbone representation structures mapped with per-residue average backbone RMSF values. The backbone color ranges from red to blue, which correspond to line thickness and denote backbone RMSF values varying from lowest to highest.

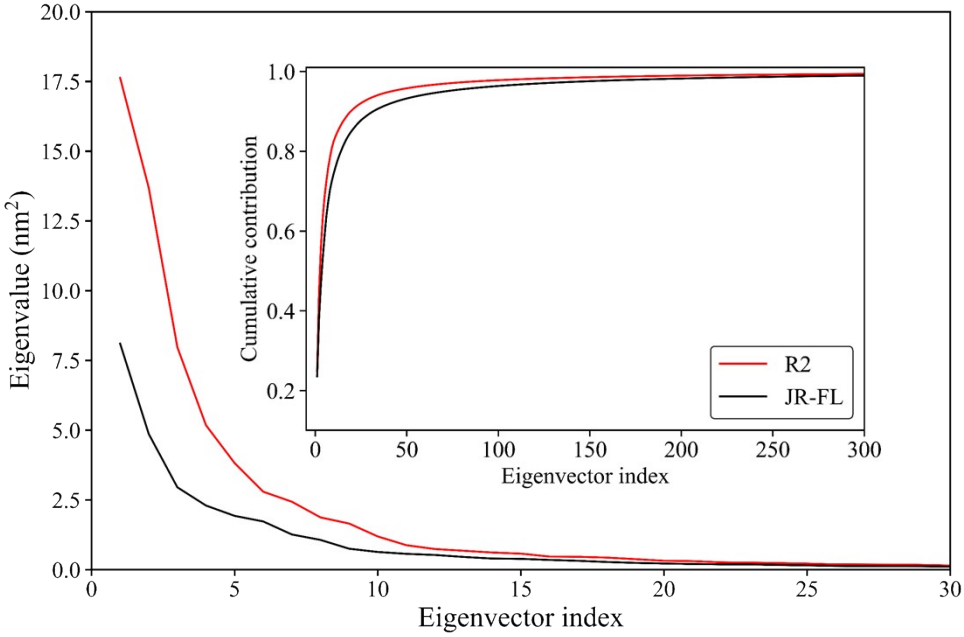

Figure S10. Eigenvalues of the first 30 eigenvectors (main plot) and cumulative contribution of all eigenvectors to the total mean square fluctuations (inset plot) for JR-FL gp120 (black line) and R2 gp120 (red line).

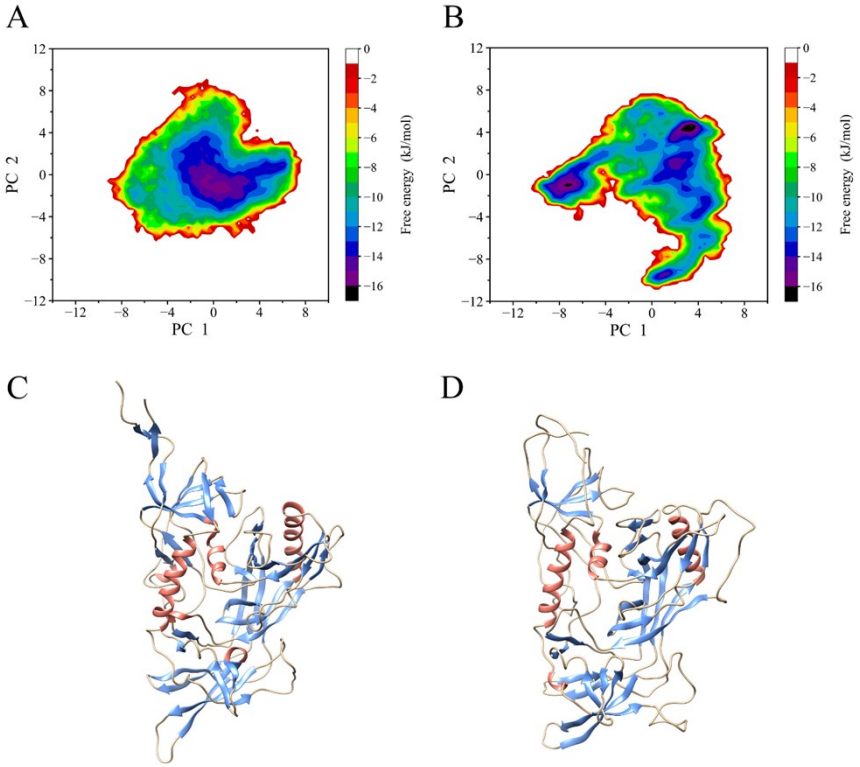

Figure S11. Constructed free energy landscapes (FELs) of the two forms of gp120 using projections of eigenvectors 1 and 2 as the reaction coordinates, and the representative structure of local energy minimum structure on the energy surface. (A) FEL of the JR-FL gp120. (B) FEL of the R2 gp120. (C) The representative structure of the minimum local energy structure on the JR-FL gp120 energy surface. (D) The representative structure of the minimum local energy structure on the R2 gp120 energy surface. The color bar denotes

the relative free energy level in kJ mol^{-1}.