Supplementary Information

Mechanistic insights of key host proteins and potential repurposed inhibitors regulating SARS-CoV-2 pathway

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Table S1: Table shows the interacting residues of target protein that remain in contact with the respective drug molecules for more than 75% of the simulation time.

| Target  | PDB ID | Drug        | Interacting Residues                                                                 |
|---------|--------|-------------|--------------------------------------------------------------------------------------|
| eIF4E2  | 2JGB   | Nafamostat  | ARG23, THR29, SER30, SER31, TYR34, ASP68, TRP80, LYS90, VAL126, SER128, ILE135, SER137, PRO180, LEU189 |
| eIF4E2  | 2JGB   | Camostat    | THR29, SER30, SER31, TRP80, ILE177, MET179, PRO180                                  |
| eIF4E2  | 2JGB   | Zotatifin   | PRO28, THR29, SER31, TRP80, SER176, ILE177, MET179, PRO180, GLU186, ARG187, LEU188, PHE190 |
| HDAC2   | 4LY1   | Nafamostat  | TYR29, MET35, ARG39, ILE40, ALA141, LEU144, HIS145, GLY154, PHE155, CYS156, HIS183, GLY305, TYR308 |
| HDAC2   | 4LY1   | Valproic Acid | TYR29, MET35, PRO37, ARG39, ILE40, PHE114, ALA141, GLY142, GLY143, LEU144, CYS156, GLY305 |
| CSK22   | 6HMB   | Silmitasertib | LEU46, GLY47, ARG48, GLY49, VAL54, VAL66, LYS69, ILE96, PHE114, ILE117, ASN119, MET164, ILE175, ASP176 |
**Figure S1:** eIF4E target and Zotatifin ligand interaction, hydrophobic interactions are shown in green and pi stacking in purple.
Figure S2: The minimum distance plot of the protein residues with that of the ligand heavy atoms. For six systems we show the distance plots for 10 independent runs for (a) HDAC2-Nafamostat, (b) eIF4E2-Nafamostat, (c) eIF4E2-Camostat, (d) CSK22-Silmitasertib, (e) eIF4E2-Zotatifin, (f) HDAC2-Valproic Acid over the metadynamics trajectories.
Figure S3: The minimum distance plot of the protein residues with that of the ligand heavy atoms with minimum distance < 0.2 nm for at least one independent run over the metadynamics trajectories for (a) HDAC2-Nafamostat, (b) eIF4E2-Nafamostat, (c) eIF4E2-Camostat, (d) CSK22-Silmitasertib, (e) eIF4E2-Zotatifin, (f) HDAC2-Valproic Acid.
Figure S4: “Normalized probability distribution” with “distance” for each of those protein residues having the minimum distance < 0.2 nm for at least in one of the independent simulations for HDAC2-Nafamostat.
Figure S5: “Normalized probability distribution” with “distance” for each of those protein residues having the minimum distance < 0.2 nm for at least in one of the independent simulations for eIF4E2-Nafamostat.
Figure S6: “Normalized probability distribution” with “distance” for each of those protein residues having the minimum distance < 0.2 nm for at least in one of the independent simulations for eIF4E2-Camostat.
Figure S7: “Normalized probability distribution” with “distance” for each of those protein residues having the minimum distance < 0.2 nm for at least in one of the independent simulations for CSK22–Silmitasertib.
Figure S8: “Normalized probability distribution” with “distance” for each of those protein residues having the minimum distance < 0.2 nm for at least one of the independent simulations for eIF4E2-Zotatifin.
Figure S9: “Normalized probability distribution” with “distance” for each of those protein residues having the minimum distance < 0.2 nm for at least in one of the independent simulations for HDAC2-Valproic Acid.