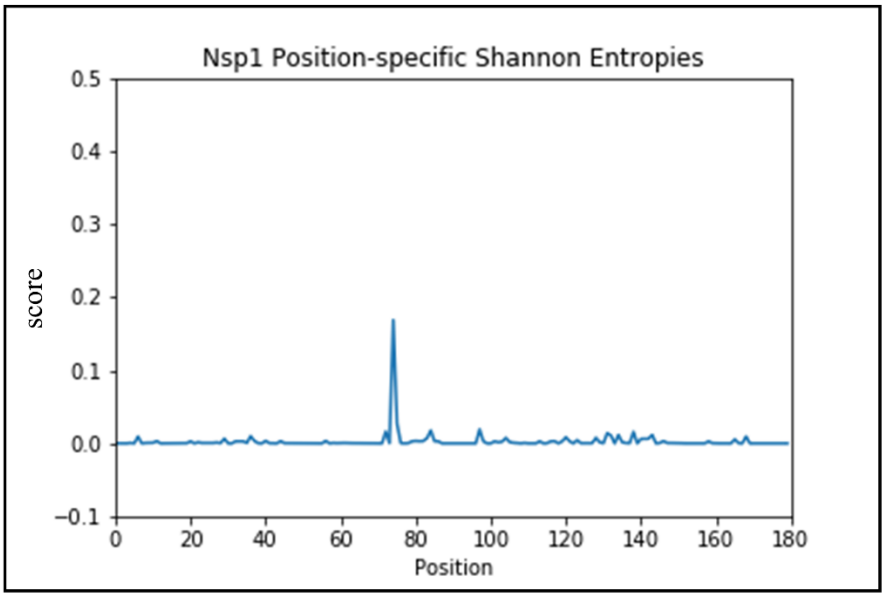
AA_position	consensus	Alignment Details
135	Ser	Asn=2,Ser=146
136	Tyr	Del=2,Tyr=146

a).

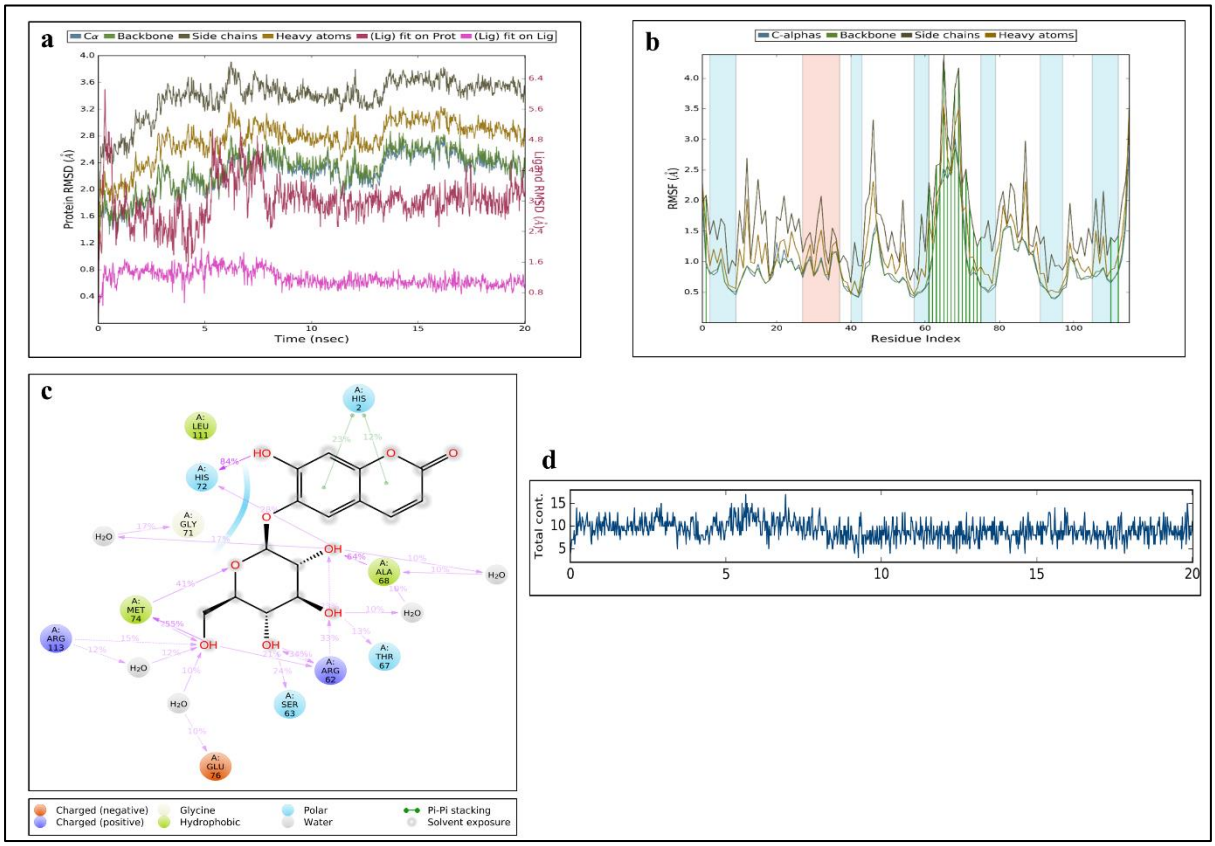
AA_position	consensus	Alignment Details
38	Val	Phe=2,Val=444
135	Ser	Asn=2,Ser=444
136	Tyr	Del=2,Tyr=444
147	Asp	Asp=444,Glu=2
169	Val	Ala=8,Val=438

b).

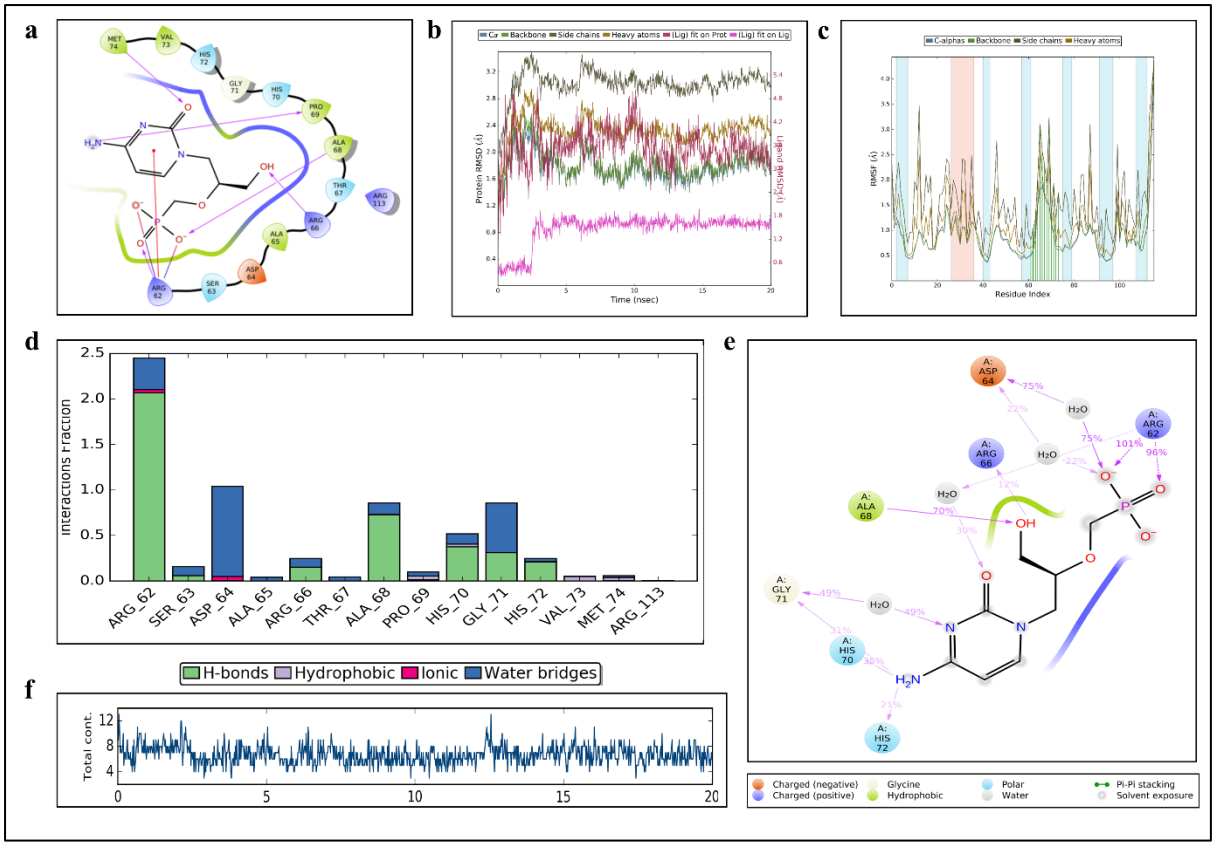


c).

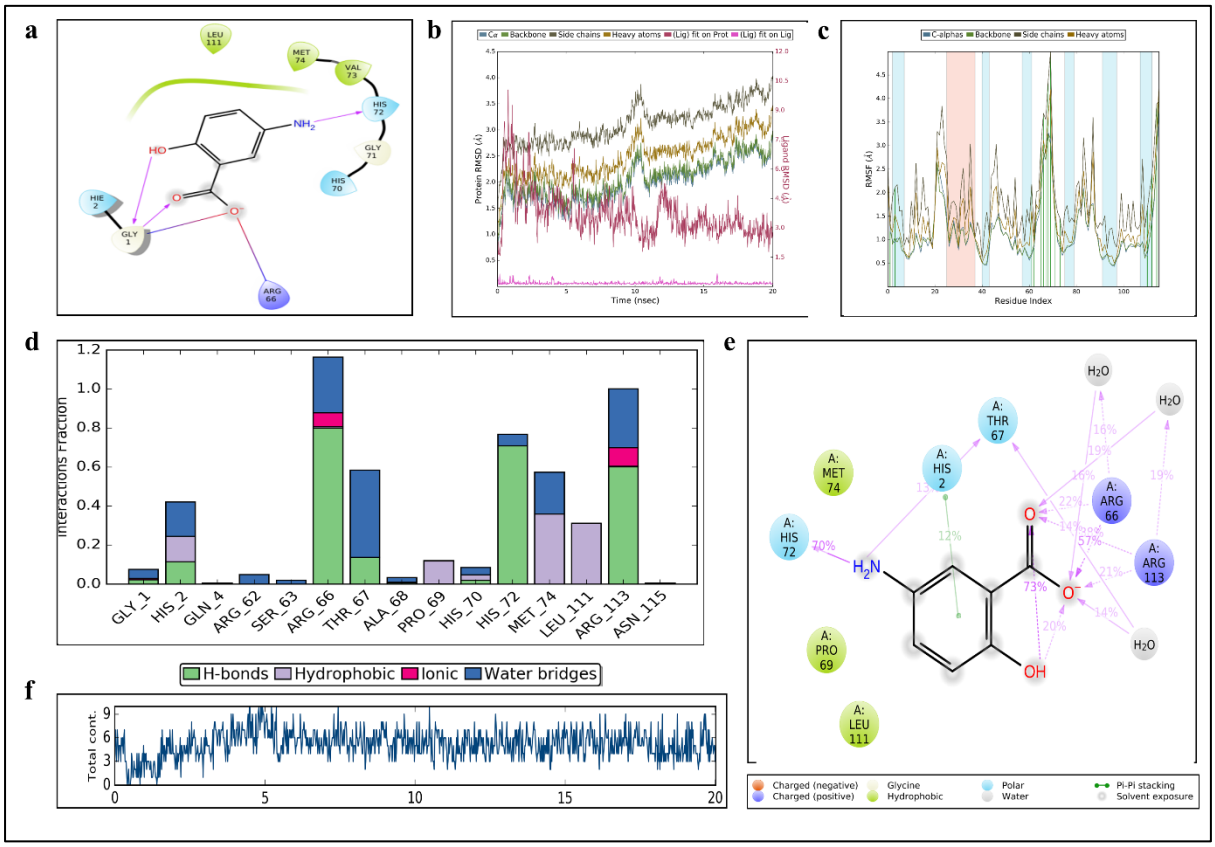
Supplementary Figure 1: Mutation analysis of Nsp1 protein sequences. **a)** Table showing Mutated regions in Indian strains till 15 May 2020 **b)** Table showing Mutated regions in Indian strains till 14 June 2020 **c)** Shannon entropy per residue



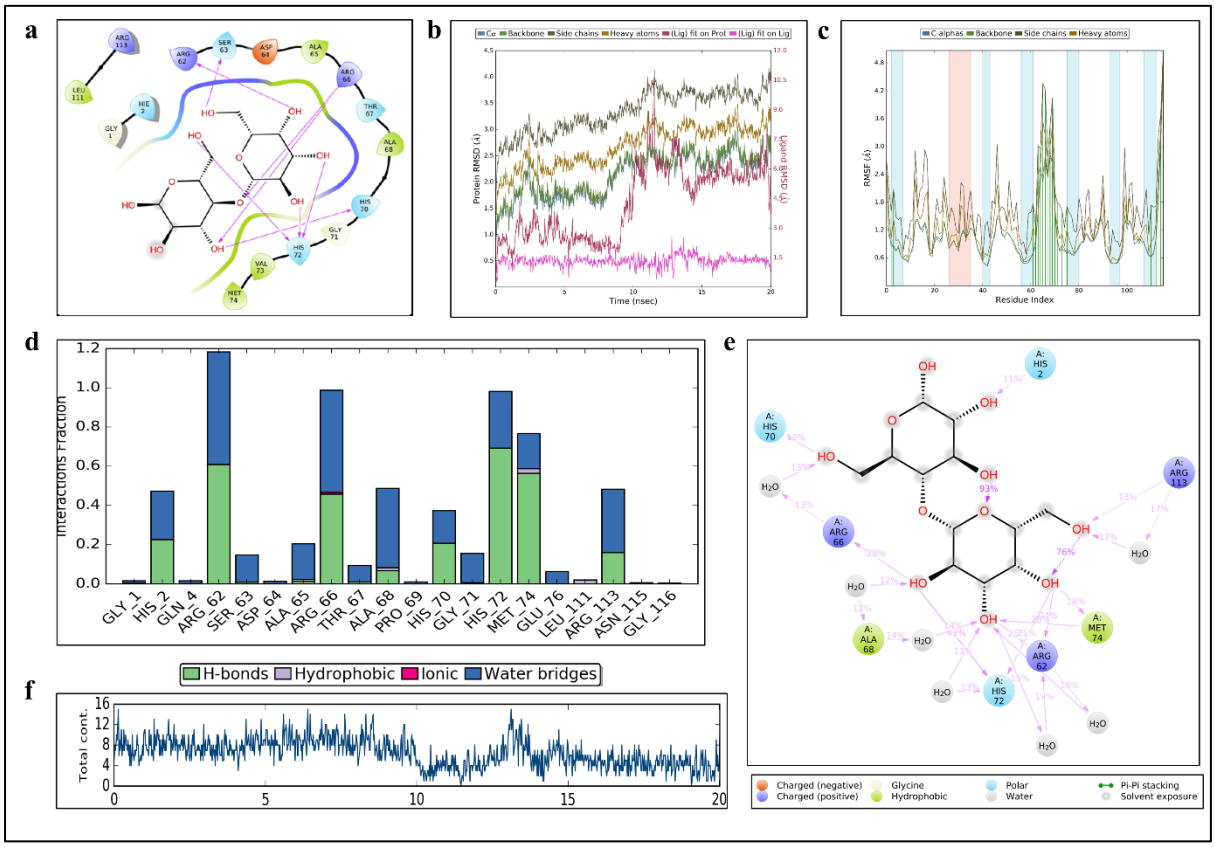
Supplementary Figure 2: MD simulation results for Nsp1-deep-Esculin. **a.** RMSD plot of Nsp1 and Esculin. **b.** Nsp1-RMSF plot **c.** Interaction of Esculin atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **d.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Esculin over the course of MD simulation.



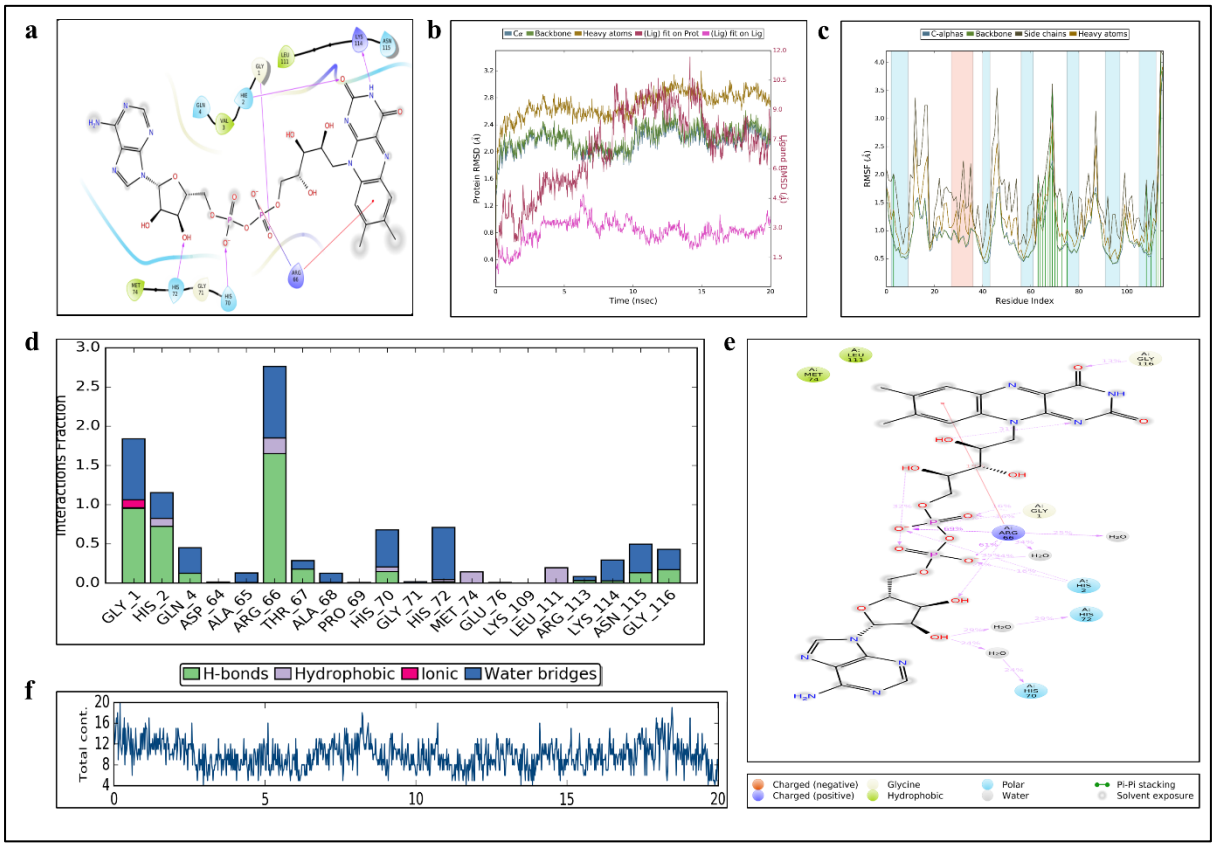
Supplementary Figure 3: Docking and MD simulation results for Nsp1-deep-Cidofovir. **a.** Cidofovir-Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Cidofovir over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Cidofovir) **c.** RMSD plot of Nsp1 and Cidofovir. **d.** Nsp1-RMSF plot **e.** Interaction of Cidofovir atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Cidofovir over the course of MD simulation



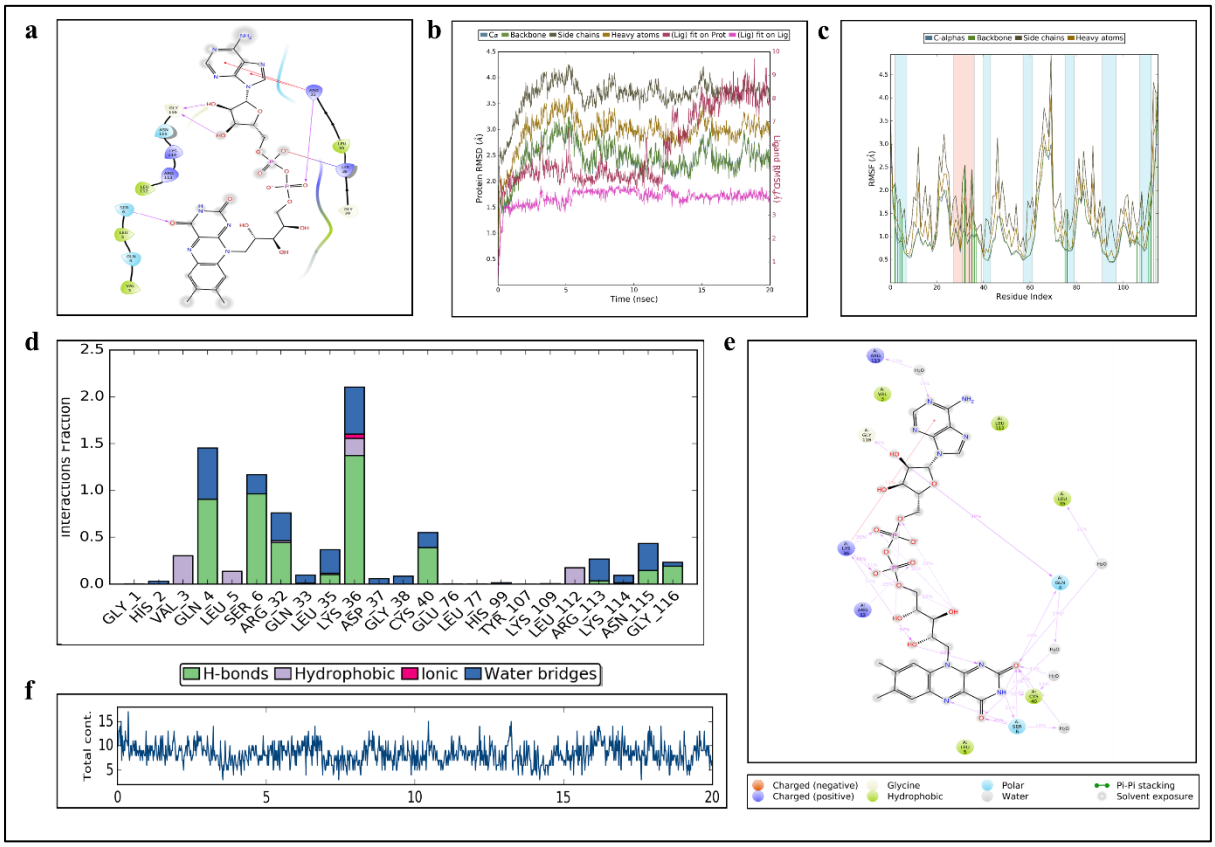
Supplementary Figure 4: Docking and MD simulation results for Nsp1-deep-Mesalazine. **a.** Mesalazine -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Mesalazine over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Mesalazine) **c.** RMSD plot of Nsp1 and Mesalazine. **d.** Nsp1-RMSF plot **e.** Interaction of Mesalazine atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Mesalazine over the course of MD simulation



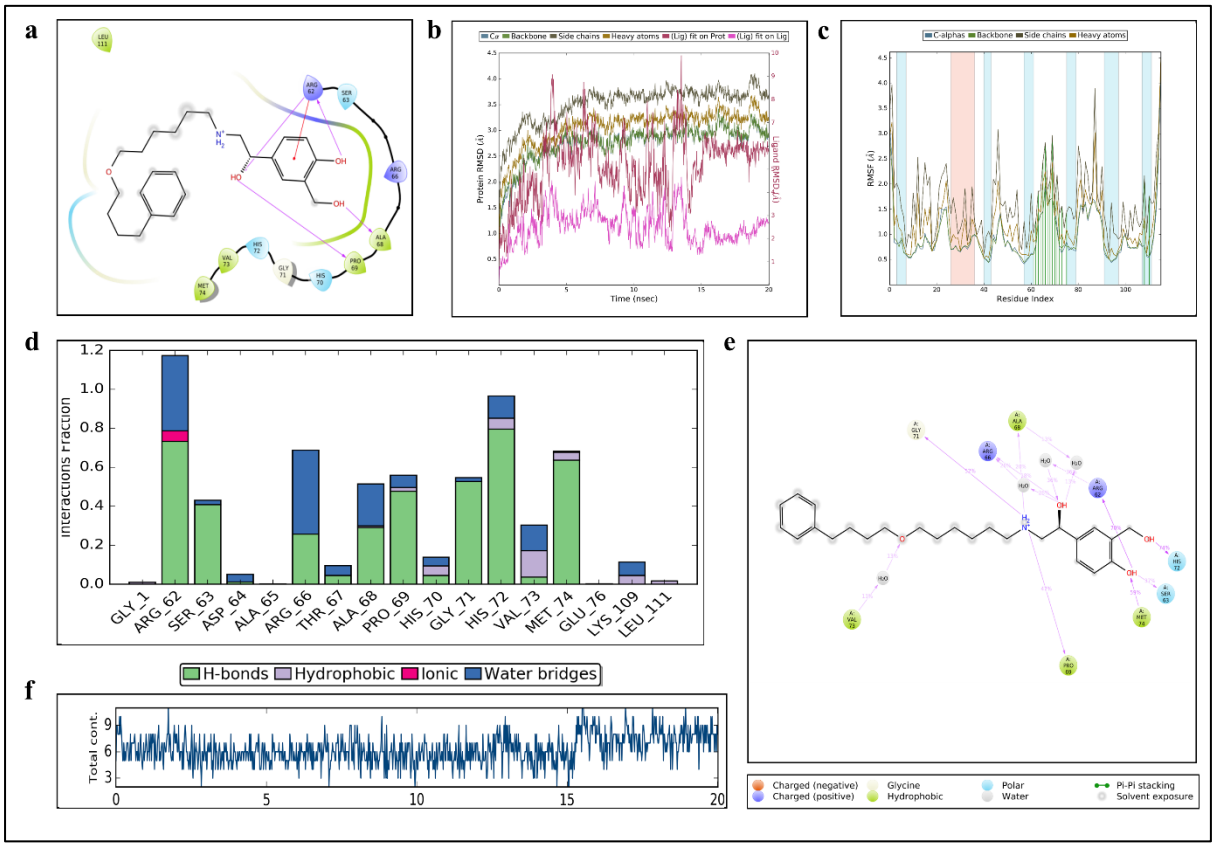
Supplementary Figure 5: Docking and MD simulation results for Nsp1-deep-Lactose. **a.** Lactose - Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Lactose over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Lactose) **c.** RMSD plot of Nsp1 and Lactose. **d.** Nsp1-RMSF plot **e.** Interaction of Lactose atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Lactose over the course of MD simulation



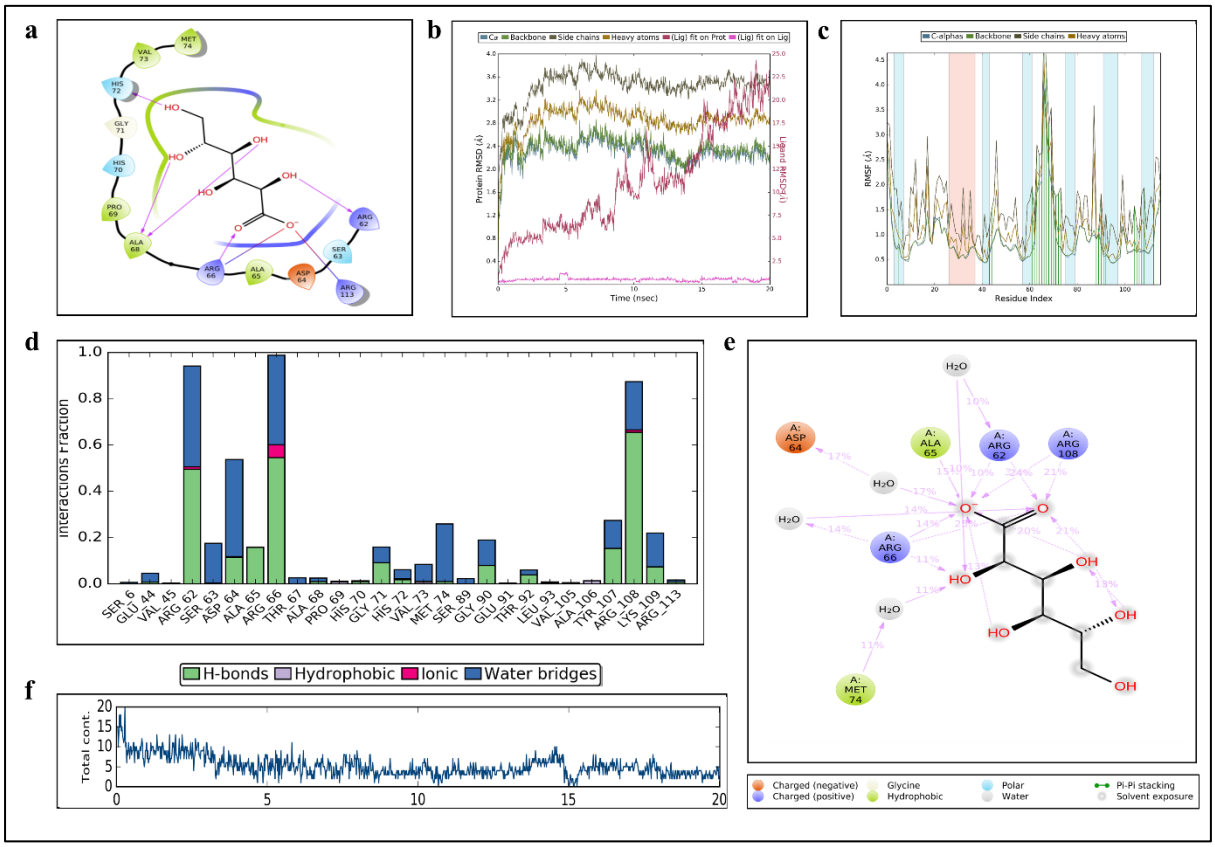
Supplementary Figure 6: Docking and MD simulation results for Nsp1-deep-FAD. **a.** FAD -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with FAD over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (FAD) **c.** RMSD plot of Nsp1 and FAD. **d.** Nsp1-RMSF plot **e.** Interaction of FAD atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and FAD over the course of MD simulation



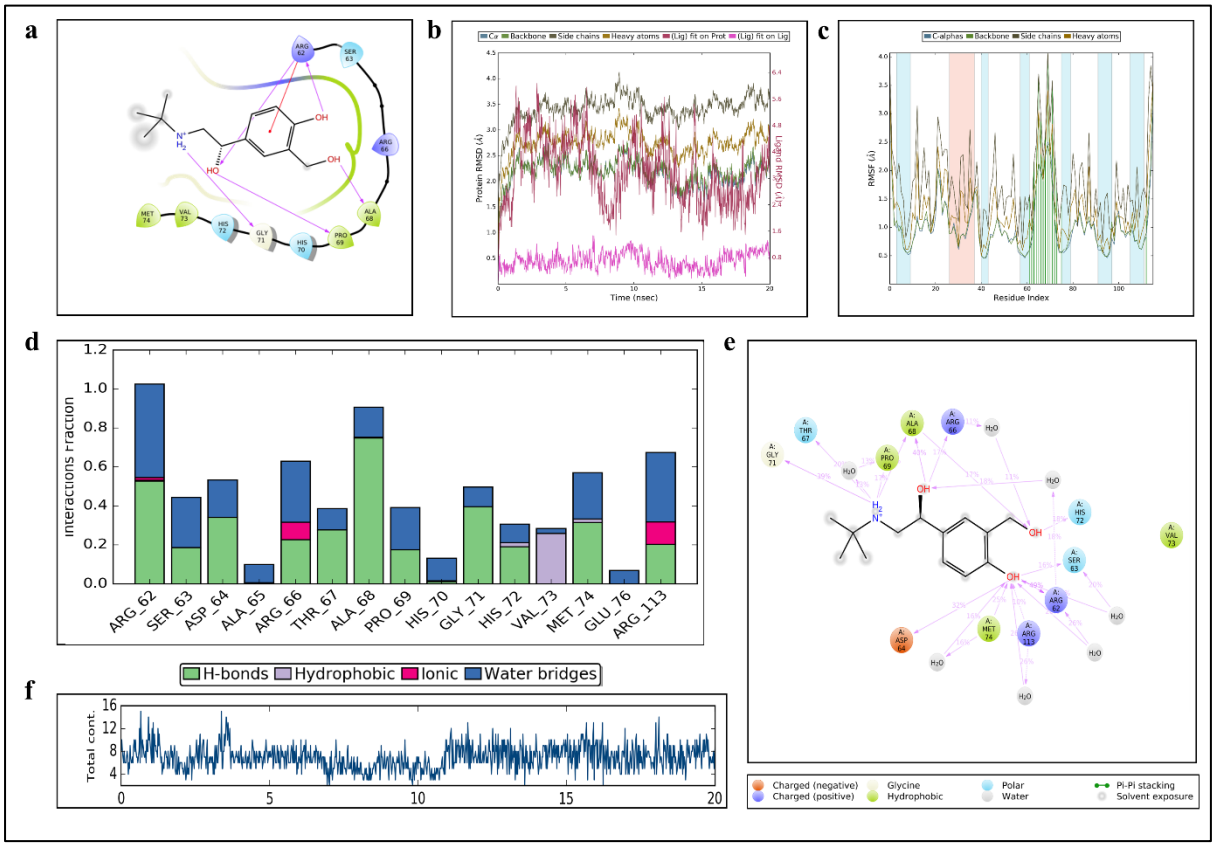
Supplementary Figure 7: Docking and MD simulation results for Nsp1-shallow-FAD. **a.** FAD -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with FAD over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (FAD) **c.** RMSD plot of Nsp1 and FAD. **d.** Nsp1-RMSF plot **e.** Interaction of FAD atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and FAD over the course of MD simulation



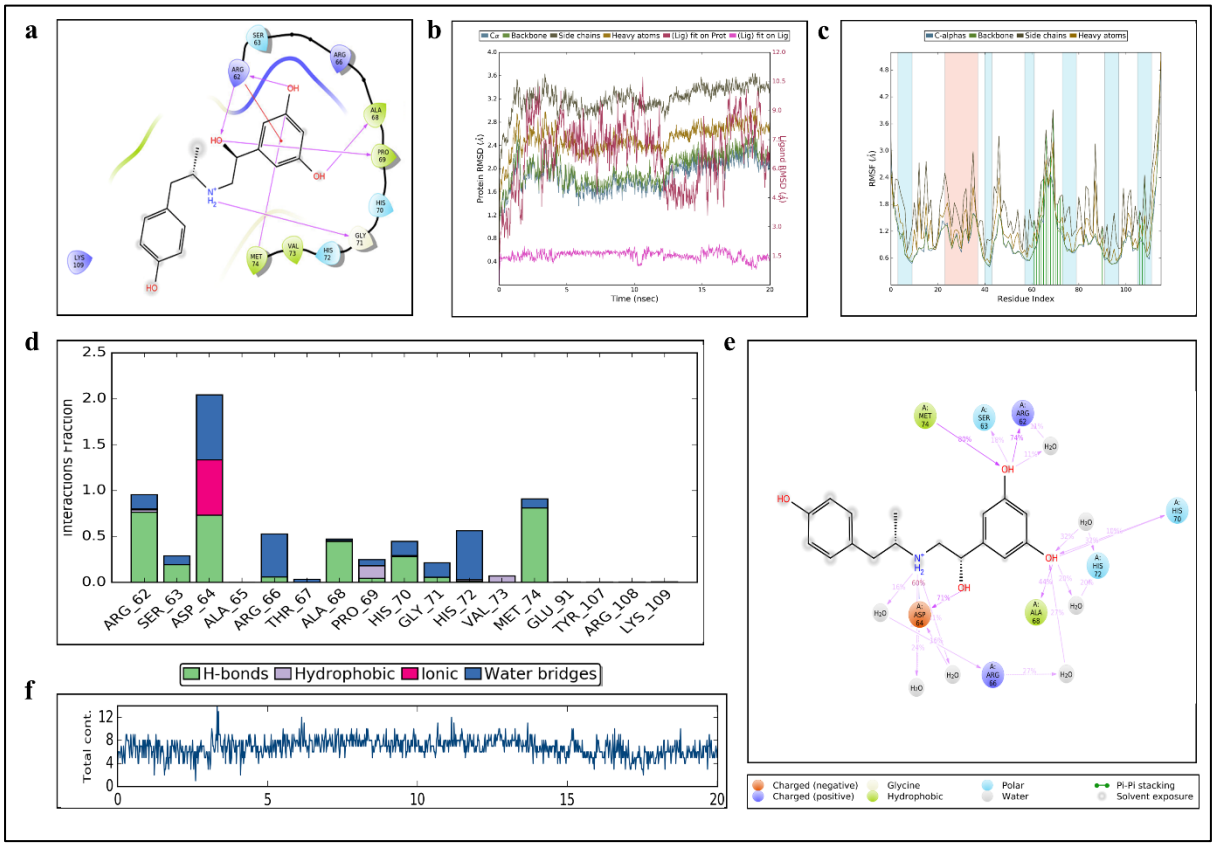
Supplementary Figure 8: Docking and MD simulation results for Nsp1-deep-Salmeterol. **a.** Salmeterol -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Salmeterol over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Salmeterol) **c.** RMSD plot of Nsp1 and Salmeterol. **d.** Nsp1-RMSF plot **e.** Interaction of Salmeterol atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Salmeterol over the course of MD simulation



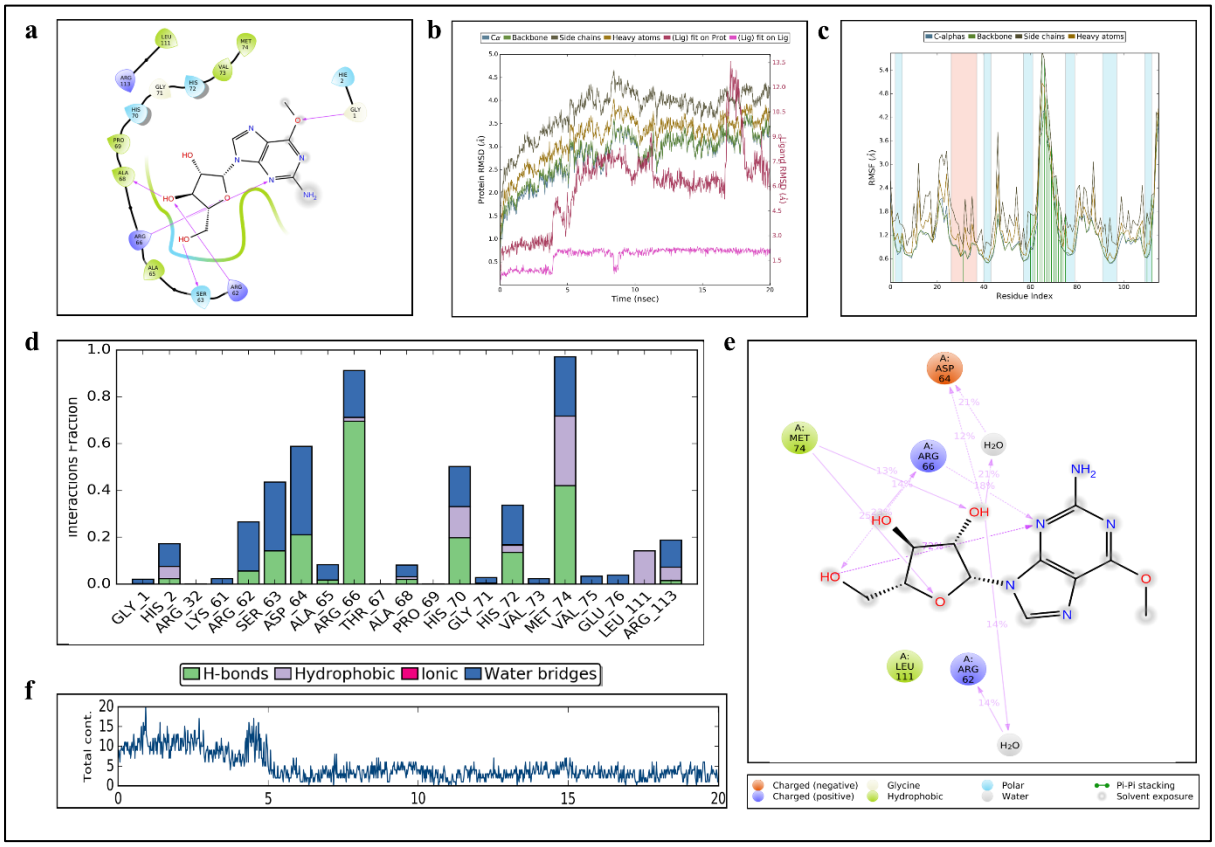
Supplementary Figure 9: Docking and MD simulation results for Nsp1-deep-Zinc-Gluconate. **a.** Zinc-Gluconate -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Zinc-Gluconate over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Zinc-Gluconate) **c.** RMSD plot of Nsp1 and Zinc-Gluconate. **d.** Nsp1-RMSF plot **e.** Interaction of Zinc-Gluconate atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Zinc-Gluconate over the course of MD simulation



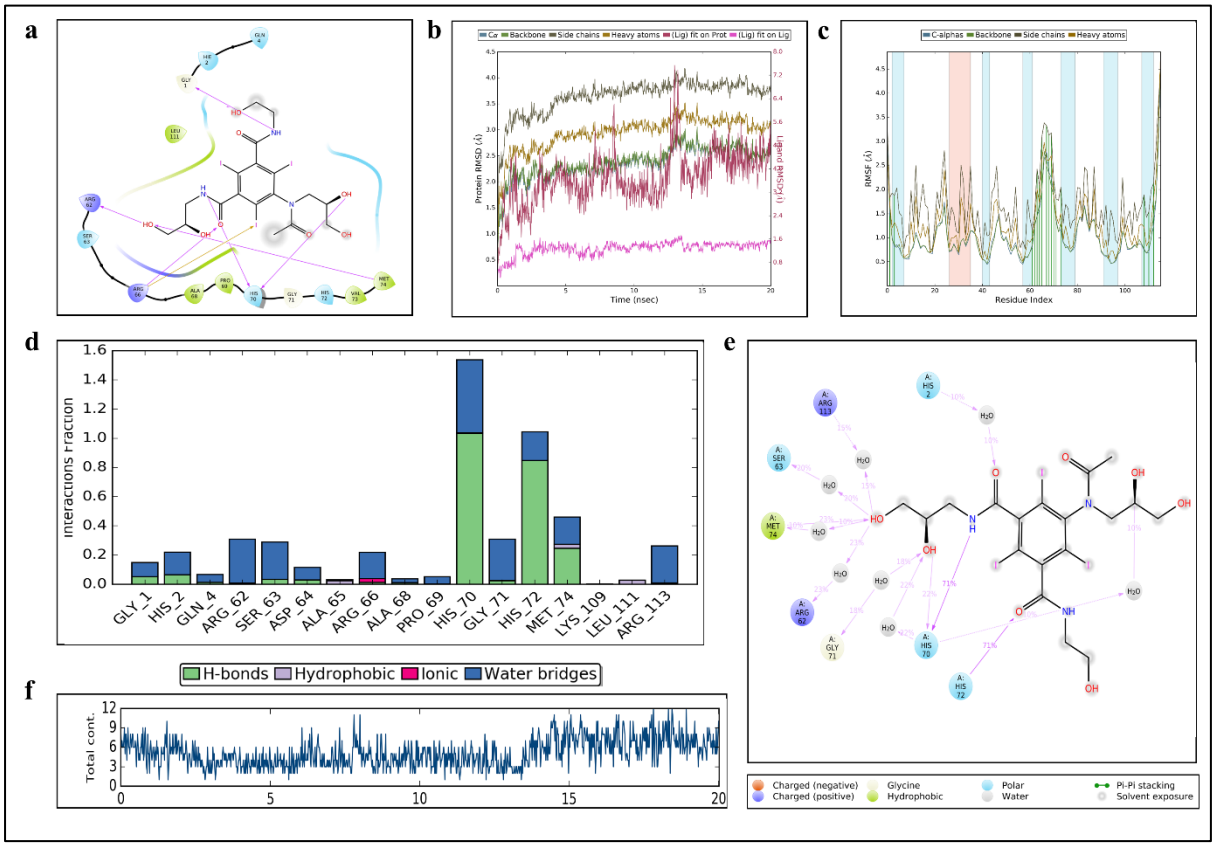
Supplementary Figure 10: Docking and MD simulation results for Nsp1-deep-Salbutamol. **a.** Salbutamol -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Salbutamol over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Salbutamol) **c.** RMSD plot of Nsp1 and Salbutamol. **d.** Nsp1-RMSF plot **e.** Interaction of Salbutamol atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Salbutamol over the course of MD simulation



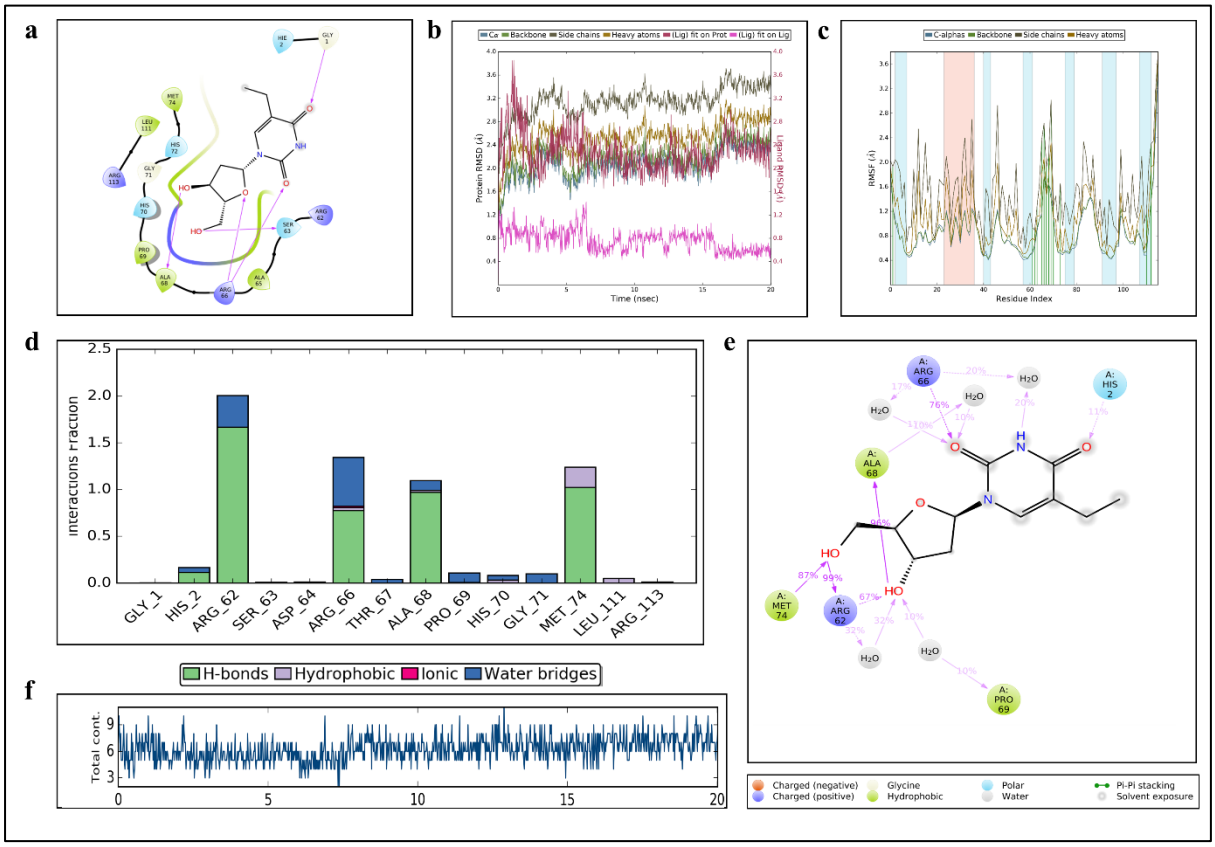
Supplementary Figure 11: Docking and MD simulation results for Nsp1-deep-Fenoterol. **a.** Fenoterol -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Fenoterol over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Fenoterol) **c.** RMSD plot of Nsp1 and Fenoterol. **d.** Nsp1-RMSF plot **e.** Interaction of Fenoterol atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Fenoterol over the course of MD simulation



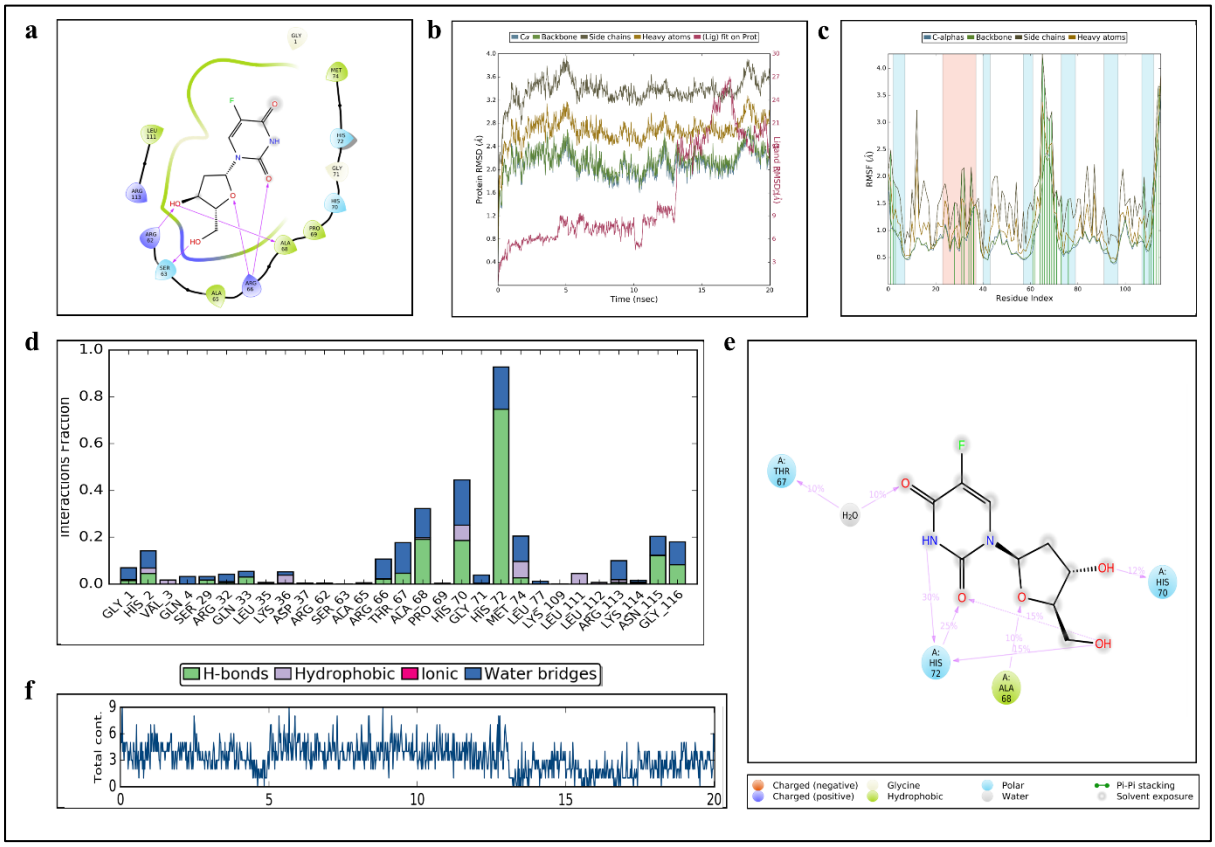
Supplementary Figure 12: Docking and MD simulation results for Nsp1-deep-Nelarabine. **a.** Nelarabine -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Nelarabine over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Nelarabine) **c.** RMSD plot of Nsp1 and Nelarabine. **d.** Nsp1-RMSF plot **e.** Interaction of Nelarabine atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Nelarabine over the course of MD simulation



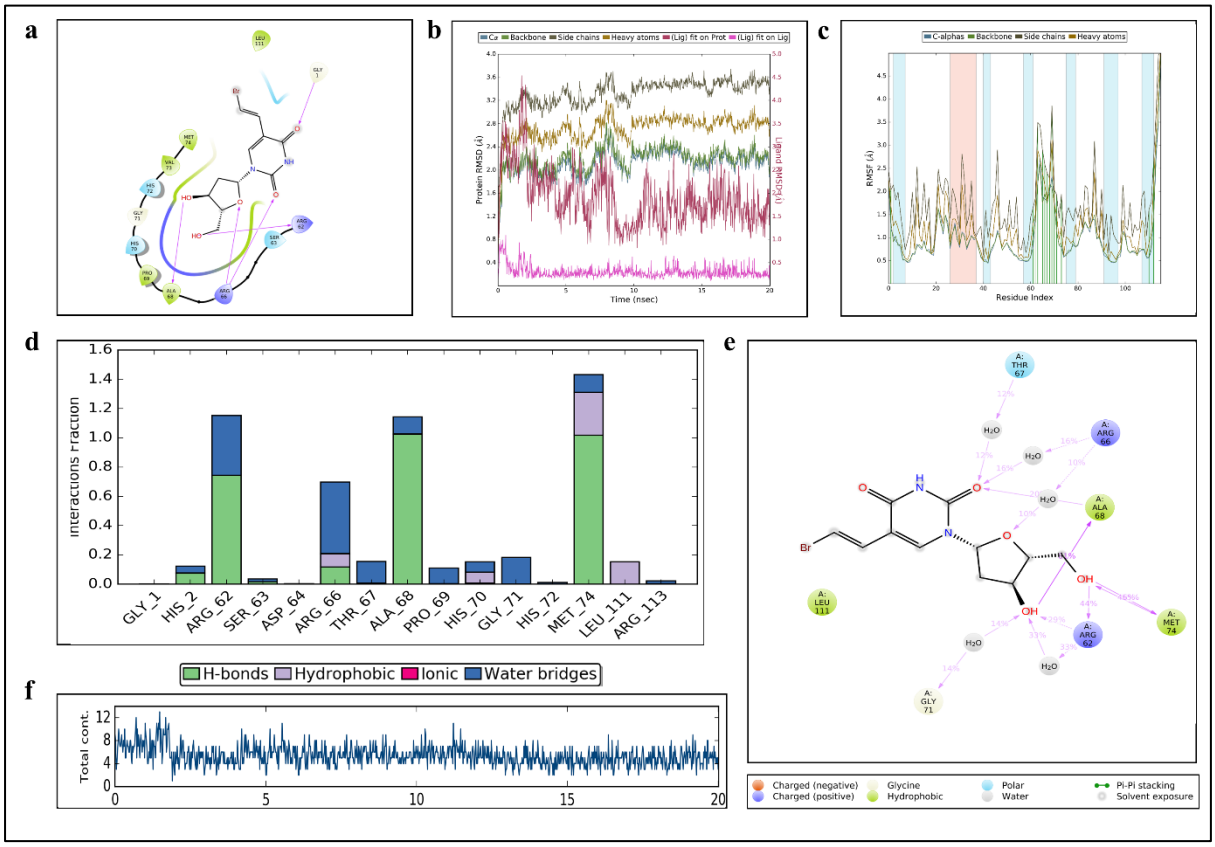
Supplementary Figure 13: Docking and MD simulation results for Nsp1-deep-Ioxilan. **a.** Ioxilan - Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Ioxilan over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Ioxilan) **c.** RMSD plot of Nsp1 and Ioxilan. **d.** Nsp1-RMSF plot **e.** Interaction of Ioxilan atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Ioxilan over the course of MD simulation



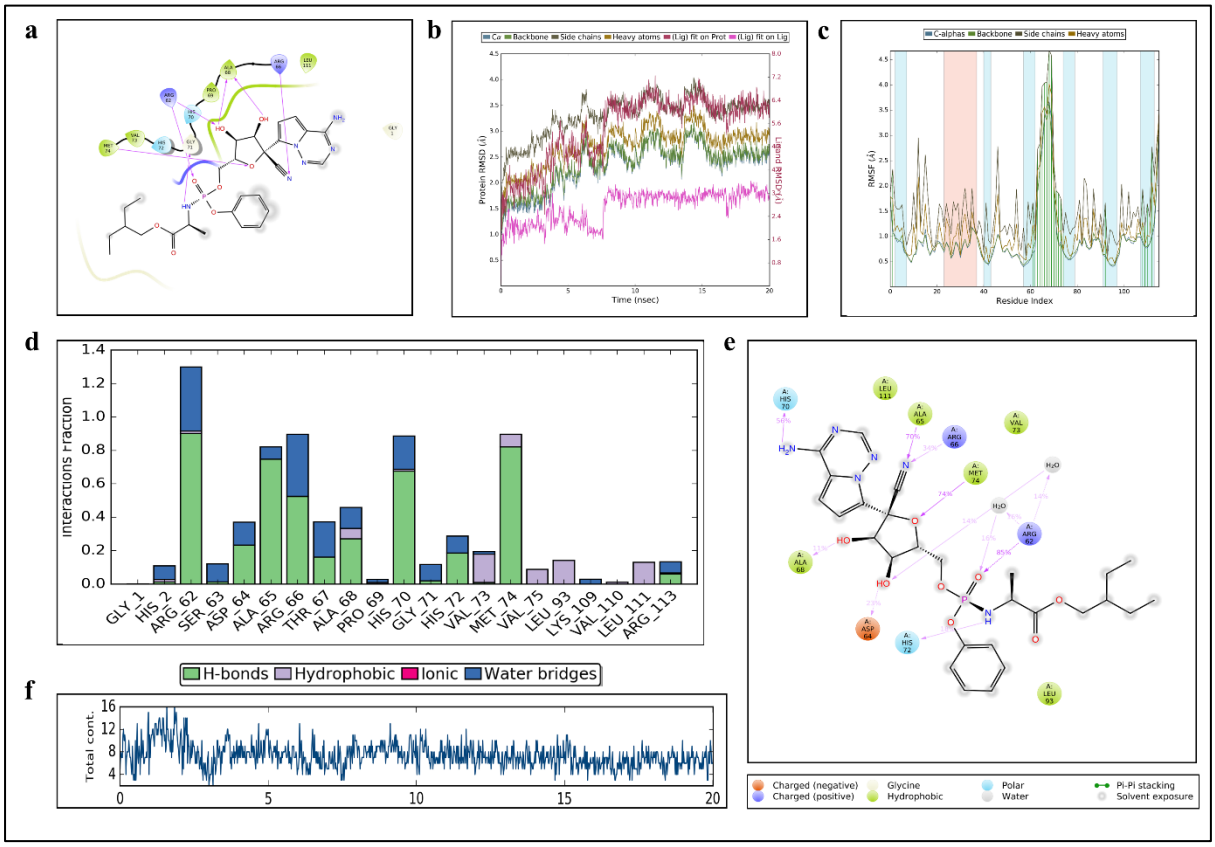
Supplementary Figure 14: Docking and MD simulation results for Nsp1-deep-Edoxudine. **a.** Edoxudine -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Edoxudine over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Edoxudine) **c.** RMSD plot of Nsp1 and Edoxudine. **d.** Nsp1-RMSF plot **e.** Interaction of Edoxudine atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Edoxudine over the course of MD simulation



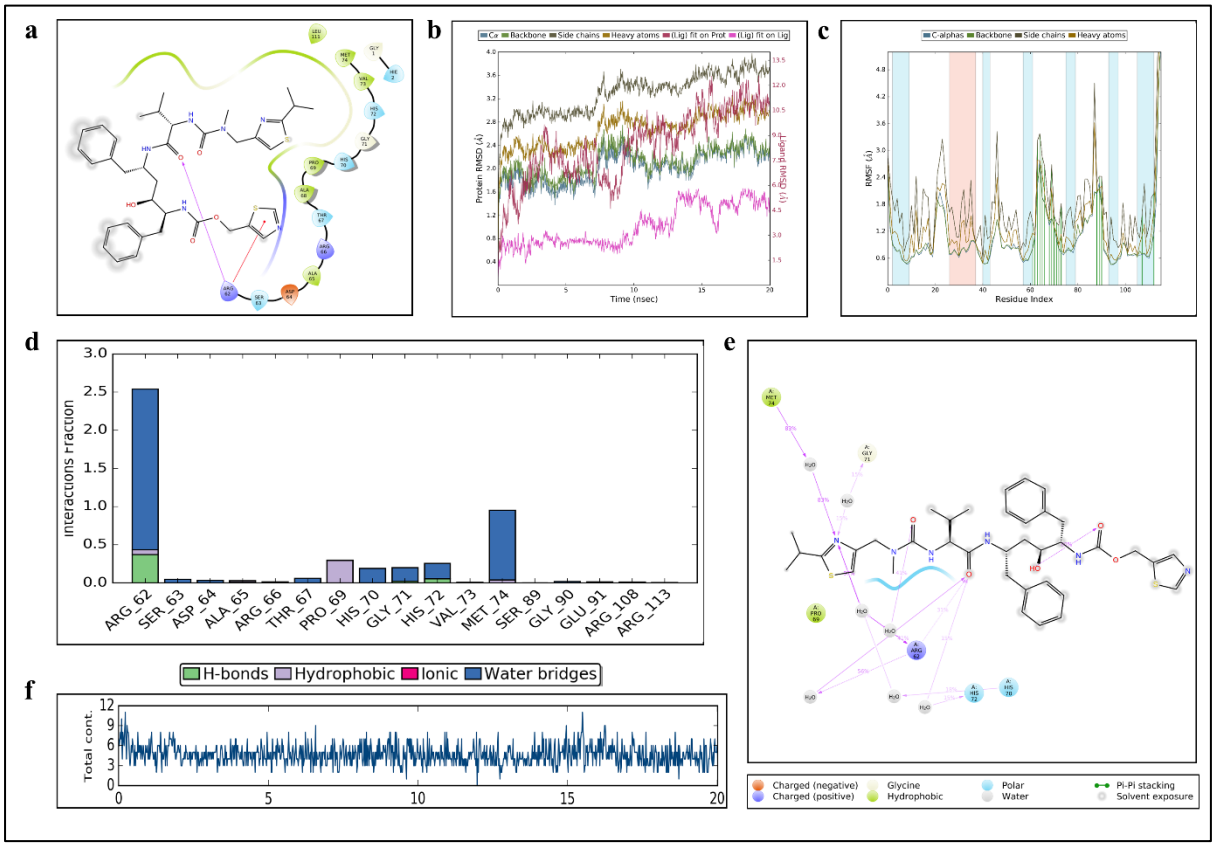
Supplementary Figure 15: Docking and MD simulation results for Nsp1-deep-Floxuridine. **a.** Floxuridine -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Floxuridine over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Floxuridine) **c.** RMSD plot of Nsp1 and Floxuridine. **d.** Nsp1-RMSF plot **e.** Interaction of Floxuridine atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Floxuridine over the course of MD simulation



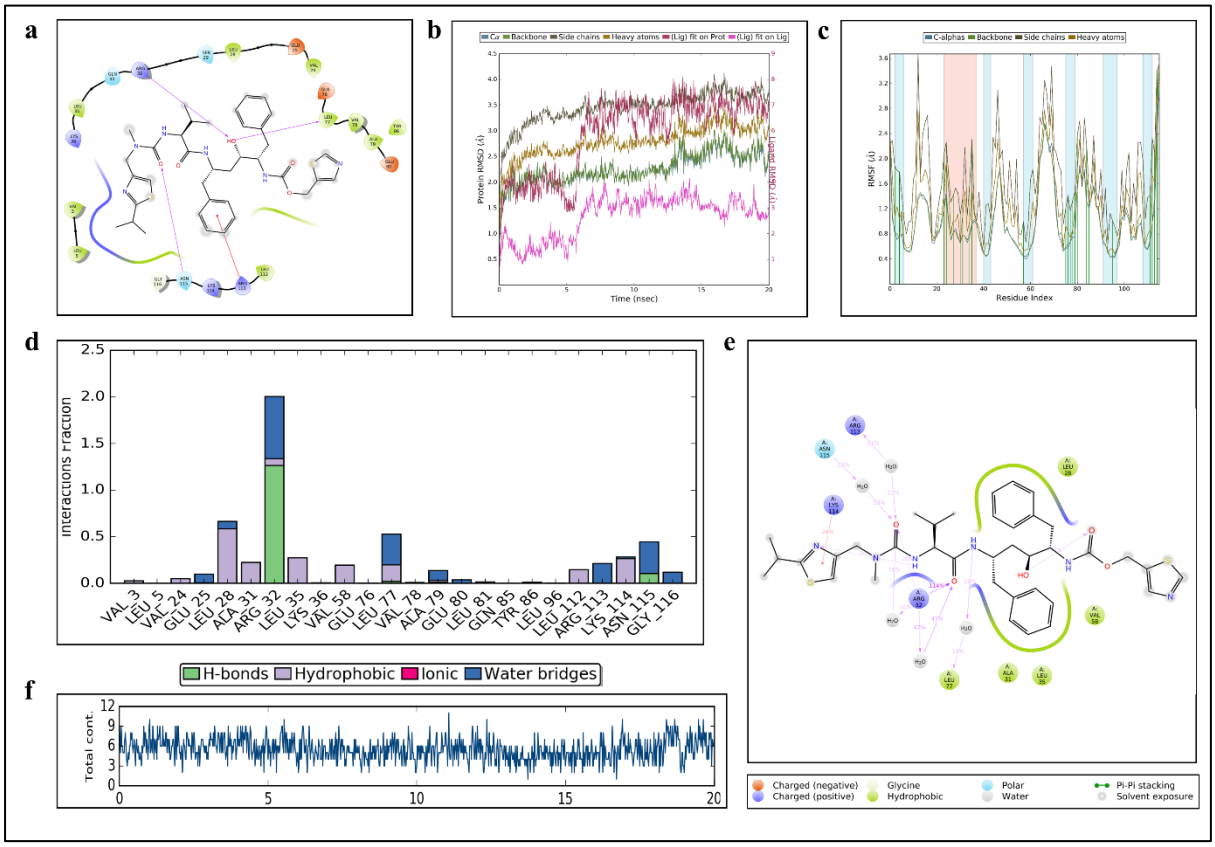
Supplementary Figure 16: Docking and MD simulation results for Nsp1-deep-Brivudine. **a.** Brivudine -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Brivudine over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Brivudine) **c.** RMSD plot of Nsp1 and Brivudine. **d.** Nsp1-RMSF plot **e.** Interaction of Brivudine atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Brivudine over the course of MD simulation



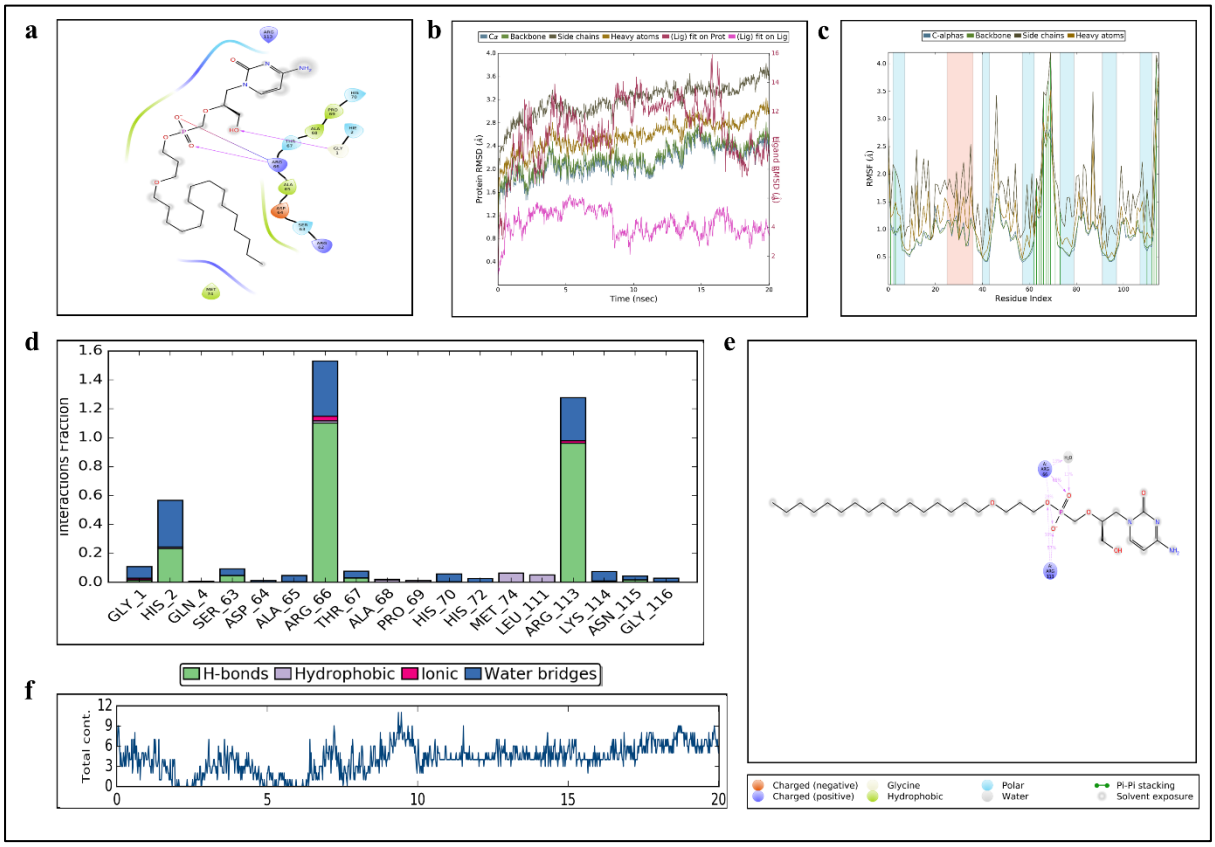
Supplementary Figure 17: Docking and MD simulation results for Nsp1-deep-Remdesivir. **a.** Remdesivir -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Remdesivir over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Remdesivir) **c.** RMSD plot of Nsp1 and Remdesivir. **d.** Nsp1-RMSF plot **e.** Interaction of Remdesivir atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Remdesivir over the course of MD simulation



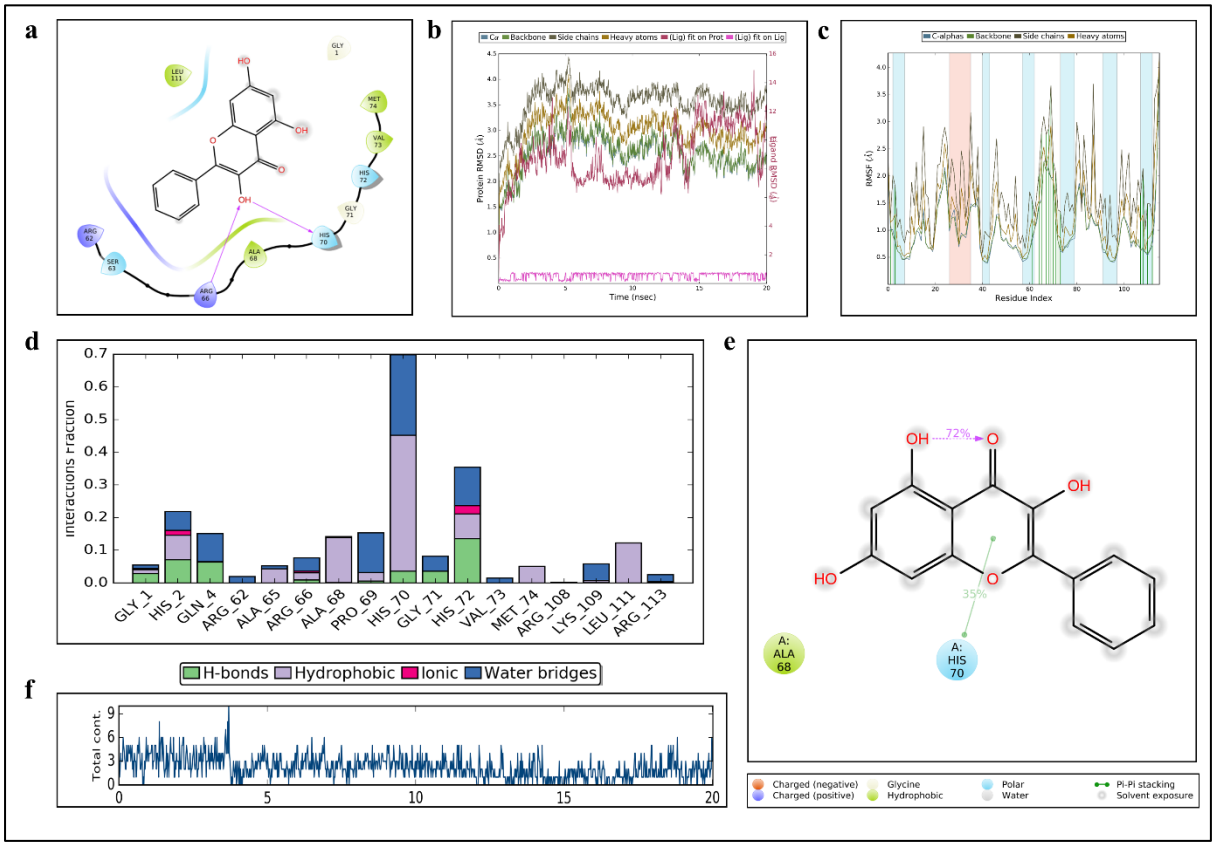
Supplementary Figure 18: Docking and MD simulation results for Nsp1-deep-Ritonavir. **a.** Ritonavir -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Ritonavir over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Ritonavir) **c.** RMSD plot of Nsp1 and Ritonavir. **d.** Nsp1-RMSF plot **e.** Interaction of Ritonavir atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Ritonavir over the course of MD simulation



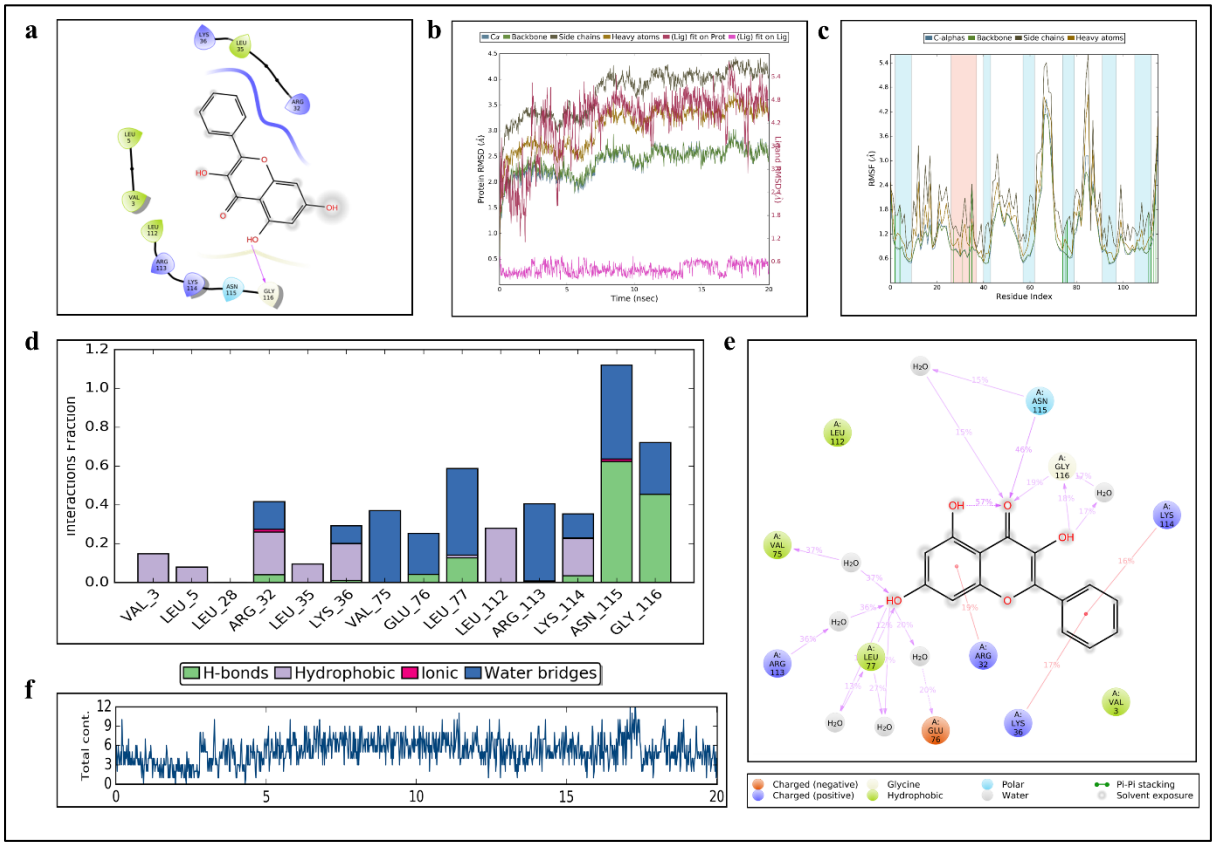
Supplementary Figure 19: Docking and MD simulation results for Nsp1-shallow-Ritonavir. **a.** Ritonavir -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Ritonavir over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Ritonavir) **c.** RMSD plot of Nsp1 and Ritonavir. **d.** Nsp1-RMSF plot **e.** Interaction of Ritonavir atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Ritonavir over the course of MD simulation



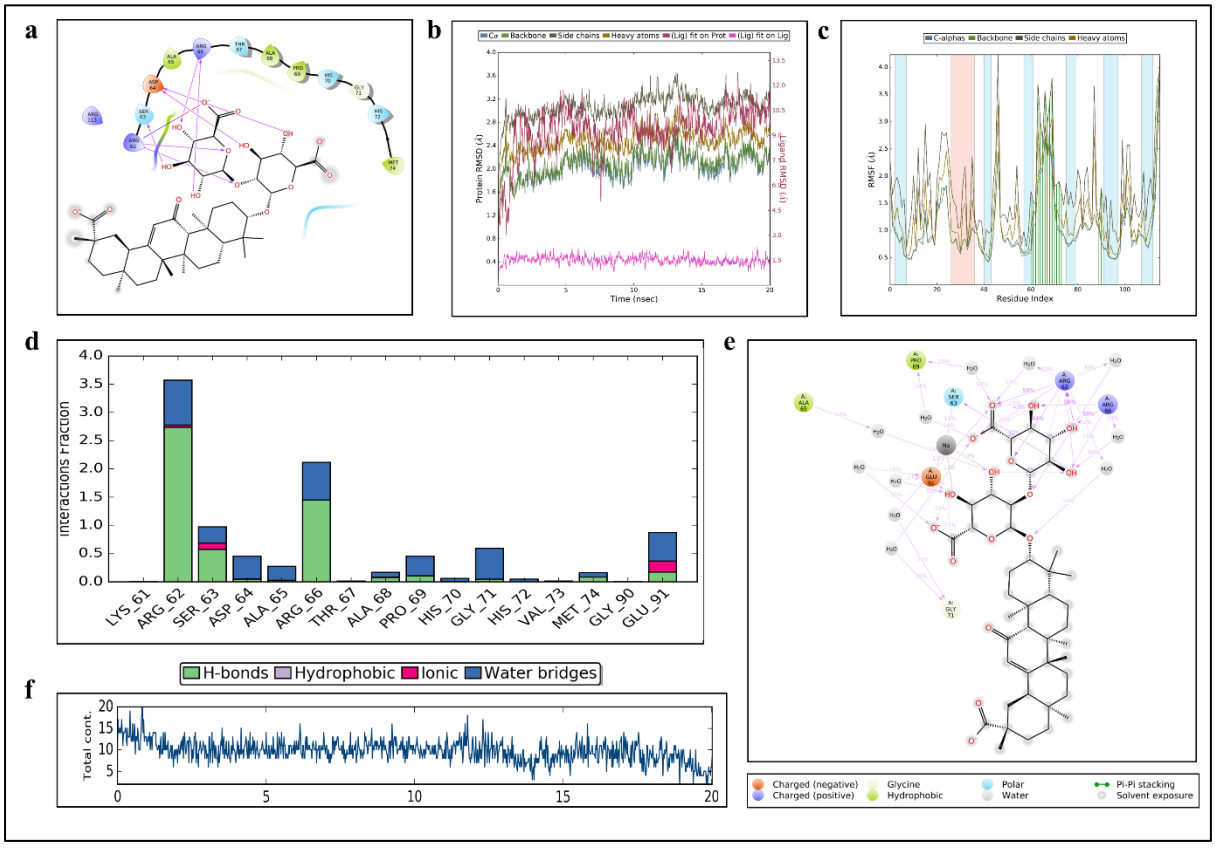
Supplementary Figure 20: Docking and MD simulation results for Nsp1-deep-Brincidofovir. **a.** Brincidofovir -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Brincidofovir over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Brincidofovir) **c.** RMSD plot of Nsp1 and Brincidofovir. **d.** Nsp1-RMSF plot **e.** Interaction of Brincidofovir atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Brincidofovir over the course of MD simulation



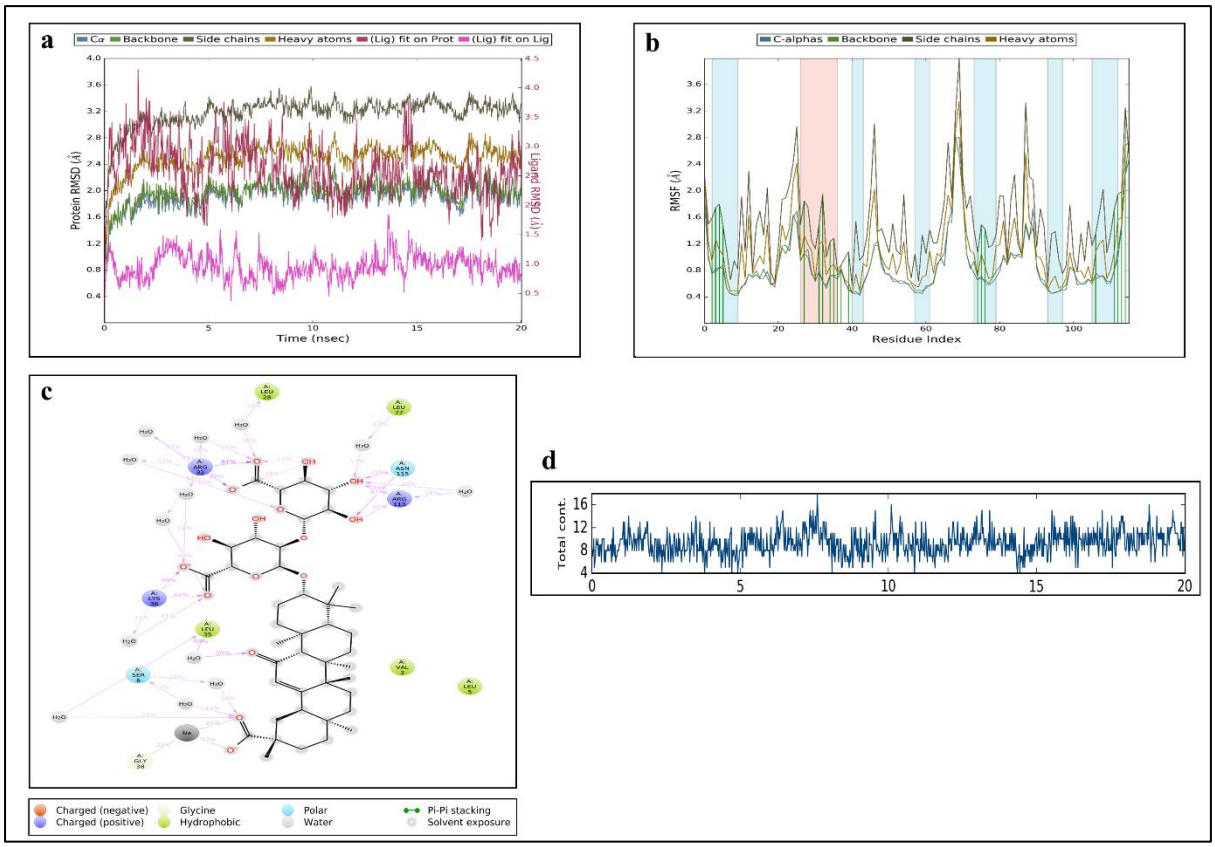
Supplementary Figure 21: Docking and MD simulation results for Nsp1-deep-Galangin. **a.** Galangin -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Galangin over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Galangin) **c.** RMSD plot of Nsp1 and Galangin. **d.** Nsp1-RMSF plot **e.** Interaction of Galangin atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Galangin over the course of MD simulation



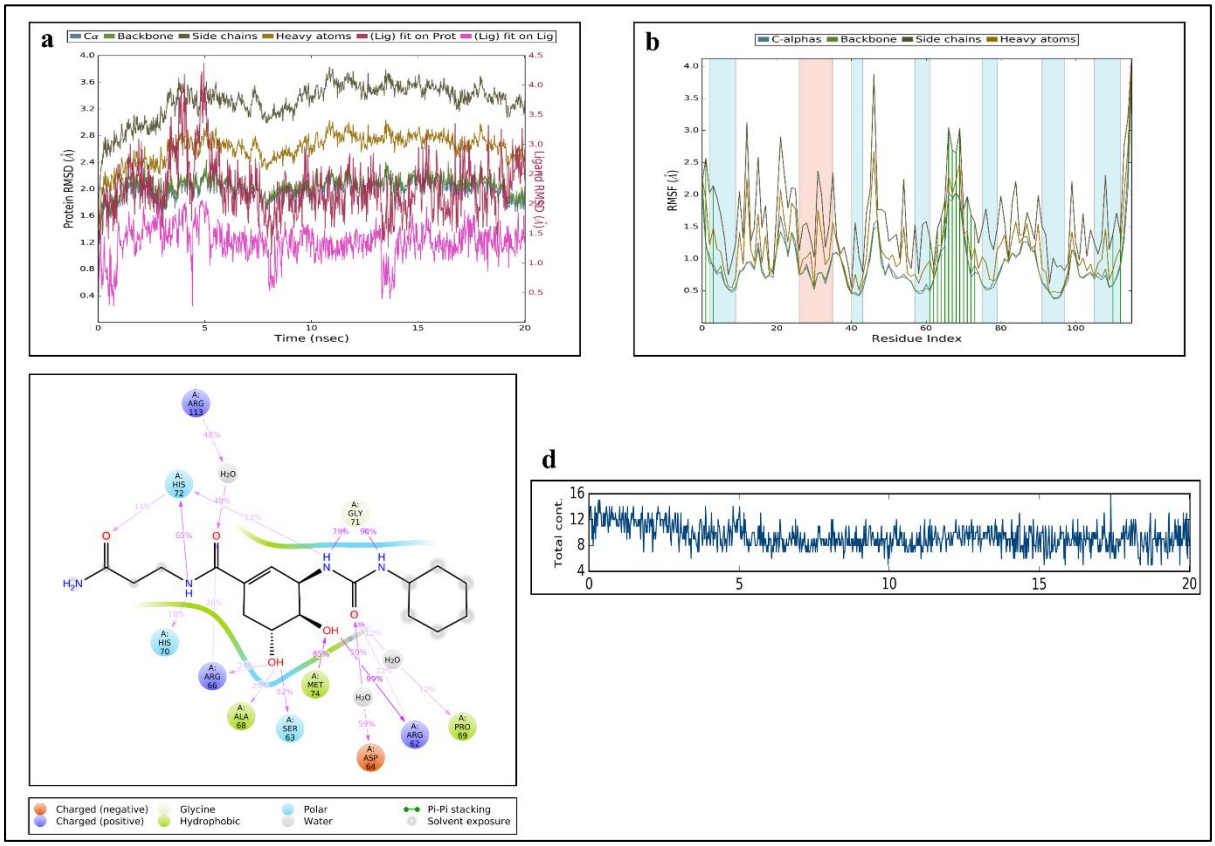
Supplementary Figure 22: Docking and MD simulation results for Nsp1-shallow-Galangin. **a.** Galangin -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Galangin over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Galangin) **c.** RMSD plot of Nsp1 and Galangin. **d.** Nsp1-RMSF plot **e.** Interaction of Galangin atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Galangin over the course of MD simulation



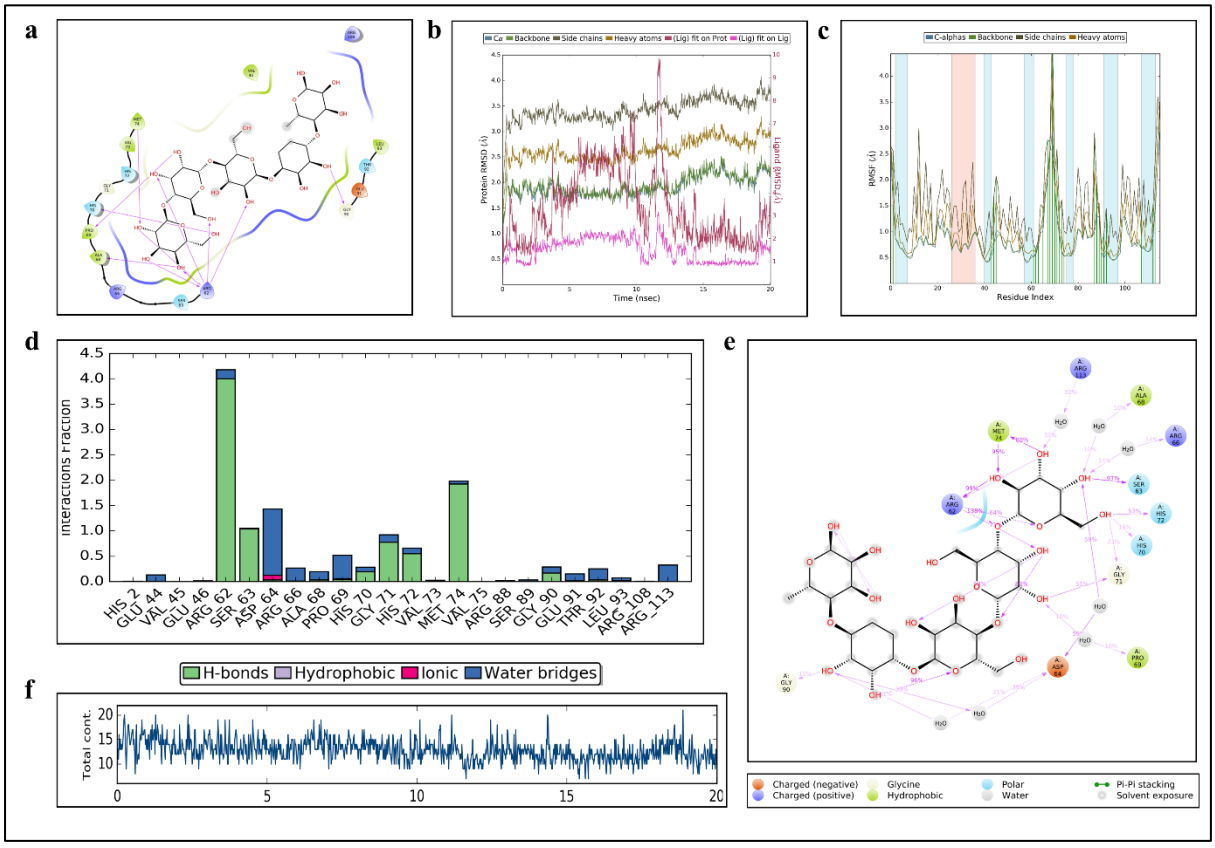
Supplementary Figure 23: Docking and MD simulation results for Nsp1-deep-Glycyrrhizic-acid. **a.** Glycyrrhizic-acid -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Glycyrrhizic-acid over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Glycyrrhizic-acid) **c.** RMSD plot of Nsp1 and Glycyrrhizic-acid. **d.** Nsp1-RMSF plot **e.** Interaction of Glycyrrhizic-acid atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Glycyrrhizic-acid over the course of MD simulation



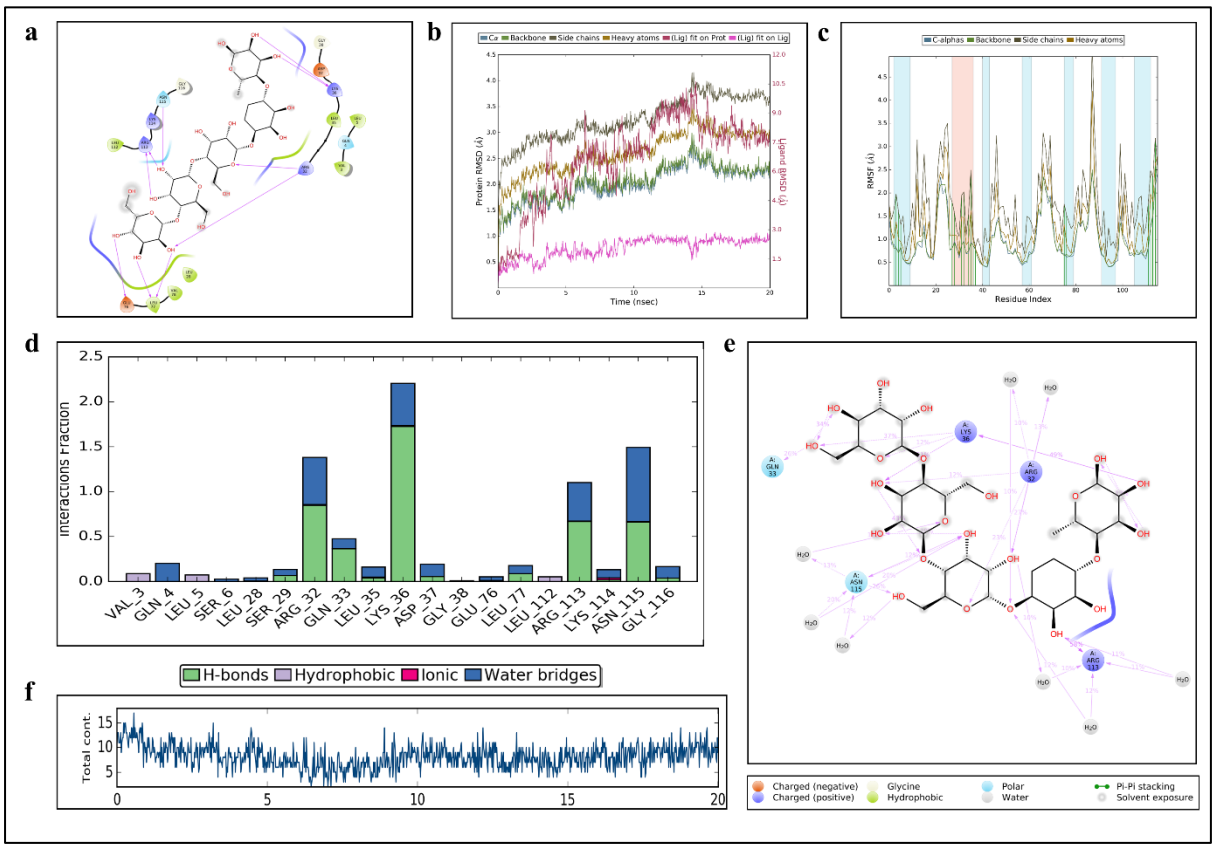
Supplementary Figure 24: MD simulation results for Nsp1-shallow-Glycyrrhizic-acid. **a.** RMSD plot of Nsp1 and Glycyrrhizic-acid. **b.** Nsp1-RMSF plot **c.** Interaction of Glycyrrhizic-acid atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **d.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Glycyrrhizic-acid over the course of MD



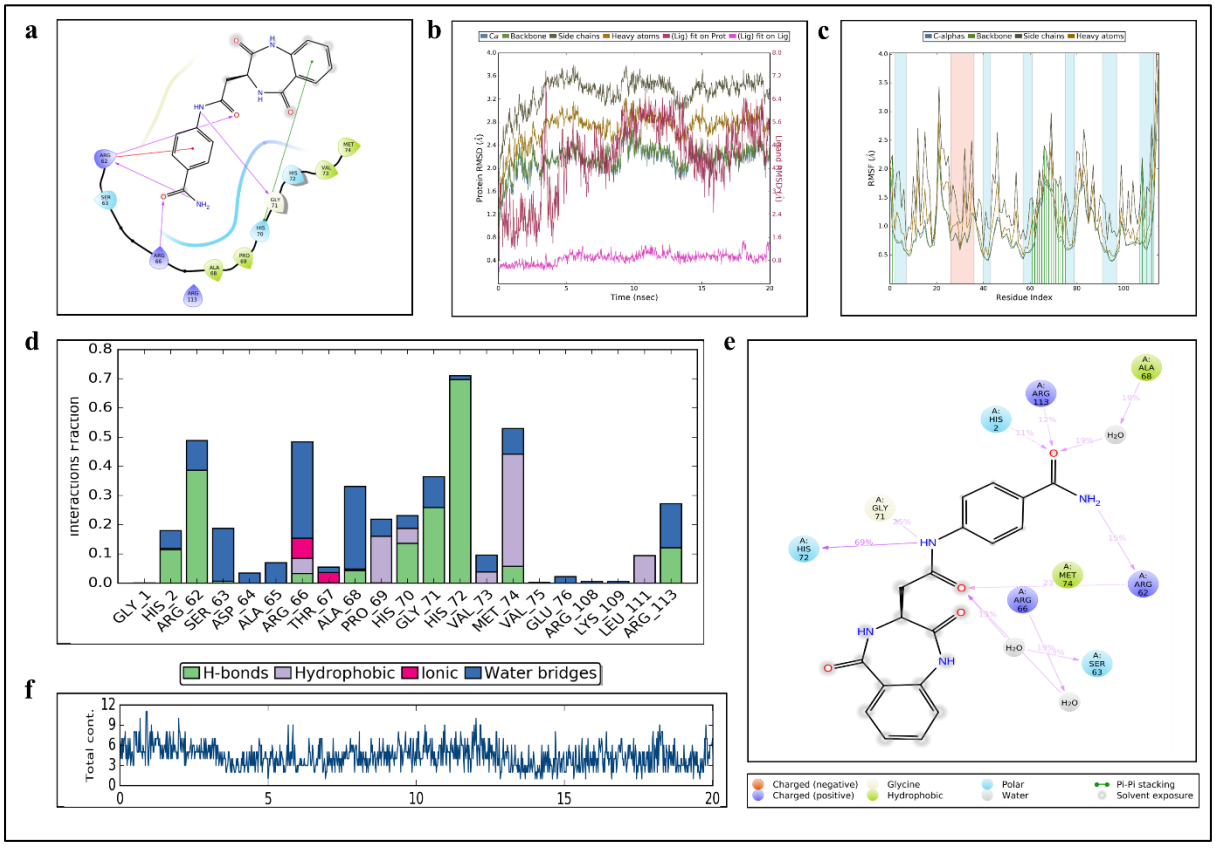
Supplementary Figure 25: MD simulation results for Nsp1-deep-SN00003849. **a.** RMSD plot of Nsp1 and SN00003849. **b.** Nsp1-RMSF plot **c.** Interaction of SN00003849 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **d.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00003849 over the course of MD simulation



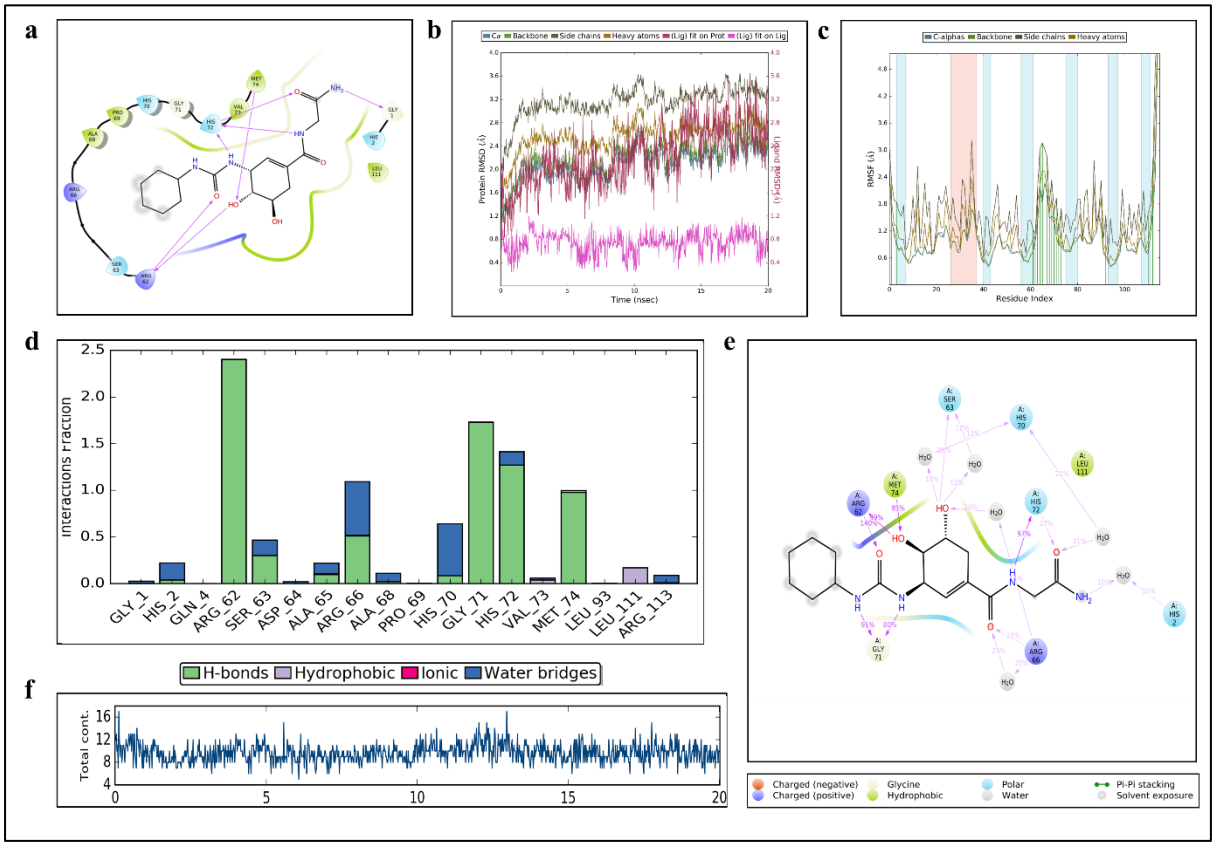
Supplementary Figure 26: Docking and MD simulation results for Nsp1-deep-SN00220639. **a.** SN00220639 -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with SN00220639 over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (SN00220639) **c.** RMSD plot of Nsp1 and SN00220639. **d.** Nsp1-RMSF plot **e.** Interaction of SN00220639 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00220639 over the course of MD simulation



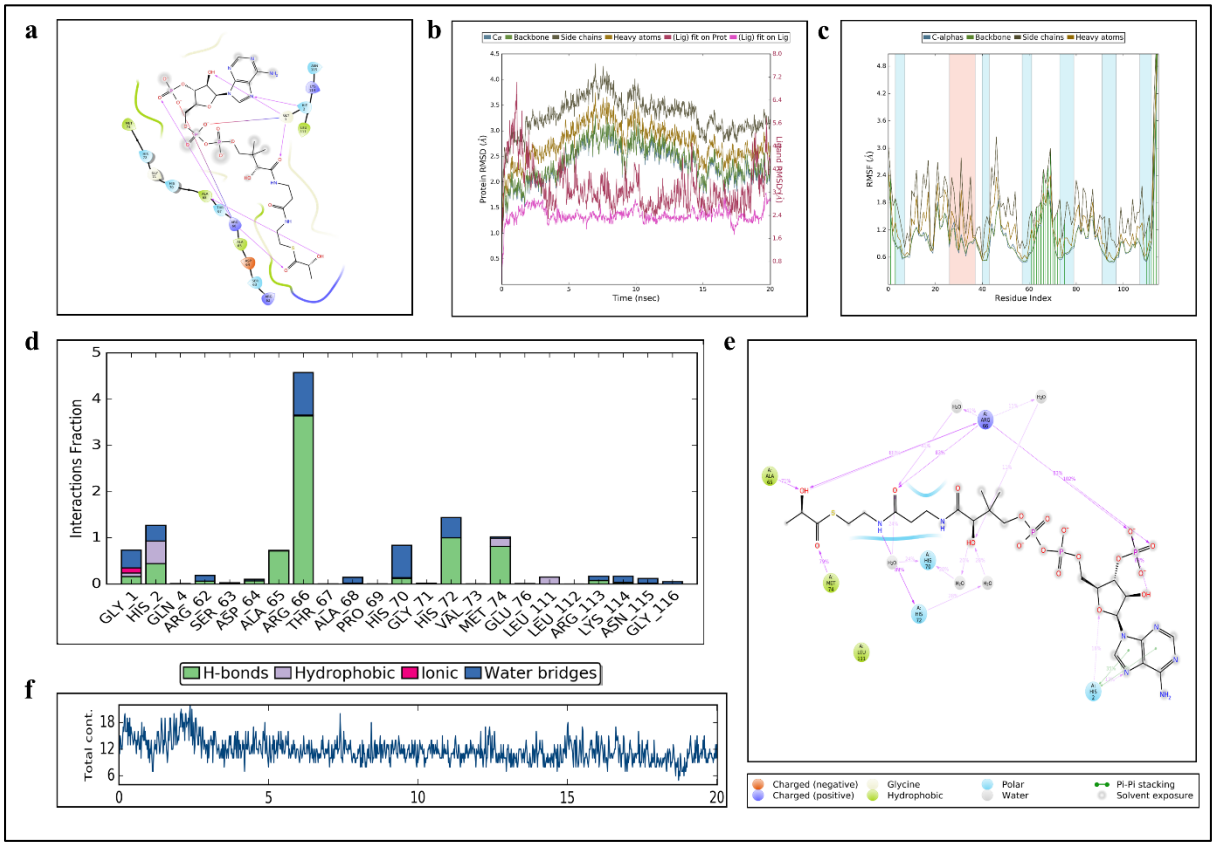
Supplementary Figure 27: Docking and MD simulation results for Nsp1-shallow-SN00220639. **a.** SN00220639 -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with SN00220639 over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (SN00220639) **c.** RMSD plot of Nsp1 and SN00220639. **d.** Nsp1-RMSF plot **e.** Interaction of SN00220639 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00220639 over the course of MD simulation



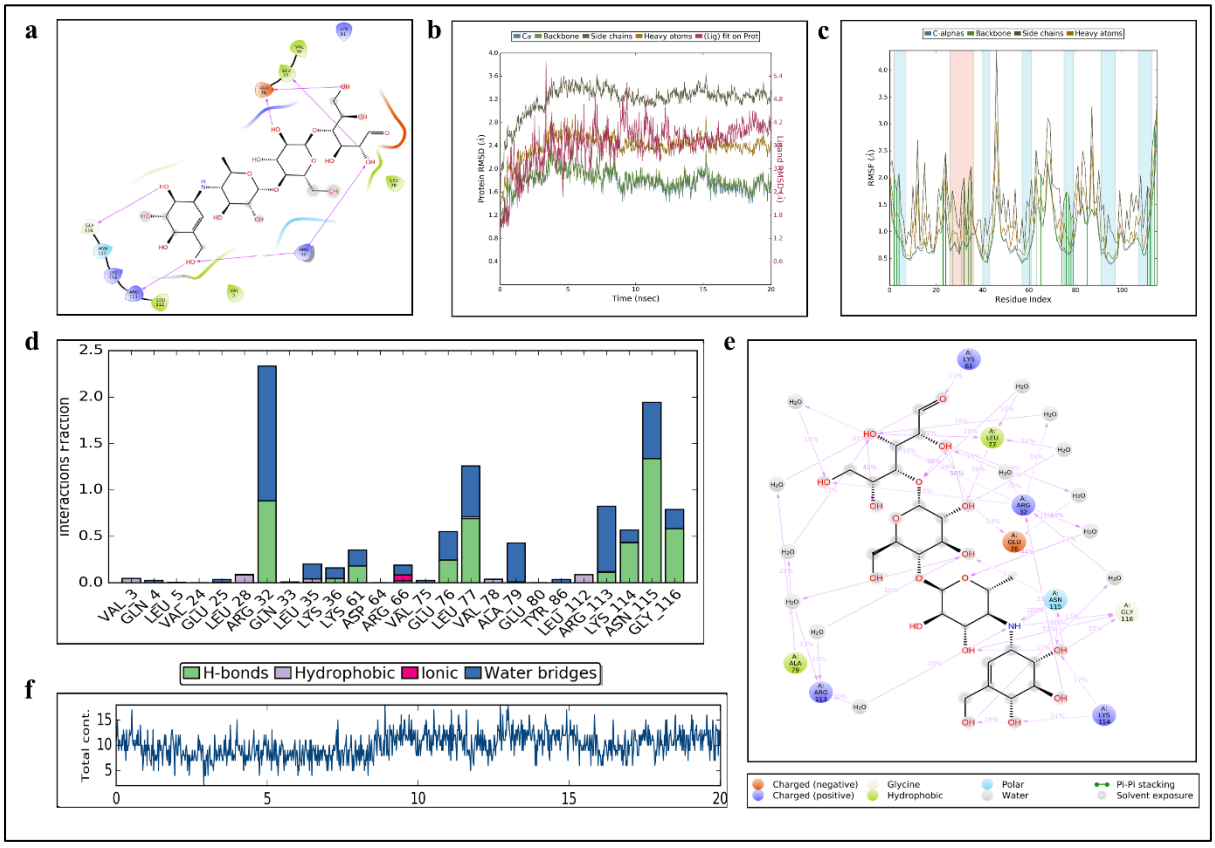
Supplementary Figure 28: Docking and MD simulation results for Nsp1-deep-SN00103215. **a.** SN00103215 -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with SN00103215 over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (SN00103215) **c.** RMSD plot of Nsp1 and SN00103215. **d.** Nsp1-RMSF plot **e.** Interaction of SN00103215 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00103215 over the course of MD simulation



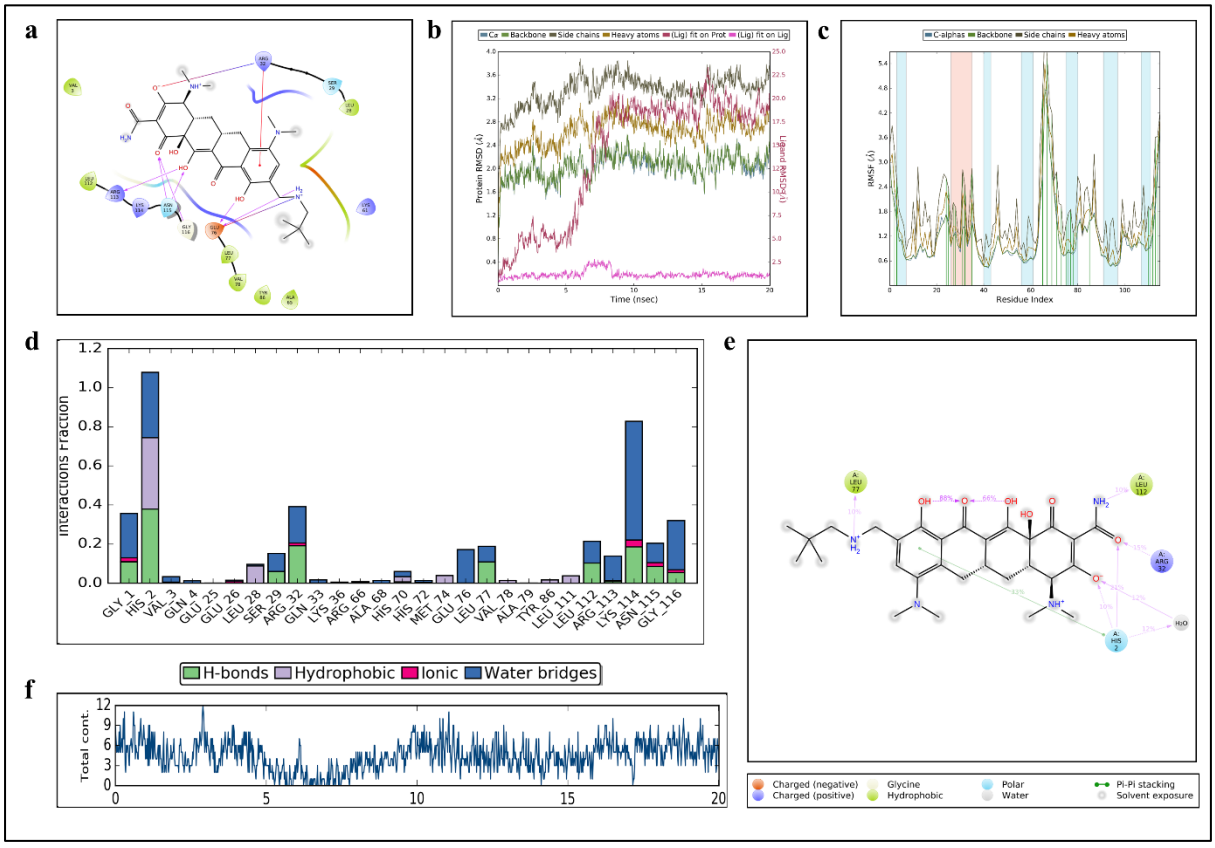
Supplementary Figure 29: Docking and MD simulation results for Nsp1-deep-SN00003832. **a.** SN00003832 -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with SN00003832 over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (SN00003832) **c.** RMSD plot of Nsp1 and SN00003832. **d.** Nsp1-RMSF plot **e.** Interaction of SN00003832 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00003832 over the course of MD simulation



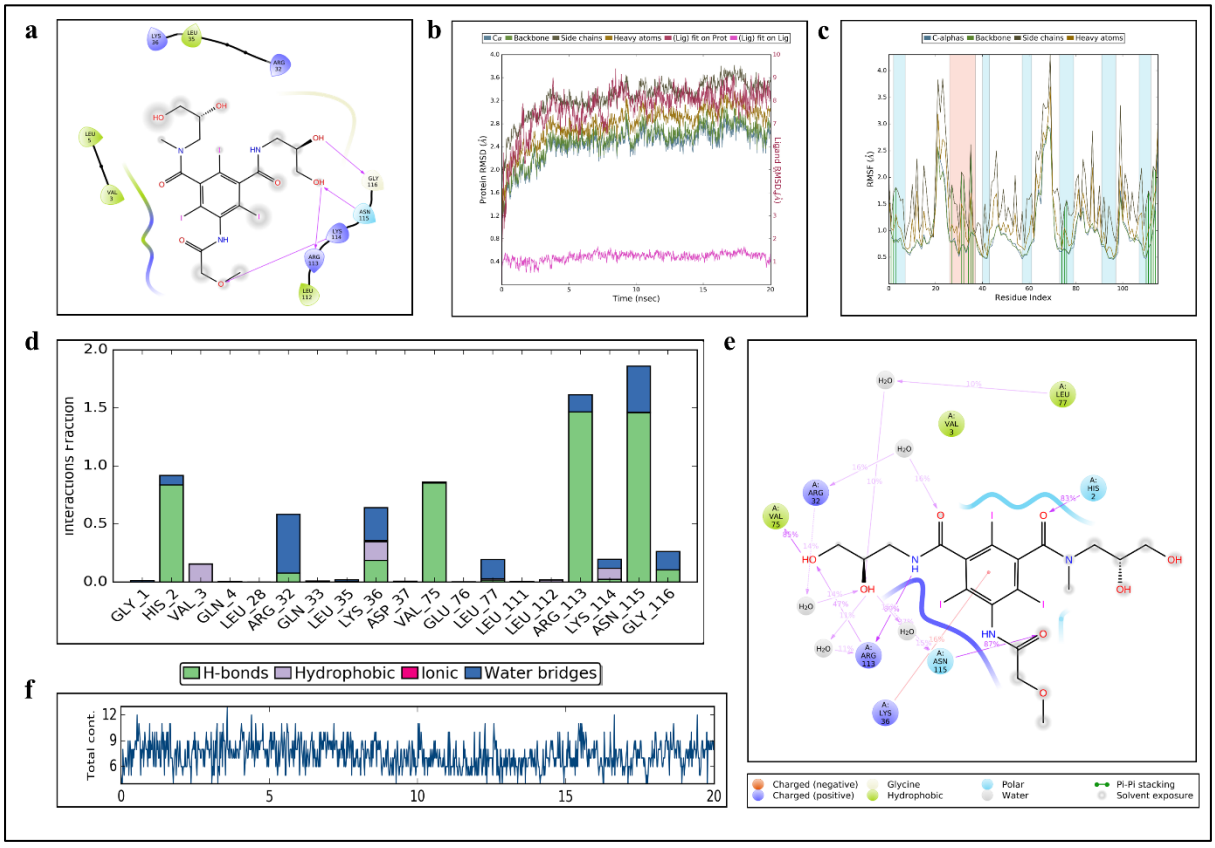
Supplementary Figure 30: Docking and MD simulation results for Nsp1-deep-SN00216190. **a.** SN00216190 -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with SN00216190 over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (SN00216190) **c.** RMSD plot of Nsp1 and SN00216190. **d.** Nsp1-RMSF plot **e.** Interaction of SN00216190 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00216190 over the course of MD simulation



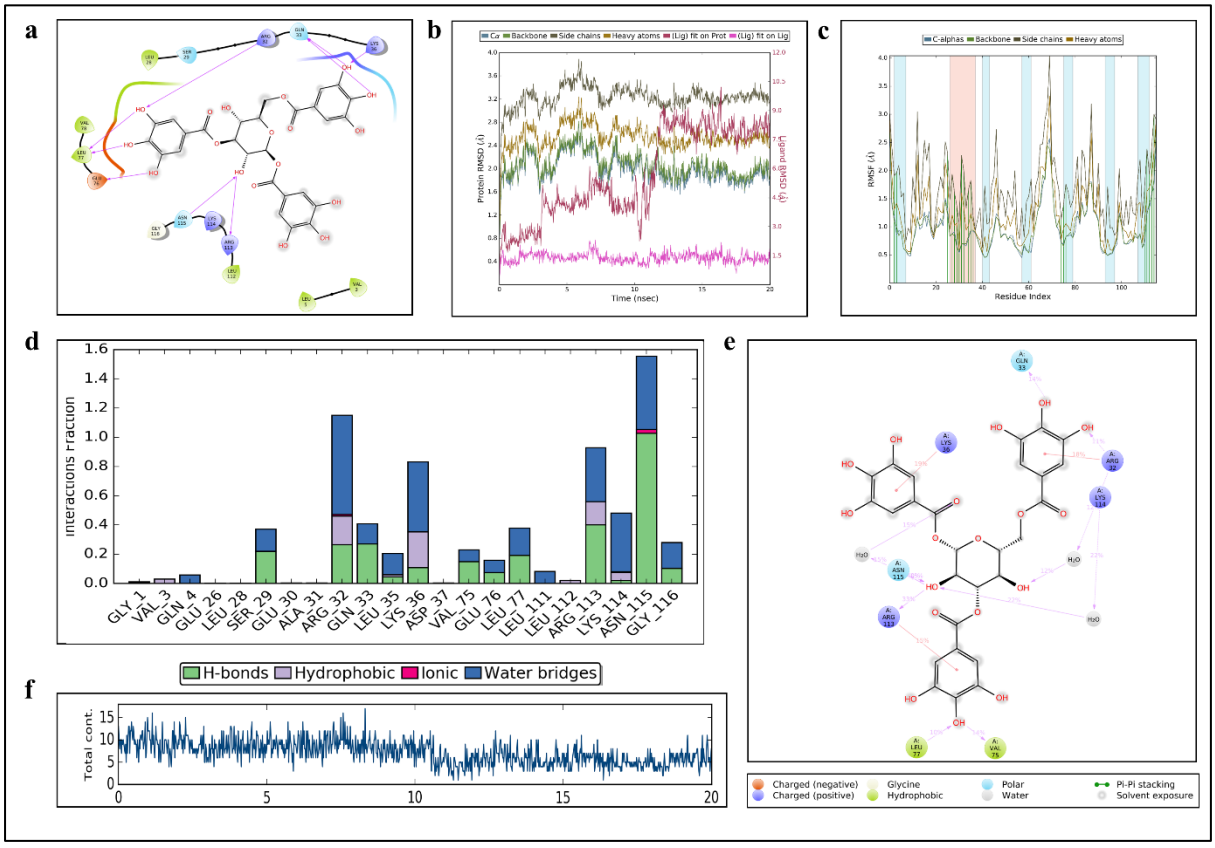
Supplementary Figure 31: Docking and MD simulation results for Nsp1-shallow-Acarbose. **a.** Acarbose -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Acarbose over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Acarbose) **c.** RMSD plot of Nsp1 and Acarbose. **d.** Nsp1-RMSF plot **e.** Interaction of Acarbose atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Acarbose over the course of MD simulation



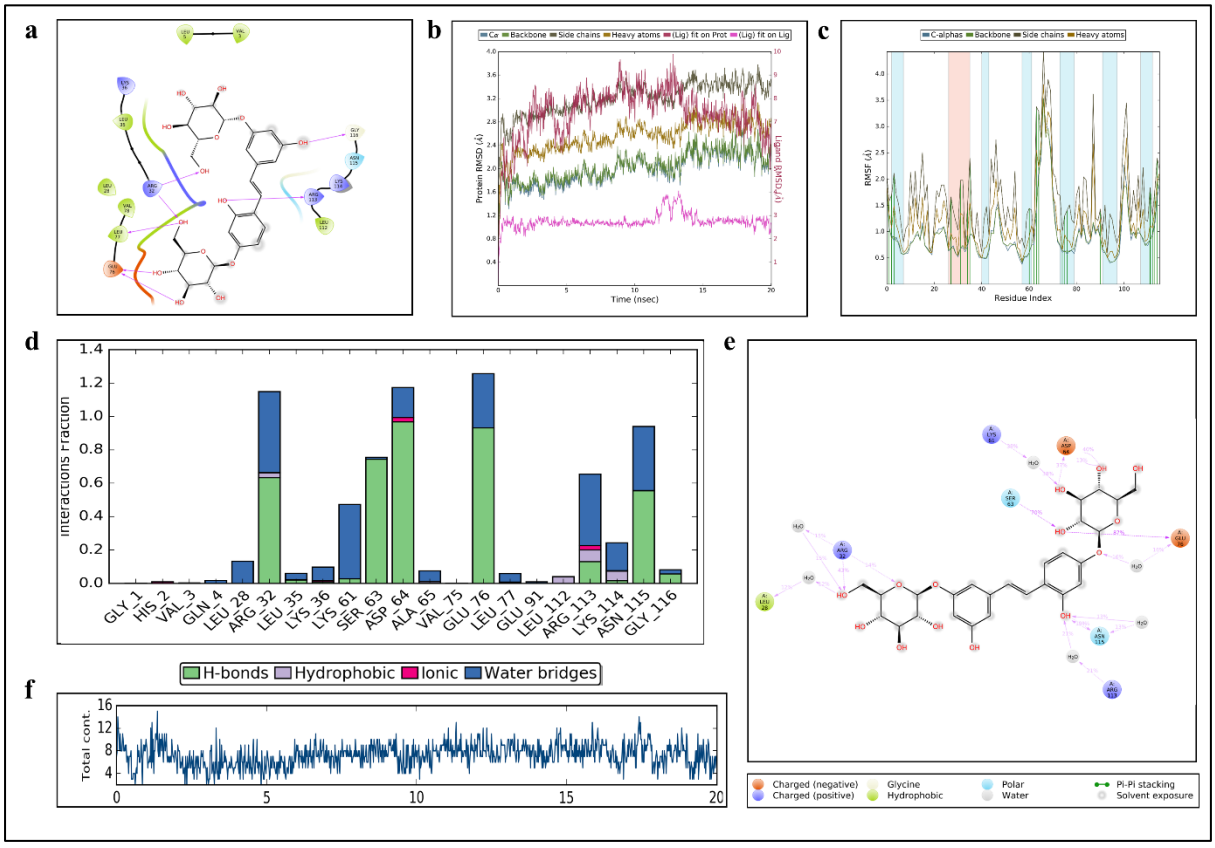
Supplementary Figure 32: Docking and MD simulation results for Nsp1-shallow-Omadacycline. **a.** Omadacycline -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Omadacycline over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Omadacycline) **c.** RMSD plot of Nsp1 and Omadacycline. **d.** Nsp1-RMSF plot **e.** Interaction of Omadacycline atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Omadacycline over the course of MD simulation



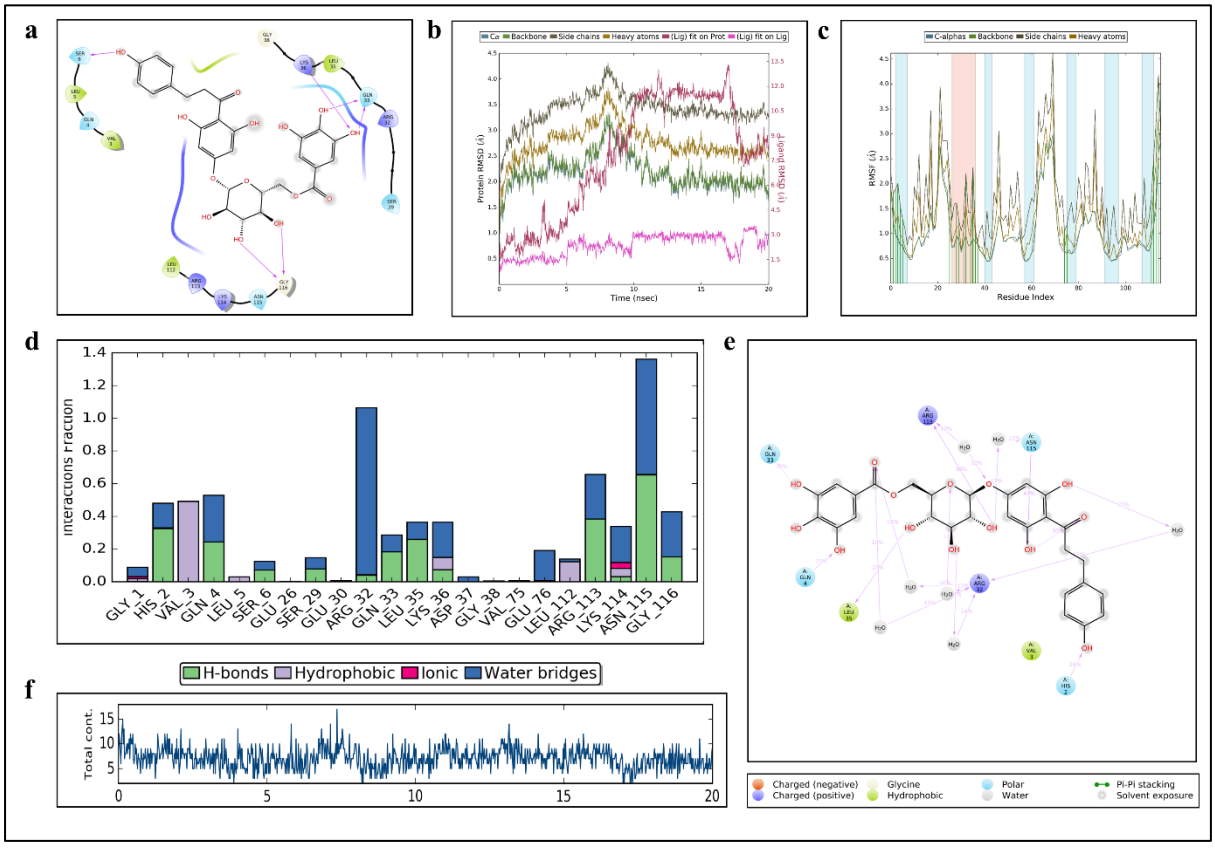
Supplementary Figure 33: Docking and MD simulation results for Nsp1-shallow-Iopromide. **a.** Iopromide -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with Iopromide over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (Iopromide) **c.** RMSD plot of Nsp1 and Iopromide. **d.** Nsp1-RMSF plot **e.** Interaction of Iopromide atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Iopromide over the course of MD simulation



Supplementary Figure 34: Docking and MD simulation results for Nsp1-shallow-SN00037405. **a.** SN00037405 -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with SN00037405 over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (SN00037405) **c.** RMSD plot of Nsp1 and SN00037405. **d.** Nsp1-RMSF plot **e.** Interaction of SN00037405 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00037405 over the course of MD simulation



Supplementary Figure 35: Docking and MD simulation results for Nsp1-shallow-SN00161170. **a.** SN00161170 -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with SN00161170 over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (SN00161170) **c.** RMSD plot of Nsp1 and SN00161170. **d.** Nsp1-RMSF plot **e.** Interaction of SN00161170 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00161170 over the course of MD simulation



Supplementary Figure 36: Docking and MD simulation results for Nsp1-shallow-SN00038342. **a.** SN00038342 -Nsp1 interactions after XP docking **b.** Interaction types and Interacting residues of Nsp1 with SN00038342 over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggests that the residue forms multiple interactions of same subtype with ligand (SN00038342) **c.** RMSD plot of Nsp1 and SN00038342. **d.** Nsp1-RMSF plot **e.** Interaction of SN00038342 atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simualtion time has been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction **f.** Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and SN00038342 over the course of MD simulation

Supplementary Table 1: ADME properties of SNDB compounds

Title	#stars	CNS	MW	donorHB	accptHB	QPlogPo/w	QPlogS	QPPCaco	QPlogBB	QPPMDCK	% Human Oral Absorption	Rule of Five
SN00103215	0	-2	352.349	4	9	0.309	-3.779	19.11	-2.5	6.864	51.689	0
SN00003832	2	-2	354.405	6.25	9.65	-1.413	-1.811	4.532	-3.084	5.284	17.46	1
SN00003849	1	-2	368.432	6	9.4	-0.953	-2.201	4.866	-3.198	5.599	20.707	1
SN00220639	16	-2	780.727	15	39.1	-7.721	0.357	0.223	-6.585	0.056	0	3
SN00216190	14	-2	839.597	8	29.8	-2.808	0.261	0.001	-6.879	0	0	3
SN00037405	10	-2	636.476	11	17.85	-2.664	-3.525	0.022	-7.813	0.005	0	3
SN00038342	9	-2	588.521	7	14.05	0.027	-4.607	0.279	-6.407	0.071	0	3
SN00161170	10	-2	568.53	10	20	-2.468	-2.32	1.177	-5.335	0.337	0	3
SN00156190	0	-2	356.418	2	5	3.803	-5.101	380.868	-1.678	174.267	95.401	0
SN00002189	0	-1	276.375	1	3.5	3.765	-4.046	1441.646	-0.874	734.611	100	0

 # Stars: Number of properties which do not fall in 95% range of similar values for known drugs; **CNS:** Central nervous system activity with -2 being inactive and 2 being active; **MW:** Molecular Weight; **donorHB:** Number of H-bond donors**; accptHB:** Number of H-bond acceptors; **QPlogPo/w:** Partition coefficient for octanol/water; **QPlogS:** Aqueous solubility with acceptable range of -6.5-0.5; **QPPCaco:** Caco-2 cell permeability in nm/sec (<25 is poor and >500 is great); **QPlogBB:** Brain/blood partition coefficient for orally delivered drugs (-3.0-1.2); **QPPMDCK:** apparent MDCK cell permeability in nm/sec (<25 is poor and >500 is great); **Rule Of Five:** Lipinski's rule of 5