Supporting information

Identification of potential molecules against COVID-19 main protease through structure-guided virtual screening approach

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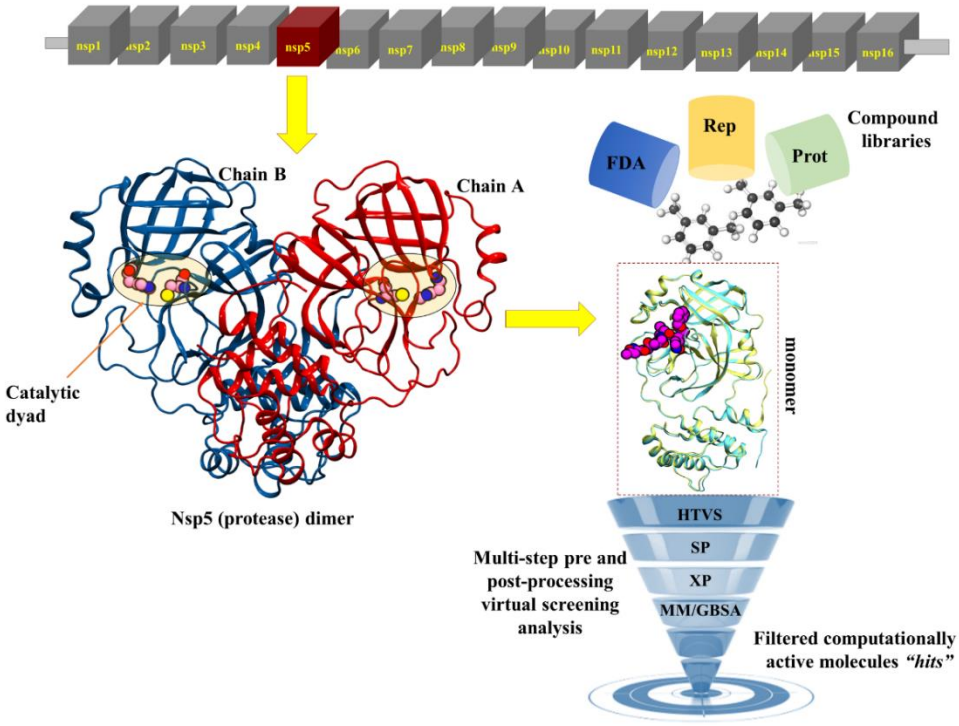
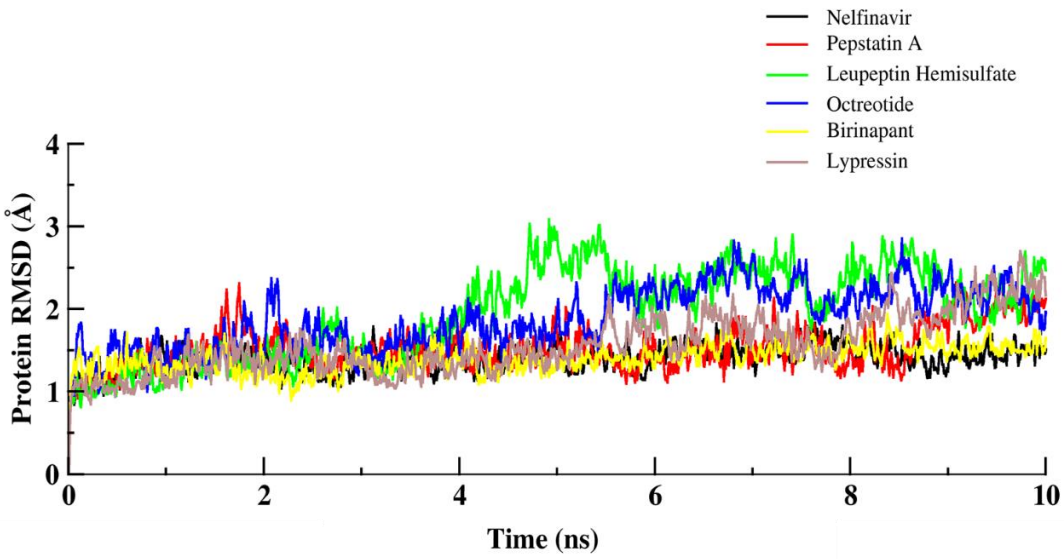
Supplementary Figures:



Supplementary Figure 1: The schematic representation of non-structural proteins of SARS-CoV-2. The targeted protein M^{pro} (main protease) is shown in red block. The modelled dimer was created. The crystal monomer 6LU7 was used for virtual screening and other post-processing analysis. **Rep** and **Prot** are repurpose and protease libraries.



Supplementary Figure 2: Protein RMSD for the top 6 hits for 10ns MD simulation.

Supplementary Table 1: List of contributions from different components to the total Prime MM/GBSA ΔG_{bind} (kcal/mol) calculated for top molecules and controls from equilibrated MD trajectory.

Molecules	**MMGBSA ΔG_{bind} Coulomb[a] (kcal/mol)**	**MMGBSA ΔG_{bind} Covalent[b] (kcal/mol)**	**MMGBSA ΔG_{bind} Hbond[c] (kcal/mol)**	**MMGBSA ΔG_{bind} Lipo[d] (kcal/mol)**	**MMGBSA ΔG_{bind} Packing[e] (kcal/mol)**	**MMGBSA ΔG_{bind} Solv GB[f] (kcal/mol)**	**MMGBSA ΔG_{bind} vdW[g] (kcal/mol)**	**Prime MMGBSA ΔG_{bind} Total[h] (kcal/mol)**
N3	-9.96	1.40	-2.49	-14.05	0	25.45	-59.48	-59.13
13b	-16.66	4.66	-1.37	-15.68	-1.7	27.21	-65.10	-68.64
Nelfinavir	-60.66	3.81	-1.44	-15.94	-2.35	58.86	-41.66	-59.38
Pepstatin A	-2.27	4.96	-2.49	-16.9	0	9.21	-66.78	-74.27
Leupeptin Hemisulfate	-111.7	3.22	-3.89	-9.84	0	115.46	-50.17	-56.92
Octreotide	-38.81	3.69	-4.53	-14.28	-1.94	42.76	-51.61	-64.72
Birinapant	-45.15	11.03	-2.5	-17.93	-3.79	49.16	-65.86	-75.04
Lypressin	-100.29	8.99	-6.16	-18.49	-0.63	88.03	-84.05	-112.60

[a]Coulomb energy

[b]Covalent binding energy

[c]Hydrogen bonding correction

[d]Lipophilic energy

[e]Pi-pi packing correction

[f]Generalised born electrostatic solvation energy

[g]Van der Waals energy

[h]Total binding free energy