Supporting Materials

# Drug repurposing: Dipeptidyl peptidase IV (DPP4) inhibitors as potential agents to treat SARS-CoV-2 (2019-nCov) infection

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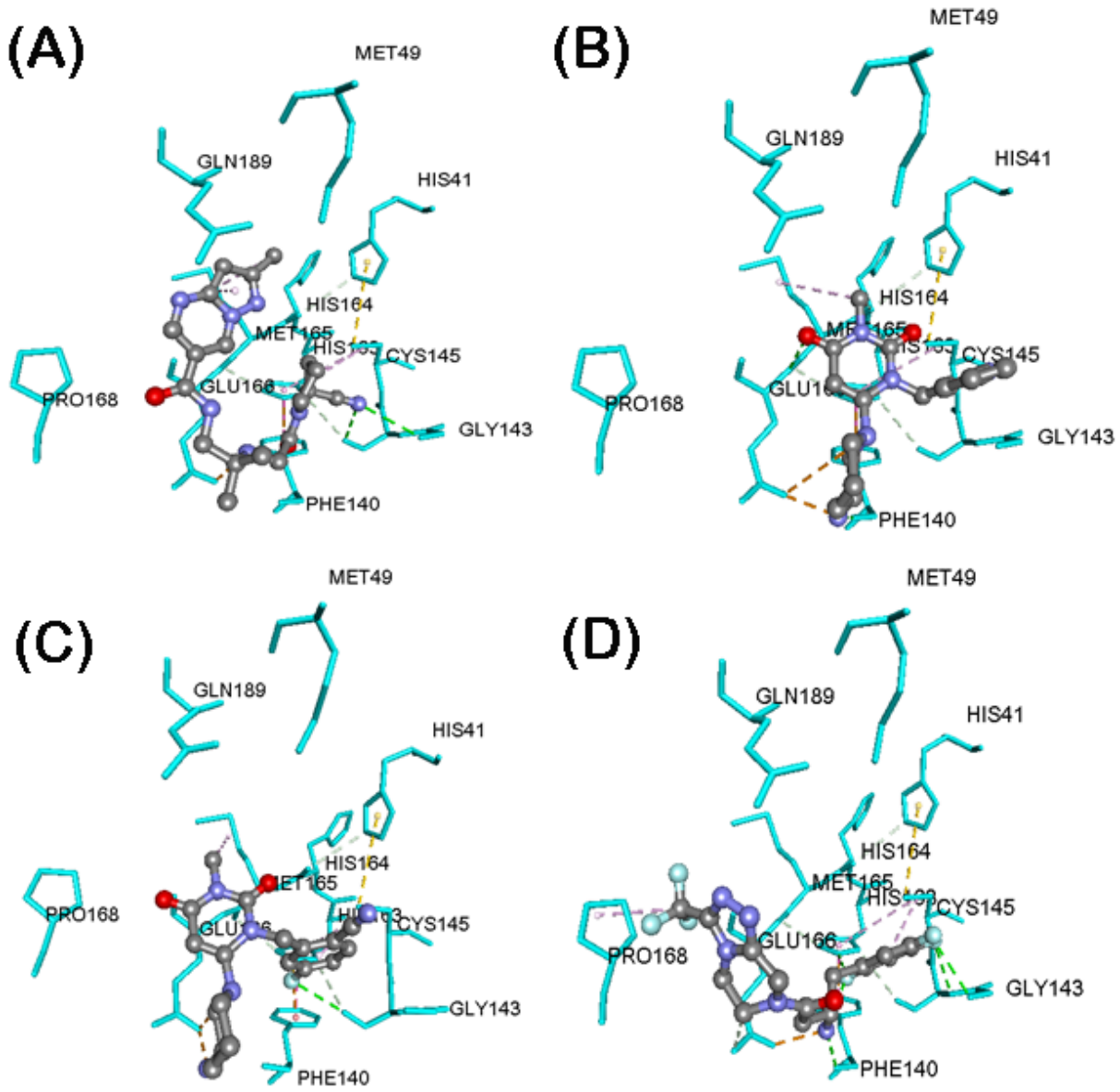


**Figure S1.** Binding modes of DPP4 inhibitors anagliptin (A), alogliptin (B), trelagliptin (C) and sitagliptin (D) in the SARS-CoV-2 $M^{pro}$ protomer (PDB ID: 6Y2F). Hydrogen atoms are not shown to enhance clarity.

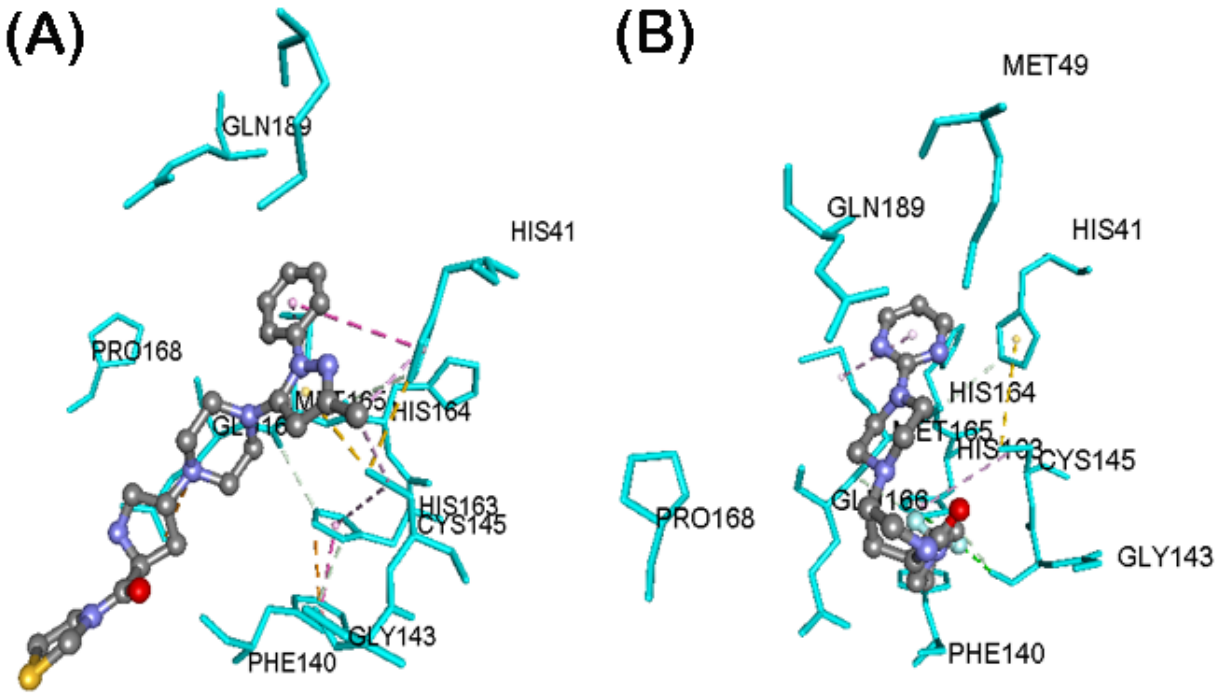


**Figure S2.** Binding modes of DPP4 inhibitors teneligliptin (A) and gosogliptin (B) in the SARS-CoV-2 $M^{pro}$ protomer (PDB ID: 6Y2F). Hydrogen atoms are not shown to enhance clarity.

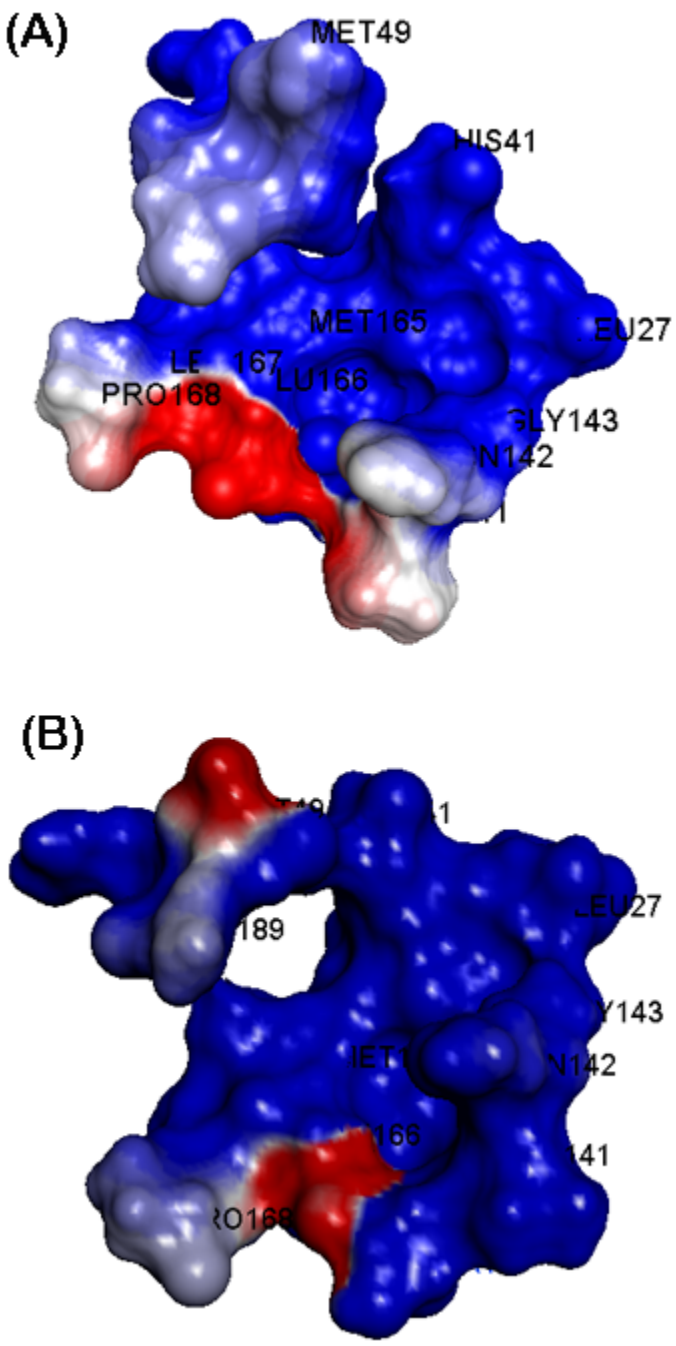


**Figure S3.** (A) Electrostatic surface potential map of SARS-CoV-2 $M^{pro}$ protomer (PDB ID: 6Y2F) and (B) dimer (PDB ID: 6Y2G). Blue and red regions represent positive and negative surface respectively.

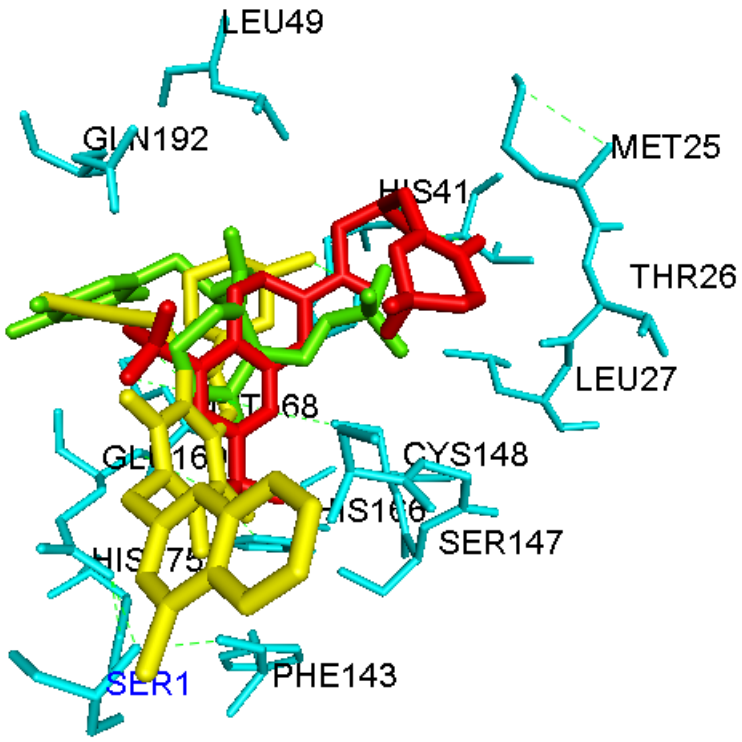


**Figure S4.** Binding modes of DPP4 inhibitors gemigliptin (red stick cartoon), linagliptin (yellow stick cartoon) and evogliptin (green stick cartoon) in the MERS-CoV $3CL^{pro}$ dimer (PDB ID: 4YLU). Hydrogen atoms are not shown to enhance clarity.

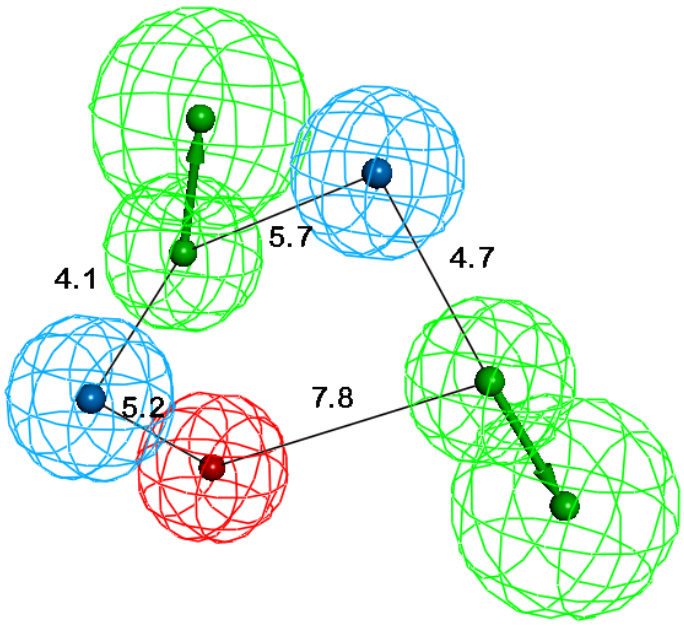


**Figure S5.** Pharmacophore model to design reversible, noncovalent SARS-CoV-2 $M^{pro}$ dimer inhibitors based on the docked poses of DPP4 inhibitors - gemigliptin, linagliptin and evogliptin. Green contours represent hydrogen bond acceptors (HBA), blue contours represent hydrophobic aliphatic (HPA) groups and red contour represents polarizable charged (POS) group. Distance parameters are provided in Angstrom units (Å).

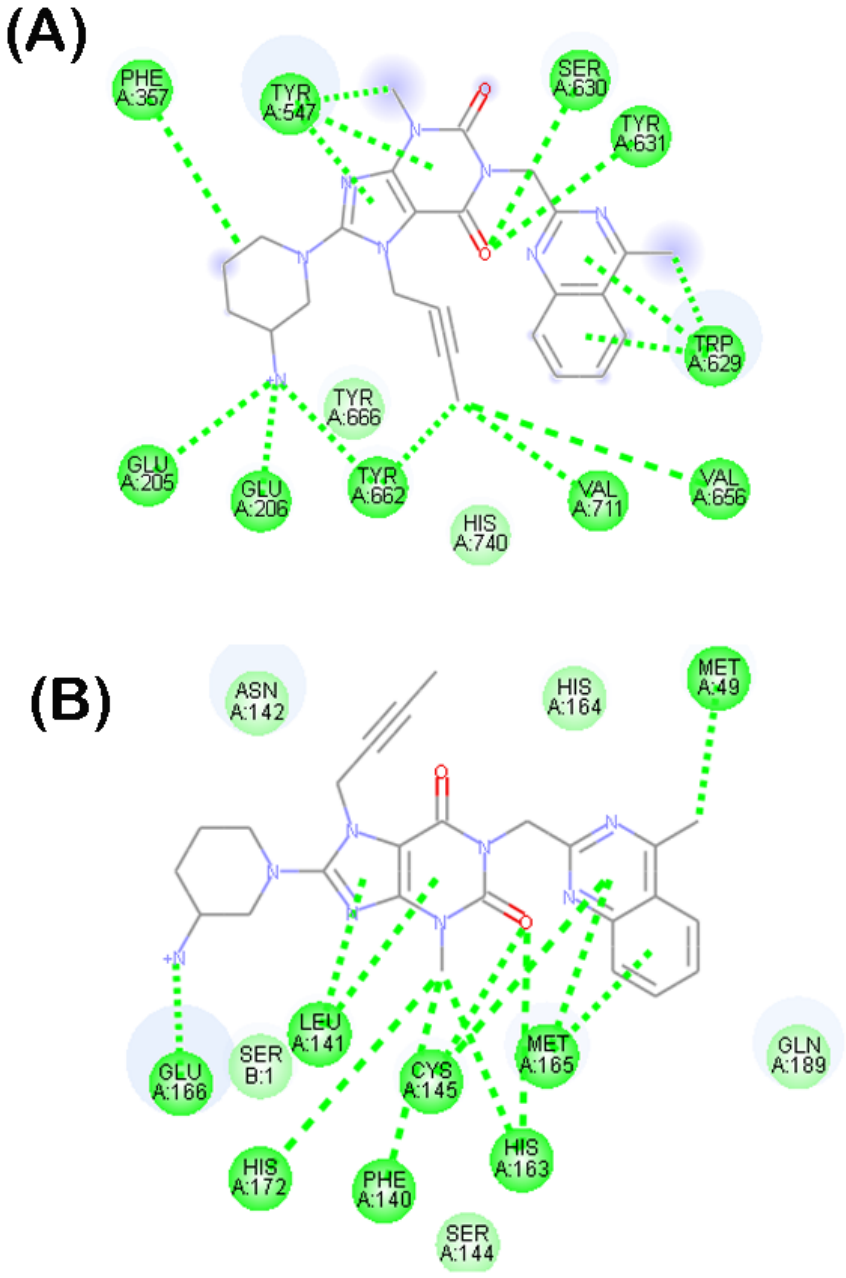


**Figure S6.** (A) 2D Interaction map of linagliptin in the active site of the serine protease DPP4 dimer (PDB ID: 2RGU). (B) 2D Interaction map of linagliptin in the active site of the cysteine protease SARS-CoV-2 $M^{pro}$ dimer (PDB ID: 6Y2G). Hydrogen atoms are not shown to enhance clarity.

**Table S1:** Physicochemical properties of DPP4 inhibitors and the SARS-CoV-2 $M^{pro}$ dimer inhibitor **1**

| Compound | No. of H-bond [1] | | No. of rotatable bonds[2] | No. of aromatic rings[3] | Polar surface area (PSA in Å$^2$)[4] | Molecular weight | Molecular volume (Å$^3$)[5] | AlogP [6] |
|---|---|---|---|---|---|---|---|---|
| | Donors | Acceptors | | | | | | |
| Vildagliptin | 2 | 3 | 3 | 0 | 0.257 | 289.37 | 254.16 | –1.05 |
| Saxagliptin | 2 | 3 | 2 | 0 | 0.299 | 315.41 | 261.36 | –0.73 |
| Anagliptin | 2 | 5 | 6 | 2 | 0.281 | 383.44 | 311.10 | –1.85 |
| Alogliptin | 2 | 3 | 3 | 1 | 0.264 | 339.39 | 271.31 | –1.29 |
| Trelagliptin | 2 | 3 | 3 | 1 | 0.257 | 357.38 | 283.66 | –1.08 |
| Sitagliptin | 1 | 3 | 5 | 2 | 0.204 | 407.31 | 289.14 | 0.92 |
| Linagliptin | 1 | 6 | 5 | 4 | 0.230 | 472.54 | 380.38 | 1.71 |
| Gemigliptin | 1 | 4 | 6 | 1 | 0.204 | 489.36 | 336.82 | 0.28 |
| Tenegliptin | 2 | 5 | 4 | 2 | 0.191 | 426.57 | 350.54 | 0.35 |
| Omarigliptin | 2 | 4 | 3 | 2 | 0.266 | 398.42 | 300.12 | –1.26 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Evogliptin | 2 | 3 | 7 | 1 | 0.200 | 401.42 | 316.93 | 0.225 |
| Gosogliptin | 1 | 5 | 3 | 1 | 0.186 | 366.40 | 282.63 | –1.06 |
| **1** | 4 | 7 | 14 | 1 | 0.268 | 593.67 | 474.71 | 1.02 |

[1] Number of hydrogen bond donors/acceptors were calculated using *Discovery Studio Structure-Based-Design* (BIOVIA Inc) program using CHARMm force field. [2] Number of rotatable bonds, [3] Number of aromatic rings, [4] Polar surface area and [5] Molecular volume were calculated using the *Discovery Studio Structure-Based-Design* (BIOVIA Inc) program after energy minimization. [6] AlogP was calculated using CHARMm force field with the *Discovery Studio Structure-Based-Design* (BIOVIA Inc) program.