Supplementary materials for

Prediction of novel inhibitors of the main protease (M-pro) of SARS-CoV-2 through consensus docking and drug reposition

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Table S1. Summary of PDB codes for SARS-CoV-2 M-pro (updated on 30.03.20).

Total structures: 87

Free-form (4)
6M03, 6Y2E, 6Y84, 6YB7

M-pro/inhibitor complex (63)

Covalently bound to M-pro through Cys145 (43)

Covalent inhibitor (4)
6LU7, 6Y2F, 6Y2G, 6Y7M

Covalent fragment (39)
5REJ, 5REK, 5REL, 5REM, 5REN, 5REO, 5REP, 5RER, 5RES, 5RET, 5REU, 5REV, 5REW, 5REY, 5RFH, 5RFI, 5RFJ, 5RFK, 5RFL, 5RFM, 5RFN, 5RFO, 5RFP, 5RFQ, 5RFR, 5RFS, 5RFT, 5RFU, 5RFV, 5RFW, 5RFX, 5RFY, 5RFZ, 5RG0, 5RG2, 5RG3

Non-covalently bound to M-pro (20)

Non-covalent inhibitor (1)
6W63

Non-covalent fragment (19)
5R7Y, 5R7Z, 5R80, 5R81, 5R82, 5R83, 5R84, 5RE4, 5RE9, 5REB, 5REH, 5REZ, 5RF1, 5RF2, 5RF3, 5RF6, 5RF7, 5RFE, 5RG1

Other interactions (20)

Fragment in the dimer interface (2)
5RF0, 5RFA

Fragment on the surface (3)
5REC, 5REE, 5RF5

Fragment in crystal contacts (15)
5RED, 5RE5, 5RE6, 5RE7, 5RE8, 5REA, 5REF, 5REG, 5REI, 5RF4, 5RF8, 5RF9, 5RFB, 5RFC, 5RFD
Table S2. Summary of *in vitro* data for known SARS-CoV-2 M-pro inhibitors (updated on 10.05.20).

| Drug name          | IC50 (μM)       | Inhibition index [5] | Glide score (kcal/mol) | FRED score (kcal/mol) | AutoDock Vina score (kcal/mol) | RMSD range (Å) |
|--------------------|-----------------|----------------------|------------------------|-----------------------|--------------------------------|-----------------|
| 11a                | 0.05 ± 0.005 [3]| -8.16                | -13.05                 | -7.50                 | [0.64-2.10]                     |                 |
| 11b                | 0.04 ± 0.002 [3]| -6.26                | -10.68                 | -8.80                 | [0.93-4.56]                     |                 |
| 11r                | 0.18 ± 0.02 [4] | -7.48                | -12.65                 | -6.50                 | [1.68-4.40]                     |                 |
| 13a                | 2.39 ± 0.63 [4] | -5.30                | -0.52                  | -7.70                 | [2.10-5.30]                     |                 |
| 13b                | 0.67 ± 0.18 [4] | -5.23                | -0.35                  | -8.40                 | [3.06-4.99]                     |                 |
| Atazanavir         | 7.53 ± 0.31 [1] | -4.28                | 1.31                   | -6.00                 | [4.40-9.42]                     |                 |
| Candesartan        | 9.45 ± 0.73 [1]| 1.166                | -4.02                  | -3.25                 | [1.74-4.35]                     |                 |
| Candesartan Cilexetil | 2.78 ± 0.31 [1]| -6.09                | -3.61                  | -7.00                 | [5.47-6.53]                     |                 |
| Carmofur           | 1.82 ± 0.06 [2]| 0.054                | -4.99                  | -4.71                 | -6.40                          | [0.99-2.64]     |
| Chloroquine        | 7.16 ± 0.23 [1]| 1.351                | -4.51                  | -6.62                 | -5.40                          | [2.69-4.43]     |
| Cimetidine         | ~ 50 [1]        | 0.014                | -1.87                  | -4.26                 | -5.00                          | [1.27-2.55]     |
| Cinanserin         | 124.93 ± 7.89 [2]| -6.15              | -7.94                  | -6.10                 | [2.16-4.53]                     |                 |
| Dipyridamole       | 0.55 ± 0.01 [1]| 0.086                | -4.60                  | -4.36                 | -6.60                          | [1.50-2.24]     |
| Disulfiram         | 9.35 ± 0.18 [2]| -0.116              | N/A                    | N/A                   | N/A                            | N/A             |
|                    | 4.67 ± 0.42 [1]|                      |                        |                       |                                |                 |
| Ebselen            | 0.67 ± 0.09 [2]| 0.271                | N/A                    | N/A                   | N/A                            | N/A             |
| Indinavir          | 43.13 ± 2.79 [1]| 0.382              | -6.62                  | 1.69                  | -8.00                          | [4.46-5.54]     |
| Maribavir          | ~ 50 [1]        | -6.21                | -5.87                  | -8.10                 | [1.20-2.32]                     |                 |
| Montelukast        | 7.29 ± 0.54 [1]| 0.339                | -5.29                  | -2.76                 | -8.00                          | [3.06-7.17]     |
| N3                 | (a) [2]         | -6.58                | 3.16                   | -8.50                 | [4.47-7.82]                     |                 |
| Drug               | IC50 ± SEM [Ref] | k<sub>obs</sub>/[I] | log<sub>10</sub> IC50 | log<sub>10</sub> IC50 | log<sub>10</sub> IC50 | Range |
|-------------------|------------------|---------------------|----------------------|----------------------|----------------------|-------|
| Omeprazole        | 20.96 ± 0.95 [1] | 1.249               | -6.18                | -4.75                | -6.20                | [1.38-2.56] |
| Oxytetracycline   | 15.15 ± 0.85 [1] | 0.403               | -5.06                | -3.16                | -6.20                | [1.35-2.21] |
| PX-12             | 21.39 ± 7.06 [2] | -4.58               | -5.02                | -4.20                | 0.91-2.49            |       |
| Roxatidine acetate| 20.31 ± 0.37 [1] | 0.109               | -4.20                | -3.90                | -5.70                | [3.98-6.36] |
| Shikonin          | 15.75 ± 8.22 [2] | -5.11               | -5.62                | -6.50                | 0.91-1.29            |       |
| Sulfacetamide     | ~ 50 [1]         | 0.002               | -3.78                | -4.51                | -5.10                | [1.37-1.63] |
| Tideglusib        | 1.55 ± 0.30 [2]  | -5.75               | -6.00                | -6.70                | 1.21-1.99            |       |
| Ubenimex          | 8.93 ± 1.21 [1]  | 0.012               | -4.83                | -5.63                | -5.60                | [2.08-3.24] |
| Valganciclovir    | 16.66 ± 0.87 [1] | 0.237               | -5.42                | -4.91                | -6.50                | [3.29-4.04] |

(a) k<sub>obs</sub>/[I]=11.300M<sup>-1</sup>s<sup>-1</sup>

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RMSD: 3.06 to 4.99
Atazanavir
RMSD: 1.74 to 4.35
Candesartan
RMSD: 5.47 to 6.53
Candesartan Cilexetil
Carmofur

RMSD: 0.99 to 2.64

Chloroquine

RMSD: 2.69 to 4.43

Cimetidine

RMSD: 1.27 to 2.55

Cinanserin

RMSD: 2.16 to 4.53
Dipyridamole

Disulfiram

Ebselen

Indinavir

RMSD: 1.50 to 2.24

RMSD: 4.46 to 5.54
Maribavir

Montelukast

N3

Omeprazole
Oxytetracycline

PX-12

Roxatidine acetate

Shikonin

RMSD: 1.35 to 2.21

RMSD: 0.91 to 2.49

RMSD: 3.98 to 6.36

RMSD: 0.91 to 1.29
**Figure S1.** Each panel shows the 2D structure and the lowest-RMSD triplet for each known M-pro inhibitor in Table S2.