Supporting Information

An *in-silico* analysis of ivermectin interaction with potential SARS-CoV-2 targets and host nuclear importin α

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**Table S1.** Non-bond interactions of ivermectin with 15 potential COVID-19 targets and importin α.

| S.No. | Target                        | Hydrogen bond interactions | Hydrophobic interactions |
|-------|-------------------------------|----------------------------|--------------------------|
|       |                               | Residues | Distance | Type  | Residues | Distance |
| 1.    | Main Protease                 | Gln189   | 1.67     | Alkyl | Pro168   | 4.88     |
|       |                               |          |          |       | Met165   | 3.76     |
|       |                               |          |          |       | Pro168   | 4.07     |
|       |                               |          |          |       | Met49    | 4.11     |
|       |                               |          |          |       | Met49    | 5.34     |
|       |                               |          |          |       | Leu50    | 4.49     |
|       |                               |          |          | π-Alkyl| His41    | 3.96     |
| 2.    | Papain-like protease          | Tyr264   | 1.88     | Alkyl | Pro248   | 5.47     |
|       |                               | Tyr268   | 2.17     | Alkyl | Pro248   | 4.87     |
|       |                               |          |          |       | Met208   | 4.90     |
|       |                               |          |          |       | Pro247   | 4.52     |
|       |                               |          |          |       | Pro247   | 5.10     |
|       |                               |          |          |       | Pro248   | 4.47     |
|       |                               |          |          | π-Alkyl| Tyr268   | 5.21     |
|       |                               |          |          | π-Alkyl| Tyr268   | 4.71     |
| 3.    | RdRp (RTP site)               | Ser549   | 1.87     | Alkyl | Pro620   | 4.90     |
|       |                               | Lys551   | 2.53     | Alkyl | Lys798   | 4.69     |
|       |                               | Lys621   | 2.18     | π-Alkyl| U20      | 5.31     |
| 4.    | RdRp (RNA site)               | Lys545   | 2.71     | Alkyl | Ala688   | 4.10     |
|       |                               | Gln573   | 1.87     | Alkyl | Ala688   | 3.70     |
|       |                               | Ala685   | 1.85     | Alkyl | Ala688   | 4.56     |
|       |                               |          |          |       | Ala688   | 4.73     |
|       |                               |          |          |       | Val557   | 4.03     |
|       |                               |          |          |       | Leu576   | 4.79     |
|       |                               |          |          |       | Lys577   | 4.30     |
| 5.    | Helicase (Nsp13; ADP site)    | Gln537   | 1.98     | Alkyl | Ala312   | 4.40     |
|       |                               | Ser539   | 2.81     | Alkyl | Ala313   | 4.38     |
|       |                               | Glu540   | 1.77     | Alkyl | Ala316   | 4.30     |
|       |                               | Glu540   | 2.01     | Alkyl | Lys320   | 5.29     |
|       |                               |          |          |       | Lys320   | 4.12     |
| 6.    | Helicase (Nsp13; NCB site)    | Arg212   | 2.81     | Alkyl | Arg178   | 4.97     |
|       |                               | Arg339   | 2.58     | Alkyl | Arg178   | 4.64     |
|       |                               | Arg339   | 2.61     | Alkyl | Ala312   | 4.96     |
|       |                               |          |          |       | Arg178   | 4.79     |
|       |                               |          |          |       | Cys309   | 4.50     |
|       |                               |          |          |       | Met378   | 4.07     |
|       |                               |          |          | π-Alkyl| Hie311   | 5.31     |
| 7.    | Nsp14 (ExoN)                  | Gln145   | 2.52     | Alkyl | Ala187   | 4.99     |
|       |                               |          |          |       | Ala187   | 4.24     |
|   |   |   |   |
|---|---|---|---|
| 8. | Nsp14 (N7-MTase) |   |   |
|   |   | Alkyl | Ala187 | 4.26 |
|   |   | Alkyl | Pro141 | 4.79 |
|   |   | Alkyl | Pro142 | 5.25 |
|   |   | Alkyl | Pro141 | 4.17 |
|   |   | π-Alkyl | His95 | 4.96 |
|   |   | π-Alkyl | Phe146 | 4.89 |
|   |   | π-Alkyl | Phe146 | 4.35 |
|   |   | π-Alkyl | Phe146 | 5.31 |
|   |   | π-Alkyl | Trp186 | 4.74 |
|   |   | π-Alkyl | Phe190 | 5.22 |
| 9. | Spike RBD | Gln493 | 2.04 | Alkyl | Leu455 | 4.87 |
|   |   | Ser494 | 2.10 | Alkyl | Leu455 | 5.10 |
|   |   | Glu484 | 2.10 | π-Alkyl | Tyr449 | 4.88 |
|   |   |   |   | π-Alkyl | Tyr449 | 5.09 |
|   |   |   |   | π-Alkyl | Phe456 | 5.02 |
|   |   |   |   | π-Alkyl | Tyr505 | 5.40 |
| 10. | Spike monomer |   |   | Alkyl | Arg403 | 4.63 |
|   |   |   |   | Alkyl | Val350 | 4.64 |
|   |   |   |   | Alkyl | Pro507 | 4.17 |
| 11. | Spike trimer | Asn334 | 2.49 | Alkyl | Pro337 | 4.21 |
|   |   | Arg357 | 3.08 | Alkyl | Val171 | 3.95 |
|   |   | Arg357 | 3.05 | π-Alkyl | Phe168 | 5.05 |
| 12. | S2 (post fusion state) | Leu1166 | 2.72 | Alkyl | Ala972 | 5.42 |
|   |   | Ala972 | 3.02 |   |   |   |
| 13. | N protein (C domain) | Arg73 | 2.30 | Alkyl | Ala90 | 3.72 |
|   |   | Gln35 | 2.47 | Alkyl | Ala90 | 5.19 |
|   |   | Gln35 | 2.34 | Alkyl | Ala90 | 4.27 |
|   |   | Gln35 | 2.58 | π-Alkyl | Trp84 | 4.70 |
|   |   | Thr36 | 2.50 | π-Alkyl | Trp84 | 3.94 |
|   |   |   |   | π-Alkyl | Trp84 | 5.28 |
|   |   |   |   | π-Alkyl | Trp84 | 5.07 |
| 14. |   |   |   | Alkyl | Ala50 | 3.77 |
|                | Np9  | 15. Nsp9 | 16 Importin α |
|----------------|------|----------|--------------|
| N protein (N   | Val7 | Val7     | Trp231       |
| domain)        | (Arg| (Alkyl  | Arg227       |
|                | 52) | (Tyr69)  | Arg227       |
|                | 4.28 | 5.31     | 5.24         |
|                | 4.31 |          | 4.21         |
|                | 4.70 |          | 5.11         |
|                | 3.85 |          | 5.44         |
|                | 4.49 |          | 5.18         |
|                | 4.53 |          | 4.81         |
|                | 4.36 |          | 4.50         |
|                | 4.50 |          | 4.90         |
|                | 4.90 |          | 5.37         |
|                | 4.87 |          | 4.87         |
Table S2. Results of docking and MM/GBSA computations of ivermectin in complex with 15 potential COVID-19 targets and importin α.

| S.N | Targets       | Docking models (Top 10) | Δ\(G_{\text{Bind}}\) (Auto Dock Vina) | MM/GBSA                                      |
|-----|---------------|-------------------------|----------------------------------------|----------------------------------------------|
|     |               |                         | \(\Delta G_{\text{Bind}}\)       | \(\Delta G_{\text{Coil}}\) | \(\Delta G_{\text{Hbond}}\) | \(\Delta G_{\text{Lipo}}\) | SolvGB | \(\Delta G_{\text{vdw}}\) | Lig SE |
| 1   | Main Protease | 1M1                     | -7.2                                 | -68.81                                      | -14.75                                      | -0.70                                      | -38.62 | 28.05 | -48.83 | 22.05 |
|     |               | 1M2                     | -6.8                                 | -79.35                                      | -10.16                                      | -0.44                                      | -53.80 | 28.52 | -59.49 | 34.37 |
|     |               | 1M3                     | -6.5                                 | -64.22                                      | -7.89                                       | -0.54                                      | -46.78 | 29.52 | -55.04 | 42.12 |
|     |               | 1M4                     | -6.3                                 | -53.20                                      | -16.79                                      | -0.85                                      | -38.61 | 34.87 | -50.42 | 28.50 |
|     |               | 1M5                     | -6.3                                 | -57.39                                      | -11.19                                      | -1.09                                      | -22.75 | 23.57 | -42.10 | 25.07 |
|     |               | 1M6                     | -6.3                                 | -63.57                                      | -14.31                                      | -0.37                                      | -37.64 | 27.09 | -46.96 | 16.29 |
|     |               | 1M7                     | -6.2                                 | -67.38                                      | -7.85                                       | -0.72                                      | -41.92 | 25.09 | -54.29 | 13.88 |
|     |               | 1M8                     | -6.1                                 | -52.35                                      | -3.32                                       | -0.41                                      | -36.94 | 29.35 | -47.20 | 12.88 |
|     |               | 1M9                     | -6.1                                 | -52.57                                      | -0.02                                       | -0.57                                      | -40.05 | 23.80 | -41.10 | 12.58 |
|     |               | 1M10                    | -6.1                                 | -43.31                                      | -6.39                                       | -0.36                                      | -27.48 | 27.41 | -43.44 | 34.20 |
| 2   | Papain-like   | 2M1                     | -7.1                                 | -18.31                                      | 18.30                                       | -1.15                                      | -40.19 | 14.80 | -36.38 | 41.06 |
|     | protease      | 2M2                     | -6.8                                 | -52.49                                      | -1.60                                       | -0.71                                      | -47.57 | 14.55 | -31.27 | 33.92 |
|     |               | 2M3                     | -6.7                                 | -60.61                                      | -7.97                                       | -0.44                                      | -52.07 | 25.94 | -42.95 | 28.76 |
|     |               | 2M4                     | -6.7                                 | -25.93                                      | 4.56                                        | -0.08                                      | -33.07 | 39.74 | -42.11 | 7.11  |
|     |               | 2M5                     | -6.6                                 | -43.53                                      | 5.53                                        | -1.08                                      | -39.01 | 39.42 | -42.59 | 15.51 |
|     |               | 2M6                     | -6.6                                 | -52.88                                      | -1.49                                       | 0.00                                       | -43.78 | 30.41 | -38.90 | 1.18  |
|     |               | 2M7                     | -6.5                                 | -43.35                                      | -3.25                                       | -1.54                                      | -43.52 | 29.35 | -38.86 | 20.73 |
|     |               | 2M8                     | -6.5                                 | -50.95                                      | 7.44                                        | -0.71                                      | -49.28 | 17.29 | -40.45 | 22.85 |
|     |               | 2M9                     | -6.4                                 | -36.14                                      | 5.60                                        | -0.83                                      | -34.69 | 33.57 | -44.13 | 20.11 |
|     |               | 2M10                    | -6.2                                 | -31.73                                      | -3.82                                       | -0.77                                      | -29.73 | 30.71 | -36.88 | 9.42  |
| 3   | RdRp (RTP site) | 3M1                     | -9.9                                 | 24.72                                       | -14.81                                      | -1.56                                      | -30.08 | 87.47 | -51.21 | 47.42 |
|     |               | 3M2                     | -9.6                                 | -29.10                                      | 3.94                                        | -1.23                                      | -27.33 | 61.01 | -68.92 | 19.48 |
|     |               | 3M3                     | -9.6                                 | 21.18                                       | -25.01                                      | -1.05                                      | -36.31 | 88.74 | -29.70 | 35.68 |
|     |               | 3M4                     | -9.6                                 | 22.81                                       | 21.83                                       | -0.85                                      | -27.23 | 52.54 | -44.43 | 39.19 |
|     |               | 3M5                     | -8.3                                 | 19.86                                       | 11.50                                       | -0.91                                      | -17.42 | 57.81 | -50.43 | 54.91 |
|     |               | 3M6                     | -8.3                                 | 25.65                                       | 4.03                                        | -1.39                                      | -41.23 | 55.95 | -68.32 | 35.62 |
|     |               | 3M7                     | -8.2                                 | 9.32                                        | -13.21                                      | -1.08                                      | -5.28  | 55.71 | -38.28 | 35.13 |
|     |               | 3M8                     | -8.1                                 | 16.16                                       | -27.62                                      | -0.84                                      | -33.08 | 97.56 | -45.68 | 45.01 |
|     |               | 3M9                     | -8.1                                 | 42.57                                       | -28.13                                      | -1.09                                      | -23.93 | 79.00 | -69.29 | 13.18 |
|     |               | 3M10                    | -8.1                                 | 42.43                                       | -0.30                                       | -1.26                                      | -23.05 | 95.62 | -50.92 | 51.14 |
| 4   | RdRp (RNA site) | 4M1                     | -8.9                                 | -38.28                                      | -1.80                                       | -0.48                                      | -41.27 | 28.94 | -43.52 | 32.69 |
|     |               | 4M2                     | -8.3                                 | -47.86                                      | -6.81                                       | -0.99                                      | -32.66 | 36.19 | -47.13 | 15.00 |
|     |               | 4M3                     | -8.2                                 | -53.11                                      | 2.46                                        | -0.46                                      | -35.35 | 23.54 | -47.18 | 14.40 |
|     |               | 4M4                     | -8.2                                 | -50.75                                      | -11.05                                      | -0.45                                      | -36.64 | 33.00 | -54.49 | 16.44 |
|     |               | 4M5                     | -8.2                                 | -70.06                                      | -22.56                                      | -0.89                                      | -37.87 | 30.74 | -47.33 | 12.87 |
|     |               | 4M6                     | -8.2                                 | -66.03                                      | -3.07                                       | -0.15                                      | -39.75 | 29.33 | -55.54 | 5.91  |
|     |               | 4M7                     | -7.9                                 | -45.50                                      | -1.77                                       | -0.46                                      | -41.99 | 32.17 | -46.89 | 20.33 |
|     |               | 4M8                     | -7.7                                 | -62.35                                      | -5.06                                       | -0.19                                      | -40.79 | 20.05 | -40.85 | 6.88  |
|   | 4M9 | 4M10 | 5M1 | 5M2 | 5M3 | 5M4 | 5M5 | 5M6 | 5M7 | 5M8 | 5M9 | 5M10 | 5 Helicase (Nsp13; ADP site) |
|---|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------------------------|
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 6 |     |      |     |     |     |     |     |     |     |     |     |     | 6 Helicase (Nsp13; NCB site) |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 7 |     |      |     |     |     |     |     |     |     |     |     |     | 7 Nsp14 (ExoN)              |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 8 |     |      |     |     |     |     |     |     |     |     |     |     | 8 Nsp14 (N7-MTase)         |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 9 |     |      |     |     |     |     |     |     |     |     |     |     | 9 Spike RBD                |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |

|   | 4M9 | 4M10 | 5M1 | 5M2 | 5M3 | 5M4 | 5M5 | 5M6 | 5M7 | 5M8 | 5M9 | 5M10 | 5 Helicase (Nsp13; ADP site) |
|---|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------------------------|
|   | -7.7 | -7.7 | -8.2 | -8.1 | -7.4 | -7.4 | -7.2 | -7 | -6.9 | -6.9 | -6.9 | -6.9 |                             |
|   | -66.23 | -59.82 | -51.45 | -58.36 | -41.60 | -43.57 | -42.84 | -43.91 | -30.56 | -32.24 | -34.07 | -52.34 |                             |
|   | 4.63 | -1.43 | 3.58 | -14.00 | 0.07 | -4.76 | -1.62 | 0.88 | -8.96 | 0.44 | -1.23 | -9.45 |                             |
|   | -0.53 | -0.26 | -0.47 | -1.08 | -1.05 | -0.94 | -0.62 | -0.79 | -1.16 | -1.28 | -1.33 | -1.38 |                             |
|   | -45.18 | -46.53 | -37.04 | -44.85 | -25.70 | -20.96 | -30.25 | -28.14 | -21.45 | -27.50 | -13.37 | -33.29 |                             |
|   | 23.45 | 33.43 | 25.60 | 40.20 | 25.30 | 26.38 | 33.94 | 23.51 | 34.31 | 29.49 | 25.09 | 29.46 |                             |
|   | -52.66 | -59.34 | -47.67 | -47.14 | -46.38 | -41.90 | -43.98 | -42.16 | -32.69 | -48.16 | -40.68 | -41.89 |                             |
|   | 9.60 | 17.73 | 10.53 | 20.30 | 15.40 | 8.24 | 15.09 | 4.90 | 25.67 | 22.49 | 9.57 | 8.68 |                             |

|   |     |      |     |     |     |     |     |     |     |     |     |     | 6 Helicase (Nsp13; NCB site) |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 7 |     |      |     |     |     |     |     |     |     |     |     |     | 7 Nsp14 (ExoN)              |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 8 |     |      |     |     |     |     |     |     |     |     |     |     | 8 Nsp14 (N7-MTase)         |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 9 |     |      |     |     |     |     |     |     |     |     |     |     | 9 Spike RBD                |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |

|   | 4M9 | 4M10 | 5M1 | 5M2 | 5M3 | 5M4 | 5M5 | 5M6 | 5M7 | 5M8 | 5M9 | 5M10 | 5 Helicase (Nsp13; ADP site) |
|---|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------------------------|
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 6 |     |      |     |     |     |     |     |     |     |     |     |     | 6 Helicase (Nsp13; NCB site) |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 7 |     |      |     |     |     |     |     |     |     |     |     |     | 7 Nsp14 (ExoN)              |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 8 |     |      |     |     |     |     |     |     |     |     |     |     | 8 Nsp14 (N7-MTase)         |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
| 9 |     |      |     |     |     |     |     |     |     |     |     |     | 9 Spike RBD                |
|   |     |      |     |     |     |     |     |     |     |     |     |     |                             |
|       | 9M4  | 9M5  | 9M6  | 9M7  | 9M8  | 9M9  | 9M10 | 10M1 | 10M2 | 10M3 | 10M4 | 10M5 | 10M6 | 10M7 | 10M8 | 10M9 | 10M10 |
|-------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-------|
| 10    | -6.8 | -6.7 | -6.4 | -6.3 | -6.2 | -6.1 | -5.8 | -5.5 | -5.5 | -5.5 | -5.4 | -5.4 | -5.3 | -5.3 | -5.2 | -5.2 | -5.2 |
| Spike | -44.81| -69.13| -41.75| -53.83| -52.18| -50.37| -48.26| -55.86| -19.44| -43.82| -55.19| -36.13| -54.61| -4.85| -29.01| -14.00| -55.30 |
| monomer| -11.13| -11.49| -0.30| 0.30 | -8.56 | -3.73 | -3.58 | -4.40 | -16.77 | -12.18 | -13.02 | -0.30 | -18.71 | 5.90 | 1.75 | 0.41 | -16.69 |
| close | -0.39 | -1.71 | -0.16 | -0.05 | -0.66 | -0.01 | -0.25 | -0.05 | -1.24 | -1.06 | -0.25 | -0.02 | -0.72 | -0.58 | -0.18 | -0.47 | -1.92 | -20.06 |
|       | -26.99| -39.45| -30.06| -37.48| -29.49| -32.47| -32.57| -39.85| -9.04  | -27.70 | -32.92 | -24.63 | -37.01 | -10.11| -22.04 | -11.45 | -32.54 |
|       | 25.76 | 24.60 | 19.32 | 14.48 | 19.94 | 16.78 | 20.11 | 17.87 | 23.55 | 19.88 | 17.14 | 12.22 | 32.33 | 3.98  | 5.34  | 8.70  | 24.58  |
|       | -35.30| -45.26| -37.66| -34.24| -31.65| -32.88| -36.46| -33.46| -13.51| -24.35| -30.20| -26.47| -38.71| -10.48| -16.68| -12.75| -33.97 |
| 11    | -8.2 | -52.79| -61.08| -52.38| -51.41| -55.82| -54.53| -71.20| -3.06 | -36.32 | -39.60| -61.34| -45.29| -29.32| -32.93| -38.38| -45.87 |
| Spike | -1.84 | -1.08 | -0.19 | -0.15 | -1.15 | 1.18  | -0.86 | -1.84 | -1.08 | -0.19 | -0.15 | -1.15 | -0.86 | 1.18  | 1.08  | -0.86 | -1.84 | -33.97 |
| trimer| -0.86 | -37.63| 22.75 | -39.60| -31.34| -45.29| -54.53| -71.20| -3.06 | -36.32 | -39.60| -61.34| -45.29| -29.32| -32.93| -38.38| -45.87 |
| open  | -28.91| -37.72| -20.74| -37.90| -39.43| -37.72| -46.38| -44.18| -30.66| -42.30 | -23.50| -48.37| -34.74| -49.10| -51.12| -48.37| -44.85 |
| 12    | -6   | -40.41| -61.08| -52.38| -51.41| -55.82| -54.53| -71.20| -3.06 | -36.32 | -39.60| -61.34| -45.29| -29.32| -32.93| -38.38| -45.87 |
| S2    | -0.32 | 1.47  | -2.92 | -3.91 | -1.00 | 1.18  | -0.86 | -1.84 | -1.08 | -0.19 | -0.15 | -1.15 | -0.86 | 1.18  | 1.08  | -0.86 | -1.84 | -33.97 |
| (post | -0.78 | -27.93| -0.19 | -0.15 | -1.15 | -0.01 | -0.86 | -1.84 | -1.08 | -0.19 | -0.15 | -1.15 | -0.86 | 1.18  | 1.08  | -0.86 | -1.84 | -33.97 |
| fusion| -22.69| -17.90| -0.22 | -28.85| -13.30| -37.05| -32.54| -22.69| -1.15 | -20.74 | -23.50| -39.43| 17.36  | -45.29| -31.34| -38.38| -45.87 |
| state | -9.36 | -39.96| -20.14| -37.90| -39.43| -37.72| -46.38| -44.18| -30.66| -42.30 | -23.50| -48.37| -34.74| -49.10| -51.12| -48.37| -44.85 |
| 13    | -6.6 | -43.08| -54.73| -33.76| -31.64| -55.04| -38.34| -40.41| 1.47  | 0.00  | -0.22 | -0.01 | -0.86 | -1.88 | -0.78 | -3.02 | -8.91 | -46.04 |
| N protein | -7.77 | -43.56| -25.14| -29.17| -28.85| -37.05| -32.54| -22.69| 1.47  | 0.00  | -0.22 | -0.01 | -0.86 | -1.88 | -0.78 | -3.02 | -8.91 | -46.04 |
| (C     | -0.50 | 24.11 | 15.14 | 27.02 | 24.59 | 12.40 | 23.92 | 18.97 | -39.96| -15.14 | -24.59 | 12.40 | -32.39 | 23.92 | -44.85| -14.87 | 23.43 |
| domain|        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |      |
| 7     |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|         | 13M9 | 13M10 | 14M1  | 14M2  | 14M3  | 14M4  | 14M5  | 14M6  | 14M7  | 14M8  | 14M9  | 14M10 |
|---------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 14      | N protein (N domain) |       |       |       |       |       |       |       |       |       |       |       |
| 15      | Nsp9 |       |       |       |       |       |       |       |       |       |       |       |
| 16      | Importin α |       |       |       |       |       |       |       |       |       |       |       |
| 8       |      |       |       |       |       |       |       |       |       |       |       |       |
| 13M9    | -5.9 | -74.91| -6.92 | -0.49 | -61.47 | 21.91 | -40.37 | 14.79 |       |       |       |       |
| 13M10   | -5.8 | -72.42| -9.56 | -0.69 | -54.56 | 26.33 | -42.68 | 18.36 |       |       |       |       |
| 14M1    | -8.2 | -54.80| -11.84| -2.62 | -34.99 | 35.80 | -50.86 | 33.29 |       |       |       |       |
| 14M2    | -8.0 | -45.67| -4.55 | -1.84 | -45.75 | 21.72 | -40.33 | 29.16 |       |       |       |       |
| 14M3    | -8.0 | -62.48| -6.83 | -1.03 | -41.21 | 24.23 | -39.69 | 14.56 |       |       |       |       |
| 14M4    | -7.7 | -52.73| -7.13 | -1.55 | -37.75 | 27.31 | -39.46 | 17.43 |       |       |       |       |
| 14M5    | -7.6 | -57.18| -0.94 | -1.74 | -41.86 | 27.04 | -47.73 | 5.46  |       |       |       |       |
| 14M6    | -7.6 | -63.69| -17.38| -1.96 | -37.56 | 34.32 | -45.23 | 24.31 |       |       |       |       |
| 14M7    | -7.5 | -53.06| -2.02 | -1.33 | -32.08 | 23.39 | -39.56 | 25.34 |       |       |       |       |
| 14M8    | -7.4 | -63.93| -25.04| -1.18 | -35.35 | 29.84 | -38.64 | 16.73 |       |       |       |       |
| 14M9    | -7.4 | -67.44| -13.89| -0.53 | -42.74 | 32.84 | -50.30 | 9.53  |       |       |       |       |
| 14M10   | -7.3 | -69.03| -3.60 | -0.11 | -54.29 | 31.69 | -58.15 | 5.48  |       |       |       |       |
| 15M1    | -5.9 | -84.70| -9.29 | -0.48 | -59.65 | 14.77 | -43.69 | 16.60 |       |       |       |       |
| 15M2    | -5.8 | -63.43| -4.59 | -0.50 | -38.36 | 10.47 | -34.39 | 8.58  |       |       |       |       |
| 15M3    | -5.6 | -51.43| -17.64| -0.77 | -32.96 | 18.49 | -26.79 | 21.47 |       |       |       |       |
| 15M4    | -5.6 | -70.78| -16.48| -0.95 | -38.69 | 13.32 | -32.88 | 8.31  |       |       |       |       |
| 15M5    | -5.6 | -73.66| -4.28 | -0.25 | -44.05 | 13.21 | -39.99 | 9.18  |       |       |       |       |
| 15M6    | -5.5 | -52.73| 0.55  | -0.11 | -29.08 | 9.00  | -39.43 | 12.51 |       |       |       |       |
| 15M7    | -5.4 | -76.54| -23.21| -0.94 | -36.04 | 17.81 | -32.67 | -0.42 |       |       |       |       |
| 15M8    | -5.4 | -42.16| 4.33  | -0.39 | -23.34 | 11.39 | -31.92 | 21.92 |       |       |       |       |
| 15M9    | -5.3 | -84.85| -12.53| -0.79 | -50.48 | 14.06 | -42.88 | 20.54 |       |       |       |       |
| 15M10   | -5.3 | -47.13| 2.59  | -0.14 | -24.60 | 10.59 | -38.12 | 17.36 |       |       |       |       |
| 16M1    | -7.4 | -43.60| -1.41 | -0.33 | -42.20 | 30.91 | -45.76 | 23.71 |       |       |       |       |
| 16M2    | -7.4 | -54.34| -1.86 | -1.53 | -43.47 | 27.75 | -44.34 | 22.27 |       |       |       |       |
| 16M3    | -7.2 | -44.89| 6.21  | -0.31 | -36.86 | 33.73 | -53.25 | 14.02 |       |       |       |       |
| 16M4    | -7.2 | -59.70| -9.28 | -0.06 | -38.76 | 31.45 | -47.79 | 13.37 |       |       |       |       |
| 16M5    | -7   | -51.09| -1.57 | -0.14 | -39.83 | 27.79 | -50.23 | 20.42 |       |       |       |       |
| 16M6    | -7   | -63.16| 1.00  | -1.04 | -34.40 | 28.67 | -52.88 | 22.07 |       |       |       |       |
| 16M7    | -6.9 | -49.50| -9.38 | -0.59 | -33.08 | 27.13 | -38.96 | 22.44 |       |       |       |       |
| 16M8    | -6.9 | -43.67| 1.96  | -1.03 | -39.78 | 42.26 | -51.11 | 10.84 |       |       |       |       |
| 16M9    | -6.9 | -66.04| -24.26| -1.45 | -35.74 | 37.83 | -45.41 | 6.34  |       |       |       |       |
| 16M10   | -6.9 | -65.63| -22.43| -1.46 | -34.64 | 27.99 | -39.93 | 10.02 |       |       |       |       |
Fig. S1. Root mean square deviation (RMSD) of ivermectin with respect to the reference conformation in Nsp9 binding pocket; rGyr: Radius of Gyration which measures the 'extendedness' of a ligand; intraHB: Intramolecular Hydrogen Bonds; MolSA: Molecular Surface Area; SASA: Solvent Accessible Surface Area; PSA: Polar Surface Area
Fig. S2. Root mean square deviation (RMSD) of ivermectin with respect to the reference conformation in importin α binding pocket; rGyr: Radius of Gyration which measures the 'extendedness' of a ligand; intraHB: Intramolecular Hydrogen Bonds; MolSA: Molecular Surface Area; SASA: Solvent Accessible Surface Area; PSA: Polar Surface Area.
Fig. S3. Analysis of hydrogen bond lengths between ivermectin and residues of Nsp9 target during the MD simulation trajectory. Snapshots were taken at 50ns (A), 60ns (B), 70ns (C), 80ns (D), 90ns (E) and 100ns (F).
Fig. S4. Analysis of hydrogen bond lengths between ivermectin and residues of importin α target during the MD simulation period. Snapshots were taken at 50ns (A), 60ns (B), 70ns (C), 80ns (D), 90ns (E) and 100ns (F).
**Fig. S5.** A timeline representation of the interactions and contacts (H-bonds, Hydrophobic, Ionic, Water bridges) between residues of Nsp9 and ivermectin in each trajectory frame. Some residues make more than one specific contact with the ligand, which is represented by a darker shade of orange, according to the scale to the right of the plot.
Fig. S6. A timeline representation of the interactions and contacts (H-bonds, Hydrophobic, Ionic, Water bridges) between residues of IMPα and ivermectin in each trajectory frame. Some residues make more than one specific contact with the ligand, which is represented by a darker shade of orange, according to the scale to the right of the plot.