

## Supplementary Materials

**Supplementary Table 1:** Binding affinity results of triplicates binding of known antivirals to the orthosteric pocket of the SARS-CoV-2 M<sup>Pro</sup> (PDB ID 6LU7) using AutoDock Vina

No.	Antivirals	Run 1	Run 2	Run 3	Average	SD
1	Nirmatrelvir	-8.6	-8.5	-8.6	-8.6	0.1
2	Ritonavir	-7.5	-7.4	-7.7	-7.5	0.2
3	Molnupiravir	-7	-7	-7	-7.0	0.0
4	Remdesivir	-7.7	-8.1	-7.9	-7.9	0.2
5	Tipranavir	-7.5	-7.6	-7.6	-7.6	0.1
6	Indinavir	-8.1	-7.9	-7.9	-8.0	0.1
7	Nelfinavir	-8.3	-8.3	-8.3	-8.3	0.0
8	Grazoprevir	-8.2	-8.1	-8.1	-8.1	0.1
9	Telaprevir	-7.1	-7.2	-7.5	-7.3	0.2
10	Boceprevir	-7.2	-7.2	-7.2	-7.2	0.0
11	Stavudine	-6.2	-6.2	-6.2	-6.2	0.0
12	Letermovir	-7.3	-7.4	-7.4	-7.4	0.1
13	Dolutegravir	-8.7	-8.7	-8.7	-8.7	0.0
14	Raltegravir	-8.7	-8.8	-8.7	-8.7	0.1
15	Lopinavir	-8	-8	-8	-8.0	0.0

**Supplementary Table 2:** Binding affinity results of triplicates binding of known antivirals to the dimer pocket of the SARS-CoV-2 M<sup>pro</sup> (PDB ID 7NT3) using AutoDock Vina

No.	Antivirals	Run 1	Run 2	Run 3	Average	SD
1	Nirmatrelvir	-8.9	-8.7	-8.7	-8.8	0.1
2	Ritonavir	-9.3	-9.4	-9.4	-9.0	0.1
3	Molnupiravir	-7.2	-7.2	-7.4	-8.1	0.1
4	Remdesivir	-8.7	-8.7	-8.8	-8.0	0.1
5	Tipranavir	-8.7	-8.8	-8.7	-8.7	0.1
6	Indinavir	-10	-10	-10.1	-10.0	0.1
7	Nelfinavir	-9.1	-9.1	-9.1	-9.6	0.0
8	Grazoprevir	-9.2	-9.2	-9.3	-9.2	0.1
9	Telaprevir	-9.8	-9.8	-9.8	-9.5	0.0
10	Boceprevir	-9	-9	-9.1	-9.4	0.1
11	Stavudine	-6.1	-6.1	-6.1	-7.6	0.0
12	Letermovir	-9.6	-9.6	-9.6	-7.9	0.0
13	Dolutegravir	-9	-9	-8.9	-9.3	0.1
14	Raltegravir	-9.6	-9.6	-9.6	-9.3	0.0
15	Lopinavir	-9	-9	-9	-9.3	0.0

**Supplementary Table 3:** Binding Affinity results of triplicates binding of known antivirals to the dimer pocket of the SARS-CoV-2 M<sup>pro</sup> (PDB ID 7EIN) using AutoDock Vina

No.	Antivirals	Run 1	Run 2	Run 3	Average	SD
1	Nirmatrelvir	-8.4	-8.4	-8.4	-8.4	0.0
2	Ritonavir	-9.4	-9.4	-8.9	-9.2	0.3
3	Molnupiravir	-8	-8	-8	-8.0	0.0
4	Remdesivir	-8.4	-8.2	-8.6	-8.4	0.2
5	Tipranavir	-9.9	-9.9	-9.7	-9.8	0.1
6	Indinavir	-10	-10	-10	-10.0	0.0
7	Nelfinavir	-8.9	-9.7	-9.7	-9.4	0.5
8	Grazoprevir	-11.1	-9.3	-9.4	-9.9	1.0
9	Telaprevir	-9.5	-8.9	-9.6	-9.3	0.4
10	Boceprevir	-8.5	-9	-8.7	-8.7	0.3
11	Stavudine	-6.3	-6.3	-6.3	-6.3	0.0
12	Letermovir	-8.3	-9.2	-8.3	-8.6	0.5
13	Dolutegravir	-9.2	-9.3	-9.3	-9.3	0.1
14	Raltegravir	-9.3	-9.1	-9	-9.1	0.2
15	Lopinavir	-9.6	-9.6	-9.6	-9.6	0.0

**Supplementary Table 4:** Binding affinity results of triplicates binding of known antivirals to the dimer pocket of the SARS-CoV-2 M<sup>Pro</sup> snapshot (MD272) using AutoDock Vina

No.	Antivirals	Run 1	Run 2	Run 3	Average	SD
1	Nirmatrelvir	-9.7	-9.7	-9.7	-9.7	0.0
2	Ritonavir	-9.5	-9.6	-9.6	-9.6	0.1
3	Molnupiravir	-7.5	-7.4	-7.6	-7.5	0.1
4	Remdesivir	-9.4	-9.3	-9.4	-9.4	0.1
5	Tipranavir	-9.7	-10.0	-9.9	-9.9	0.2
6	Indinavir	-10.0	-10.5	-10.0	-10.2	0.3
7	Nelfinavir	-10.1	-9.8	-10.1	-10.0	0.2
8	Grazoprevir	-10.6	-9.1	-10.7	-10.1	0.9
9	Telaprevir	-9.5	-9.5	-9.5	-9.5	0.0
10	Boceprevir	-8.7	-8.6	-9.1	-8.8	0.3
11	Stavudine	-6.5	-6.8	-6.5	-6.6	0.2
12	Letermovir	-8.8	-8.7	-8.7	-8.7	0.1
13	Dolutegravir	-10.0	-10.1	-10.0	-10.0	0.1
14	Raltegravir	-10.0	-9.8	-10.0	-9.9	0.1
15	Lopinavir	-10.4	-10.4	-9.9	-10.2	0.3

**Supplementary Table 5:** Pockets predicted by DogSitecorer. 7NT3, 7EIN, MD272 are a dimer structure, whereas 6LU7 is a monomer.

Protein	Pocket label	Pocket ID (DogSitecorer)	Volume	Surface	HA	HD	Hydrophobic interactions	Hydrophobicity	Druggability Score
7NT3	P1	P_0	1341.94	1352.76	68	33	65	0.39	0.806642
	P2	P_1	606.19	931.81	61	21	57	0.41	0.820398
		P_2	587.18	697.16	55	21	28	0.27	0.733178
		P_3	519.2	598.42	34	15	34	0.41	0.686779
		P_4	315.36	414.62	12	7	21	0.52	0.649737
	P0	P_5	286.37	435.96	30	10	20	0.33	0.640625
		P_6	279.58	352.59	10	5	14	0.48	0.538673
		P_7	248.64	442.56	22	7	17	0.37	0.521937
MD272	P1	P_0	1466.43	1314.21	84	31	55	0.32	0.806896
	P2	P_1	671.2	874.76	47	17	44	0.41	0.80739
	P0	P_2	607.01	756.86	48	17	38	0.37	0.776935
		P_5	311.74	407.09	16	2	22	0.55	0.551235
7EIN	P1	P_0	2732.44	3396.64	182	68	139	0.36	0.811352
		P_1	351.39	490.43	16	7	25	0.52	0.802892

		P_2	345.2	455.35	21	11	19	0.37	0.554048
	P0	P_3	307.53	418.99	18	10	14	0.33	0.57547
	P2	P_7	163.95	296.36	10	3	12	0.48	0.259547
6LU7		P_0	634.24	995.93	43	21	61	0.49	0.791922
		P_1	416.19	595.23	31	13	19	0.3	0.807977
	P0	P_2	370.69	625.38	25	15	28	0.41	0.708625
		P_3	338.18	582.16	24	7	28	0.47	0.592275

**Supplementary Table 6:** Summary of the top three druggable pockets of M<sup>pro</sup>, featuring drug scores, volume, surface area measurements and residues involved.

Protein	Pocket label	Pocket (Dogsite scorer)	Drug Score	Volume (Å <sup>3</sup> )	Surface area (Å <sup>2</sup> )	Residues
7NT3	P0	P5	0.64	286.37	435.96	ChainB: Arg40, His41, Cys44, Asp48, Met49, Pro52, Tyr54, His164, Met165, Glu166, Leu167, Phe181, Val186, Asp187, Arg188, Gln189, Thr190, Ala191, Gln192
	P1	P0	0.81	1341.94	1352.76	ChainA: Gly2, Phe3, Arg4, Lys5, Met6, Ala7, Val125, Tyr126, Gln127, Arg131, Lys137, Gly138, Gly170, Val171, His172, Thr199, Trp207, Ile281, Leu282, Gly283, Ser284, Ala285, Leu286, Leu287, Glu288, Glu290, Phe291 ChainB: Ser1, Gly2, Phe3, Arg4, Lys5, Met6, Ala7, Val125, Tyr126, Gln127, Lys137, Gly138, Thr169, Val171, His172, Trp207, Ile281, Leu282, Gly283, Ser284, Ala285, Leu286, Glu288, Phe291
	P2	P1	0.82	606.19	931.81	ChainA: Ala116, Tyr118, Ser123, Ser139, Phe140, Leu141 ChainB: Ser1, Gly2, Phe3, Arg4, Lys5, Met6, Phe8, Val104, Gln110, Thr111, Gln127, Asn151, Asp153, Ser158, Ile213, Asn214, Glu290, Phe291, Thr292, Phe294, Aspr295, Val296, Arg298, Gln299, Cys300, Ser301
MD272	P0	P2	0.78	607.01	756.86	Thr25, Leu27, His41, Cys44, Thr45, Ser46, Met49, Pro52, Tyr54, Phe140, Leu141, Asn142, Gly143, Ser144, Cys145, His163, His164, Met165, Glu166, Leu167, Pro168, His172, Phe181, Phe185, Val186, Asp187, Arg188, Gln189, Thr190, Ala191, Gln192, Ala193
	P1	P0	0.81	1466.43	1314.21	Ser1, Gly2, Phe3, Arg4, Lys5, Met6, Ala7, Thr111, Val125, Tyr126, Gln127, Cys128, Ala129, Arg131, Thr135, Ile136, Lys137, Gly138, Thr169, Gly170, Val171, Trp207, Ile281, Leu282, Gly283, Ser284, Ala285, Leu286, Glu288, Asp289, Glu290, Phe291, Thr292, Asp295, Arg298, Gln299 Phe310, Arg311, Lys312, Ala314, Val432, Tyr433, Gln434, Lys444, Gly445, Gly447, Val478, His479, Trp514, Asn521, Asp523, Leu589, Gly590, Ser591, Ala592, Leu593, Glu595, Phe598

	P2	P1	0.81	671.20	874.76	Arg311, Lys312, Met313, Phe315, Val411, Ile413, Gln414, Pro415, Gly416, Gln417, Thr418, Phe419, Ser420, Gln434, Cys435, Pro439, Asn458, Asp460, Ser465, Cys467, Ile507, Thr508, Val509, Asn510, Glu547, Pro548, Leu549, His553, Ile556, Glu597, Phe598, Thr599, Pro600, Phe601, Asp602, Arg605, Gln606
7EIN	P0	P3	0.58	307.53	418.99	ChainA: Thr25, Thr26, Leu27, Pro39, His41, Val42, Met49, Phe140, Leu141, Asn142, Gly143, Ser144, Cys145, His163, His164, Met 165, Glu166, His172 ChainB: Ser1
	P1	P0	0.81	2732.44	3396.64	ChainA: Ser1, Gly2, Phe3, Arg4, Lys5, Met6, Ala7, Phe8, Pro9, Ser10, Gly11, Lys12, Val13, Gln110, Thr111, Phe112, Ala116, Tyr118, Ser123, Gly124, Val125, Tyr126, Gln127, Cys128, Ala129, Ile136, Lys137, Gly138, Ser139, Phe140, Leu141, Ser144, Asn151, Ile152, Tyr154, Asp155, Gly170, Val171, His172, Trp207, Ala210, Ile213, Asn214, Gln256, Leu282, Gly283, Ser284, Ala285, Leu286, Glu288, Glu290, Phe291, Thr292, Phe294, Asp295, Arg298, Gln299, Cys300 ChainB: Ser1, Gly2, Phe3, Arg4, Lys5, Met6, Ala7, Phe8, Pro9, Glu14, Ile106, Pro108, Gln110, Thr111, Phe112, Ala116, Tyr118, Ser121, Pro122, Ser123, Gly124, Val125, Tyr126, Gln127, Cys128, Ala129, Lys137, Gly138, Ser139, Phe140, Leu141, Asn151, Gly 170, Val171, His172, Ile200, Asn203, Trp207, Ile213, Asn214, Glu240, Ile249, Leu282, Gly283, Ser284, Ala285, Leu286, Glu288, Glu290, Phe291, Thr292, Pro293, Phe294, Asp295, Arg298, Gln299, Cys300
	P2	P7	0.26	163.95	296.36	Pro108, Gln110, Ile200, Val202, Asn203, His246, Ile249, Thr292, Pro293
6LU7	P0	P2	0.71	370.69	625.38	Gln19, Thr26, Leu27, Asn28, His41, Met49, Cys117, Tyr118, Asn119, Gly120, Phe140, Leu141, Asn142, Gly143, Ser144, Cys145, His163, His164, Met165, Glu166, His172

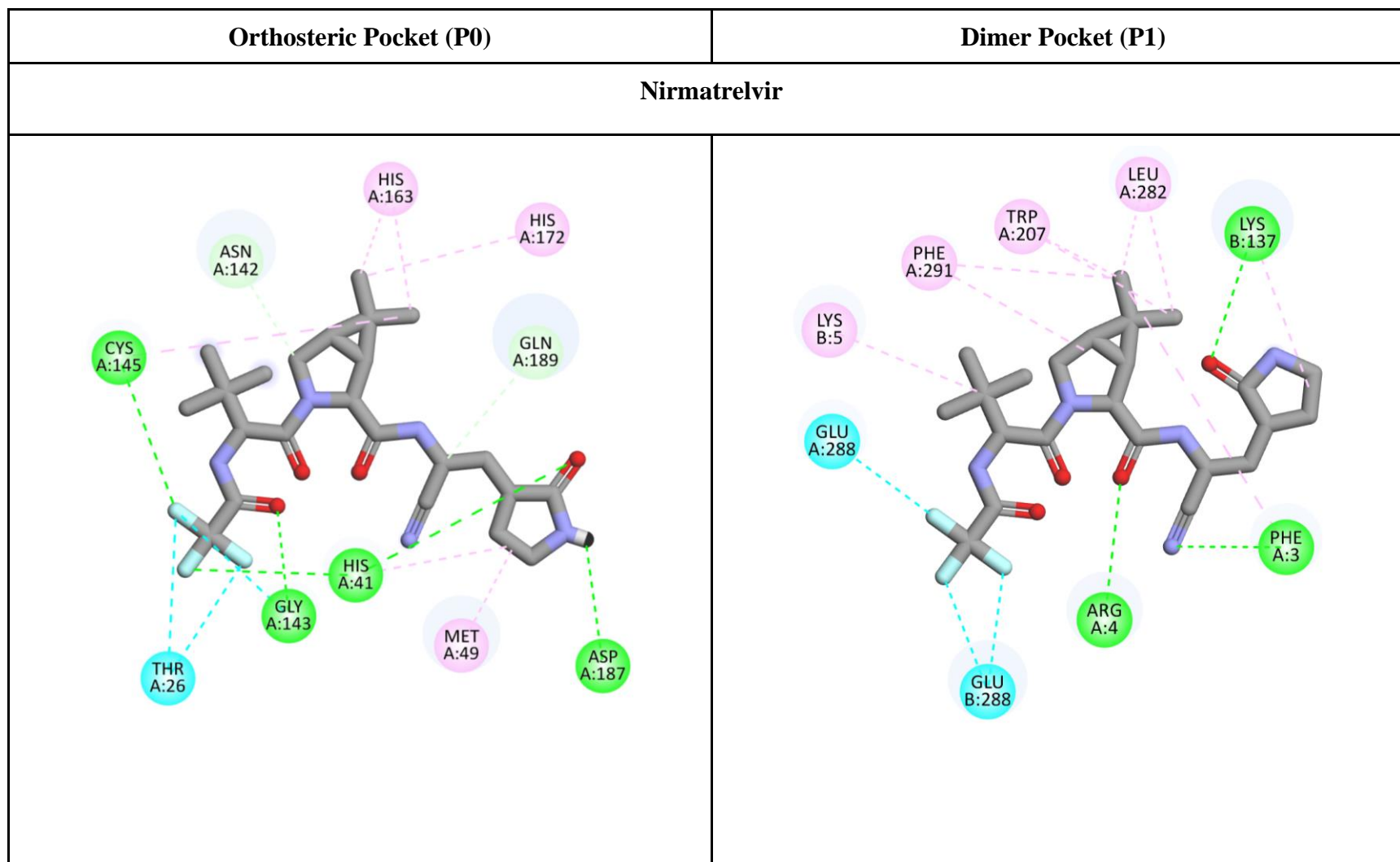


**Supplementary Table 7:** Summary of amino acid interactions between PDB ID: 7NT3 with the top 3 antivirals that exhibit highest docking binding affinities to the dimer pocket of the SAR-CoV-2 M<sup>pro</sup>.

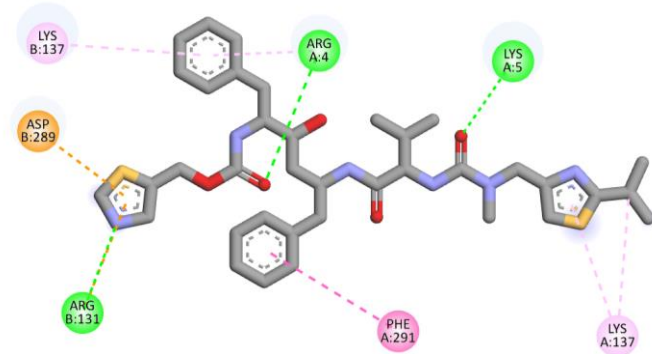
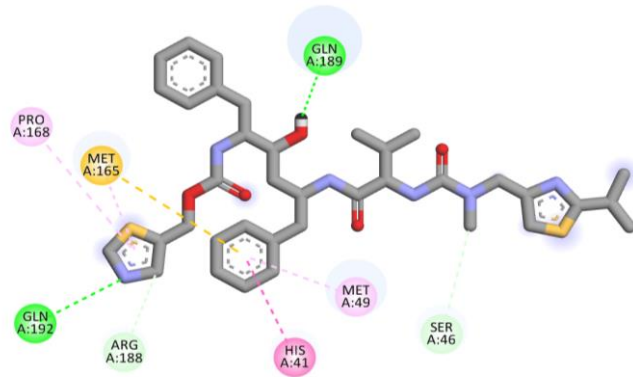
Ligand	Pose	Residues	Distance (Å)	Interaction	
Indinavir	1	ARG4 (A)	2.06	Conventional hydrogen bond	
		LEU282 (A)	2.99		
		ARG131 (B)	2.71		
		GLU288 (B)	2.61		
	1	GLY283 (A)	3.45	Carbon / Pi-Donor hydrogen bond	
		LYS5 (B)	2.64		
		ARG4 (B)	5.15	Alkyl / Pi-Alkyl	
		LYS5 (B)	3.82		
	LYS137 (B)	4.66			
	1	GLU288 (A)	4.95	Pi-Anion	
		2	ARG4 (A)	2.15	Conventional hydrogen bond
			GLY283 (A)	2.21	
			GLU288 (B)	2.64	
	2	LEU282 (A)	3.21	Carbon / Pi-Donor hydrogen bond	
		LYS5 (B)	2.69		
		ARG4 (B)	5.03	Alkyl / Pi-Alkyl	
		LYS5 (B)	3.90		
	2	LEU282 (A)	3.85	Pi-Sigma	
		3	LYS5 (A)	2.07	Conventional hydrogen bond
			GLU288 (B)	2.19	
			GLU288 (B)	3.62	
3	ARG4 (A)	5.23	Alkyl / Pi-Alkyl		
	LYS137 (A)	5.17			
	LEU286 (A)	5.50			
	ARG 4 (B)	5.13			
	LYS137 (B)	4.57			
	GLU288 (A)	3.87	Pi-Anion/ Pi-Cation		
	GLU290 (A)	4.23			
	ARG 4 (B)	4.19			
LYS137 (B)	4.26				
GLU288 (B)	4.26				
Grazoprevir	1	LYS137 (A)	3.05	Conventional hydrogen bond	
		THR199 (A)	2.93		
		GLU288 (A)	3.70		Carbon hydrogen bond
		LYS137 (A)	4.16		Alkyl / Pi-Alkyl
		LEU286 (A)	4.61		
		ALA285 (B)	4.25		
	LYS5 (A)	4.64	Pi-Cation		
	TYR239 (A)	5.84	Pi-Sulfur		
	2	LYS5 (B)	2.31	Conventional hydrogen bond	
		GLY283 (B)	2.39		
		ASN214 (B)	3.18	Carbon hydrogen bond	
		SER284 (B)	3.44		
		LEU286 (A)	4.44		
	PHE291 (B)	5.22	Pi-Sulfur		
	3	LEU282 (B)	2.35	Conventional hydrogen bond	
		SER284 (B)	2.45		
		ASN214 (B)	3.23	Carbon hydrogen bond	
		LYS5 (B)	4.44	Alkyl / Pi-Alkyl	
PHE291 (B)	5.40				

<b>Ligand</b>	<b>Pose</b>	<b>Residues</b>	<b>Distance (Å)</b>	<b>Interaction</b>			
Lopinavir	1	LYS5 (A)	2.42	Conventional hydrogen bond			
		GLY283 (A)	2.82				
		SER284 (A)	2.76				
		SER284 (B)	2.94				
			LYS5 (A)	5.40	Alkyl / Pi-Alkyl		
			LYS5 (B)	3.95			
			LYS137 (B)	5.07			
			LEU286 (B)	4.06			
	2		ARG4 (A)	2.23	Conventional hydrogen bond		
			LYS5 (A)	2.62			
			GLU288 (A)	2.03			
			LYS5 (B)	2.60			
			LYS137 (A)	4.63	Pi-Alkyl		
			ARG4 (B)	4.34	Pi-Cation		
			3		LYS5 (A)	2.55	Conventional hydrogen bond
					GLY283 (A)	2.16	
	GLU288 (B)	2.26					
	GLY283 (A)	3.16			Carbon hydrogen bond		
		GLU288 (A)	5.00	Pi-Anion/ Pi-Cation			
		ARG4 (B)	4.20				
		ARG4 (A)	4.39		Alkyl / Pi-Alkyl		
		LYS5 (A)	5.14				
LYS137 (A)	5.05						
ARG4 (B)	4.25						
		LYS5 (B)	3.77				

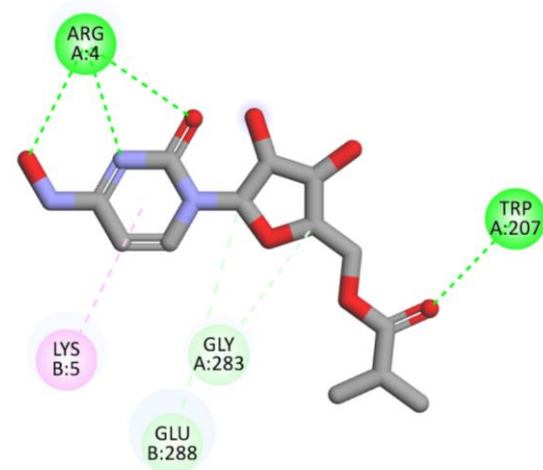
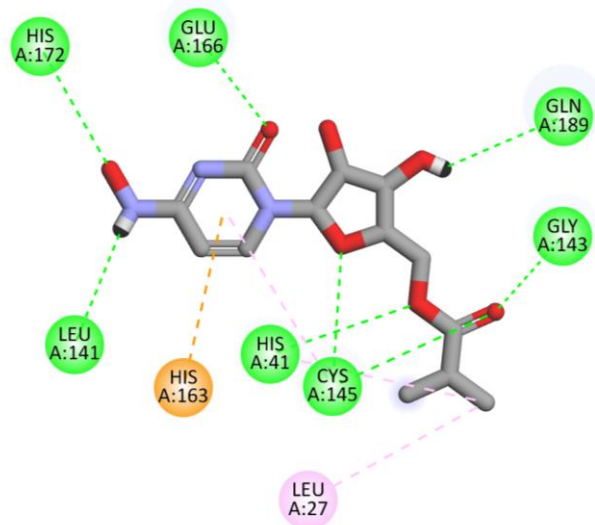
**Supplementary Table 8:** Docking of known antivirals to the SARS-CoV-2 M<sup>pro</sup>. Interactions between M<sup>pro</sup> and the antivirals at the catalytic site (left) and the dimer pocket (right).



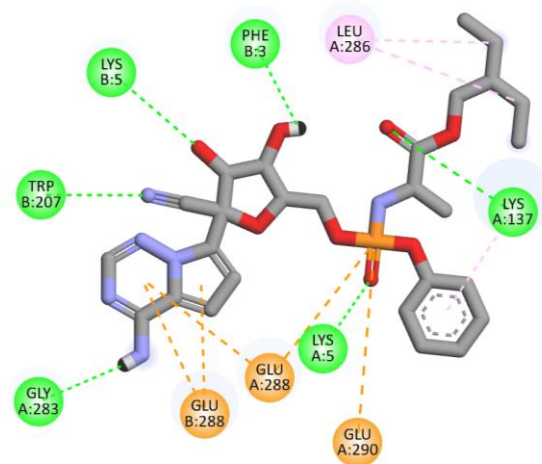
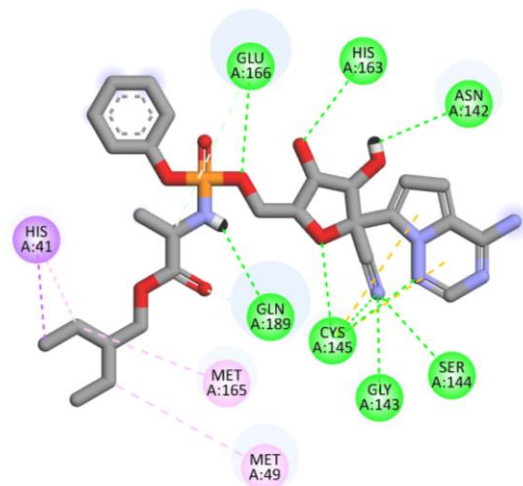
## Ritonavir



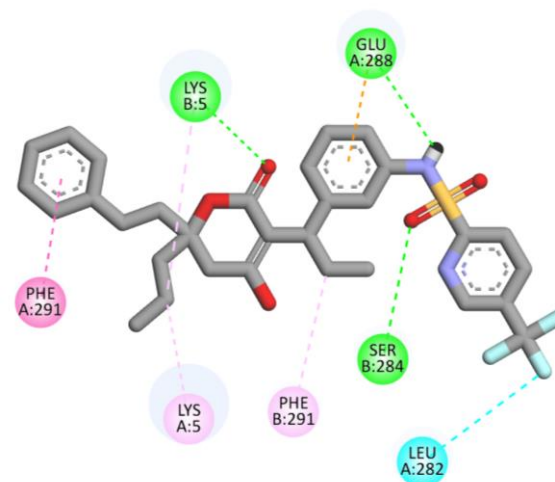
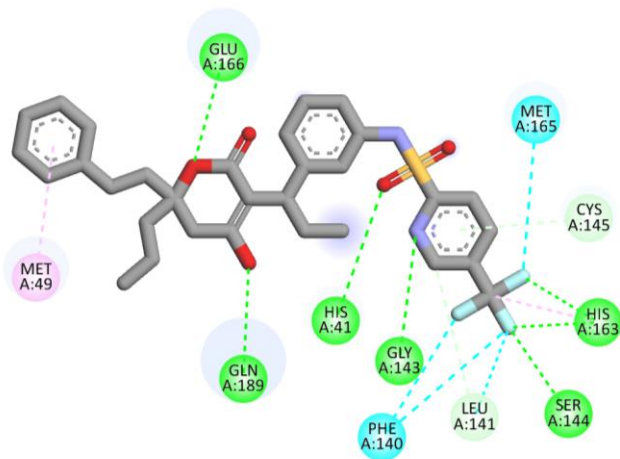
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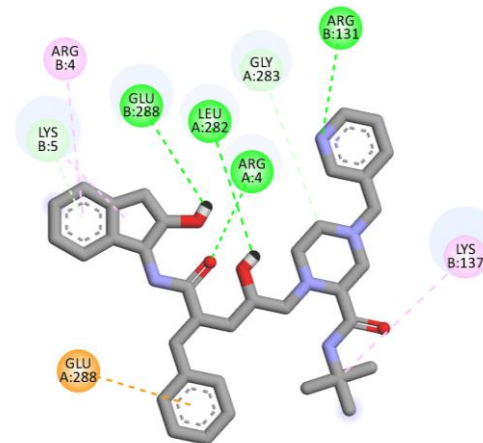
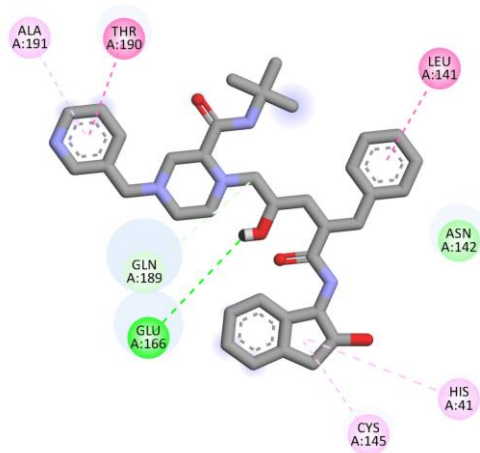
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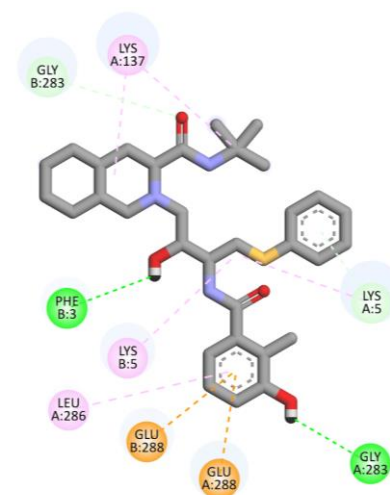
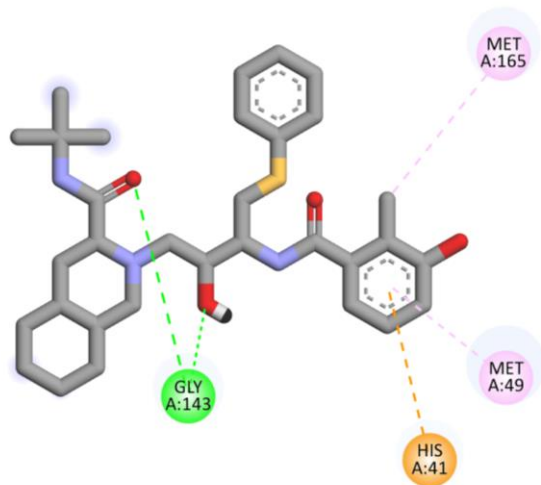
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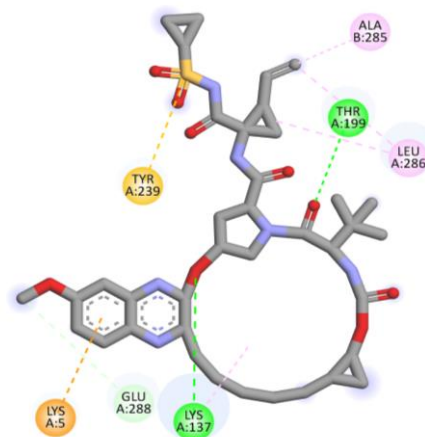
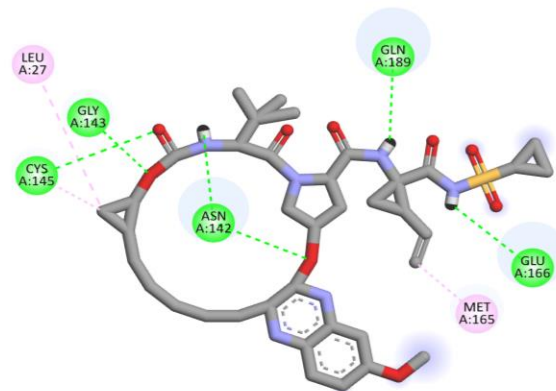
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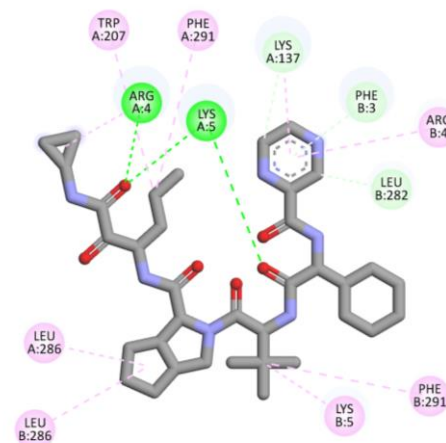
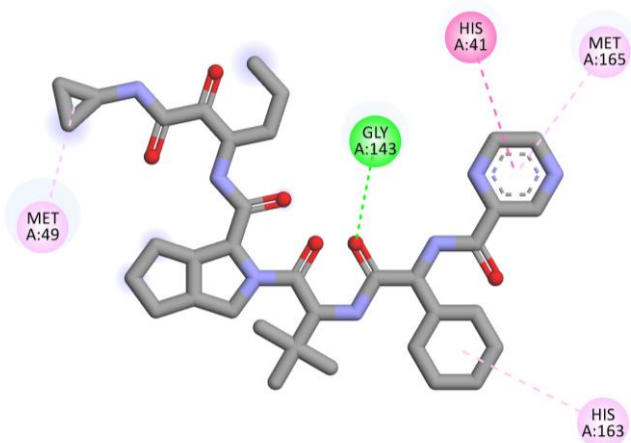
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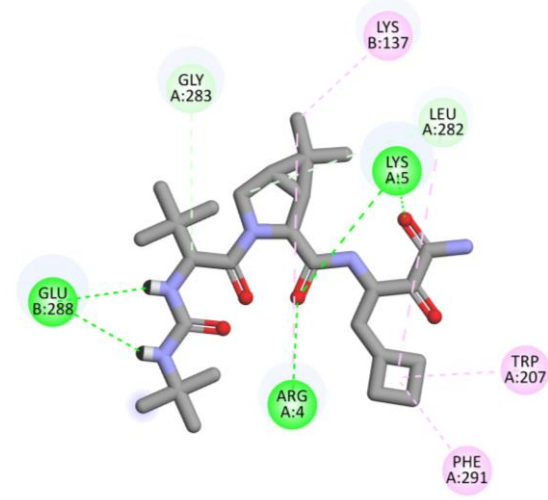
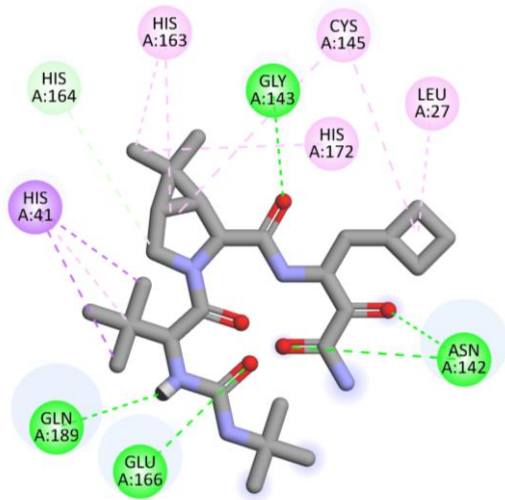
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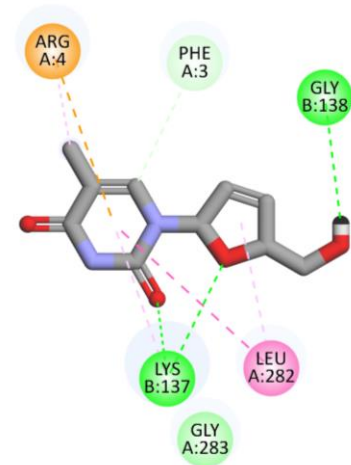
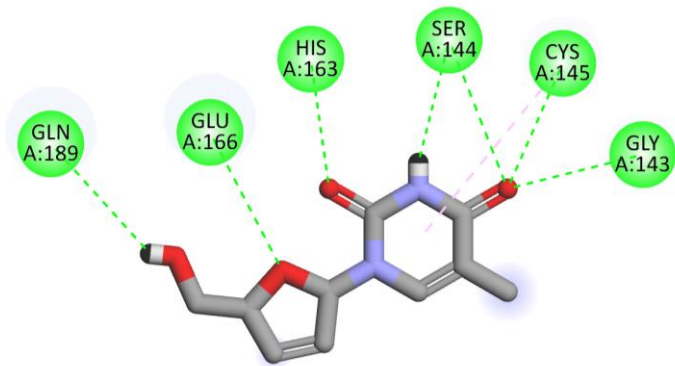
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## Boceprevir

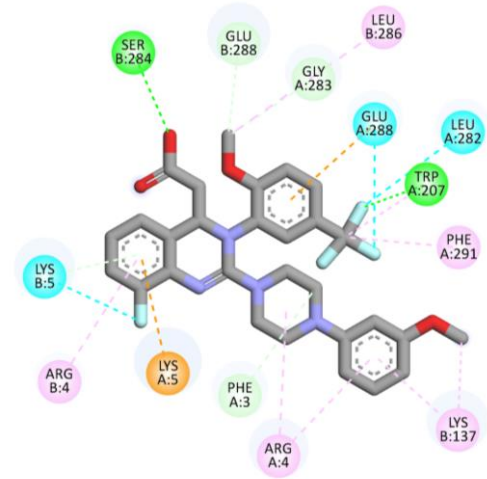
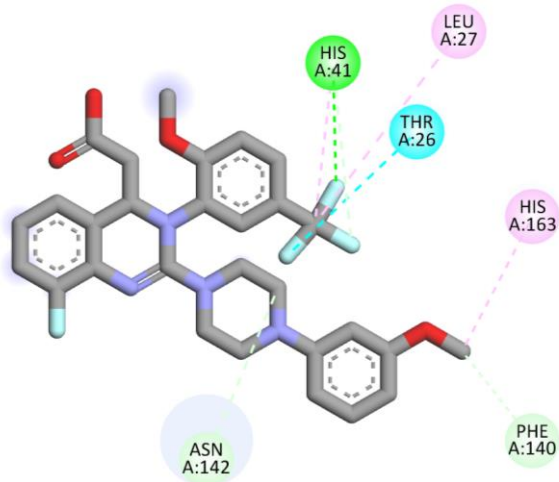


## Stavudine

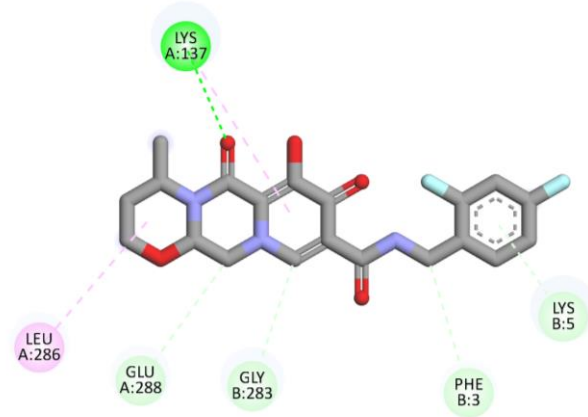
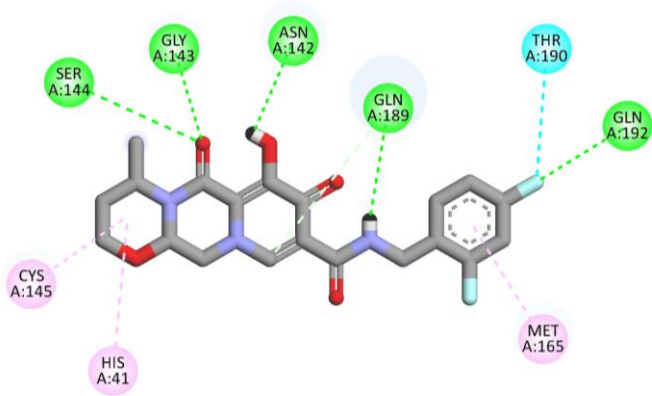




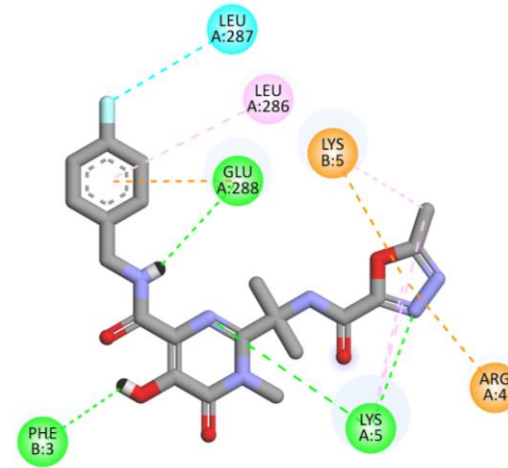
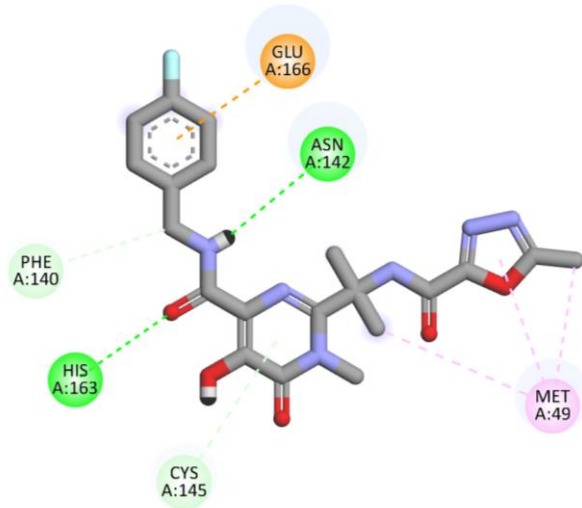
## Letermovir



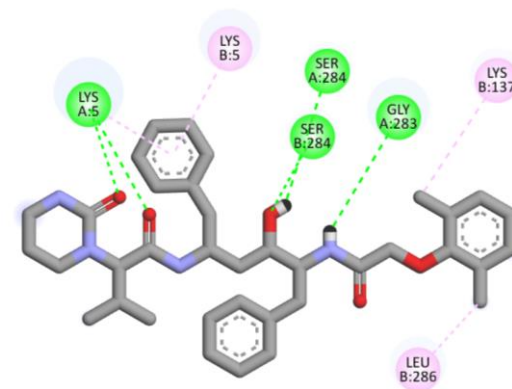
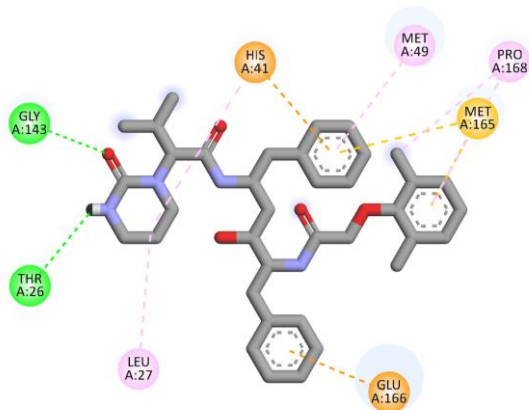
## Dolutegravir

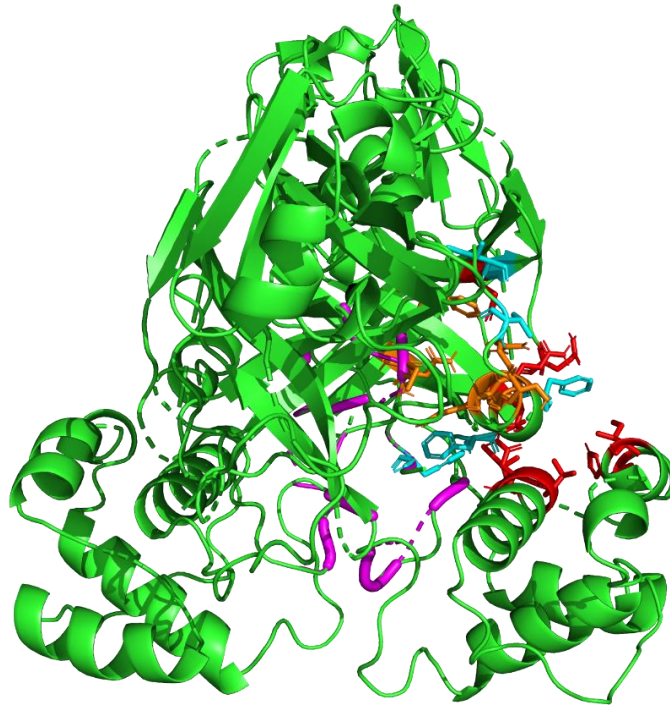


## Raltegravir



## Lopinavir





**Supplementary Fig. 1:** Side view of SARS-CoV-2 M<sup>pro</sup>, showing the position of dimer pocket of Site #2, Site #5 (Alzyoud et al., 2022) and P1. Residues involved in Site #2 (represented in red sticks), Site #5 (represented in blue and orange sticks) and P1 (represented in purple cartoon) via Pymol.

4WMF   MERS-CoV	SGLVKMSHPS-DVEACMVQVTCGSM TLNGLWLDNTVWCPRHVMCPADQLSDPNYDALLIS	59
7NT3   SARS-CoV-2	SGFRKMA-FPSGKVEGCMVQVTCGTTTLNGLWLDVVYVCPRHVICTSEDMLNPNYEDLLIR	60
1UK3   SARS-CoV	--FRKMAFPSPGKVEGCMVQVTCGTTTLNGLWLDVVYVCPRHVICTAEDMLNPNYEDLLIR	58
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4WMF   MERS-CoV	MTNHSFSVQKHIGAPANLRVVGHAMQGTLLKLTVDVANPSTPAYFTTVPKGAAFSVLAC	119
7NT3   SARS-CoV-2	KSNHNFVQA---GNVQLRVIGHSMQNCVLLKVDANPKTPKYKFRVRIQPGQTFSVLAC	117
1UK3   SARS-CoV	KSNHSFLVQA---GNVQLRVIGHSMQNCVLLKVDTSNPKTPKYKFRVRIQPGQTFSVLAC	115
	:**.* ** . :****:***. :*:**.*:*** **.* : : ** :*****	
4WMF   MERS-CoV	YNGRPTGFTVVMRPNYTIKGSFLCGSAGSVGYTKEGVSINFCYMHQMELANGTHTGSAF	179
7NT3   SARS-CoV-2	YNGSPSGVYQCAMRPNHTIKGSFLNGSCSVGFNIDYDCVSFCYMHMELPTGVHAGTDL	177
1UK3   SARS-CoV	YNGSPSGVYQCAMRPNHTIKGSFLNGSCSVGFNIDYDCVSFCYMHMELPTGVHAGTDL	175
	*** * : . : .****.*:***** **.*:***. : . : .****:* ** . * : * : :	
4WMF   MERS-CoV	DGTYMGAFMDKQVHQVQLTDKYCSVNVVAVLYAAIILNGCAWFKPNRTSVVSNFNEWALAN	239
7NT3   SARS-CoV-2	EGNFYGPFDVDRQTAQAAGDTITVNVLAIAAINGDRWFLNRFITTLNDFNLVAMKY	237
1UK3   SARS-CoV	EGKFYGPFDVDRQTAQAAGDTITLNLVLAIAAINGDRWFLNRFITTLNDFNLVAMKY	235
	:* : ** * : * : . * . ** . :****:*****:*** ** : : * : . ** * :	
4WMF   MERS-CoV	QTFEFVGTQ--SVDMLAVKTVGVAIEQLLYAI-QQLYTGFQKQILGSTMLEDEFTPEDVN	296
7NT3   SARS-CoV-2	NYEPLTQDHDVILGPLSAQTGIAVLDMCASLKELLQNGMNGRTILGSALLEDEFPFDVV	297
1UK3   SARS-CoV	NYEPLTQDHDVILGPLSAQTGIAVLDMCAALKELLQNGMNGRTILGSTILEDEFPFDVV	295
	: : . : . * : : * : * : : : * . * : : * : * : * : * : * : * : * : *	
4WMF   MERS-CoV	MQIMGVMSGLVKMSHPSGDVEACMVQVTCGSM TLNGLWLDNTVWCPRHVMCPADQLSDP	356
7NT3   SARS-CoV-2	RQCSGVTSFRKMA-FPSGKVEGCMVQVTCGTTTLNGLWLDVVYVCPRHVICTSEDMLNP	357
1UK3   SARS-CoV	RQCSGV--SGFRKMAFPSPGKVEGCMVQVTCGTTTLNGLWLDVVYVCPRHVICTAEDMLNP	353
	* ** * : * : .****.*:*****: *****:.*:*****: * : : : *	
4WMF   MERS-CoV	NYDALLISMTNHSFSVQKHIGAPANLRVVGHAMQGTLLKLTVDVANPSTPAYFTTVPKPG	416
7NT3   SARS-CoV-2	NYEDLLIRKSNHNFVQA---GNVQLRVIGHSMQNCVLLKVDANPKTPKYKFRVRIQPG	414
1UK3   SARS-CoV	NYEDLLIRKSNHSFLVQA---GNVQLRVIGHSMQNCVLLKVDTSNPKTPKYKFRVRIQPG	410
	** : ** * : * . * ** . :****:***. :*:**.*:*** **.* : : **	
4WMF   MERS-CoV	AAFSVLACYNGRPTGFTVVMRPNYTIKGSFLCGSAGSVGYTKEGVSINFCYMHQMELAN	476
7NT3   SARS-CoV-2	QTFSVLACYNGSPSGVYQCAMRPNHTIKGSFLNGSCSVGFNIDYDCVSFCYMHMELPT	474
1UK3   SARS-CoV	QTFSVLACYNGSPSGVYQCAMRPNHTIKGSFLNGSCSVGFNIDYDCVSFCYMHMELPT	470
	:***** * : . : .****.*:***** **.*:***. : . : .****:* ** .	
4WMF   MERS-CoV	GTHTGSAFDGTMYGAFMDKQVHQVQLTDKYCSVNVVAVLYAAIILNGCAWFKPNRTSVVS	536
7NT3   SARS-CoV-2	GVHAGTDLGNFYGPFDVDRQTAQAAGDTITVNVLAIAAINGDRWFLNRFITTLNDFNLVAMKY	534
1UK3   SARS-CoV	GVHAGTDLGNFYGPFDVDRQTAQAAGDTITLNLVLAIAAINGDRWFLNRFITTLNDFNLVAMKY	530
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4WMF   MERS-CoV	FNEWALANQTFEFVGTQ--SVDMLAVKTVGVAIEQLLYAI-QQLYTGFQKQILGSTMLEDE	593
7NT3   SARS-CoV-2	FNLVAMKYNYEPLTQDHDVILGPLSAQTGIAVLDMCASLKELLQNGMNGRTILGSALLEDE	594
1UK3   SARS-CoV	FNLVAMKYNYEPLTQDHDVILGPLSAQTGIAVLDMCAALKELLQNGMNGRTILGSTILEDE	590
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4WMF   MERS-CoV	EFTPEDVNMQIMGV	607
7NT3   SARS-CoV-2	EFPPFDVVRQCSG-	607
1UK3   SARS-CoV	EFTPFDVVRQCSG-	603
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**Supplementary Fig. 2:** Sequence comparison of M<sup>pro</sup> of MERS-CoV, SARS-CoV and SARS-CoV-2 coronaviruses. Residues involved in the dimer pocket of SARS-CoV-2 M<sup>pro</sup> are indicated in black box.