

Supplementary Material

Table S1. Literature survey of transcriptomics studies focused on expression of SARS-CoV-2 RdRp in infected human cell line and patient samples.

Cell Line/ Patient Sample	Method	Reference
Normal human bronchial epithelial (NHBE) and human adenocarcinomic alveolar basal epithelial cells (A549)	RNA-Seq	[29]
Throat/nasal swab grown in <i>Cercopithecus aethiops</i> kidney epithelial cells (Vero CCI-81)	RT-qPCR	[30]
Throat swab samples	RT-qPCR	[31]
Human lung and colon samples	RT-qPCR	[32]
RT-qPCR = reverse transcriptase quantitative PCR; RNA-Seq = ribonucleic acid sequencing		

Table S2. Identification of SARS-CoV-2 RdRp peptides found in infected human cell line and patient samples.

Project ID	Cell Line/ Patient Sample	Peptide sequences	Positions	Accession ID
PXD017710	Colan carcinoma cell line	HDFFKFRIDVDMVPHISR	4491-4508	QOE87934.1
		NVTPTITQMNLKYAISAKNR	4926-4945	QOF20355.1
		DEDDNLIDSYFVVKRPTFSNYQHEETIYNLLKDCPAVAK	4452-4490	QPM30612.1
		GATVLIGTSKFYGGWHNMLK	4976-4995	QLC46995.1
		QCDDYVYLPYPDPSRILGAGCFVDDIVK	5214-5241	QNO75717.1
		QALLKTVQFCDAIR	4576-4589	QMS52714.1
PXD018581	Lung carcinoma cell line	FLPFQQFGRDIADTTDAVR	4929-4947	QOL77454.1
		HFFFAQDGNAAISDYDYRYNLPTMCDIRQLLFVVEVADK	4831-4870	QNO32046.1
		HFDEGNCGLKEILVTYNCCDDDYFNKK	4525-4552	QKJ68603.1
PXD019686	Nasal swab simili	AFDIYNDKVAGFAKFLK	4426-4442	QOQ08810.1
		AFDIYNNKVAGFAKFLK	4426-4442	QKR84563.1

Table S3. Viral RdRp amino acid sequences used for phylogenetic analysis

<p>>SARS-CoV UniProt ID: P0C6X7 (Severe acute respiratory syndrome coronavirus)</p> <p>SADASTFLNRVCGVSAARLTPCGTGTSTDVVYRAFDIYNEKVAGFAKFLKTNCCRFQEKD EEGNLLDSYFVVKRHTMSNYQHEETIYNLVKDCPAVAVHDDFFKFRVDGDMVPHISRQRLT KYTMADLVYALRHFDEGNCDTLKEILVTYNCCDDDYFNKKDWYDFVENPDILRVYANLGE RVRQSLLKTVQFCDAMRDAGIVGVLTLDNQDLNGNWYDFGDFVQVAPGCGVPIVDSYYSL LMPILTLTRALAAESHMDADLAKPLIKWDLKDYDFTEERLCLFDRYFKYWDQTYHPNCIN CLDDRCILHCANFNVLSTVFPPTSFGPLVRKIFVDGVPFVVSTGYHFRELGVVHNQDVN LHSSRSLFKELLVYAADPAMHAASGNLLLDKRTTCFSVAALTNNVAFQTVKPGNFNKDFY DFAVSKGFFKEGSSVELKHFFFAQDGNAAISDYDYRYNLPMTCDIRQLLFVVEVVVKYF DCYDGGCINANQVIVNNLDKSAGFPFNKWGKARLYYDSMSYEDQDALFAYTKRNVIPITIT QMNLKYAISAKNRARTVAGVSICSTMTNRQFHQKLLKSIAATRGATVVIGTSKFYGGWHN MLKTVYSDVETPHLMGWDYPKCDRAMPNMLRIMASLVLARKHNTCCNLSHRFYRLANCA QVLSEMVMCGGSLYVKPGGTSSGDATTAYANSVFNICQAVTANVNALLSTDGNKIADKYV RNLQHRLYECLYRNRDVEHFVDEFYAYLRKHFSMMILSDDAVVCYNSNYAAQGLVASIK NFKAVLYYQNNVFMSEAKCWTETDLTKGPHEFCSQHTMLVKQGDDYVYLPYPDPSRILGA GCFVDDIVKTDGTLMIERFVSLAIDAYPLTKHPNQEYADVHFLYLQYIRKLHDELTHGML DMYSVMLTNDNTSRYWEPEFYEAMYPHTVLQ</p>
<p>>SARS-CoV-2 UniProt ID: P0DTD1 (Severe acute respiratory syndrome coronavirus 2)</p> <p>SADAQSFLNRVCGVSAARLTPCGTGTSTDVVYRAFDIYNDKVAGFAKFLKTNCCRFQEKD EDDNLIDSYFVVKRHTFSNYQHEETIYNLLKDCPAVAKHDDFFKFRIDGDMVPHISRQRLT KYTMADLVYALRHFDEGNCDTLKEILVTYNCCDDDYFNKKDWYDFVENPDILRVYANLGE RVRQALLKTVQFCDAMRNAGIVGVLTLDNQDLNGNWYDFGDFIQTTPGSGVPVVDSDYYSL LMPILTLTRALTAESHVDTDLTKPYIKWDLKDYDFTEERLKLFDRIYFKYWDQTYHPNCVN CLDDRCILHCANFNVLSTVFPPTSFGPLVRKIFVDGVPFVVSTGYHFRELGVVHNQDVN LHSSRSLFKELLVYAADPAMHAASGNLLLDKRTTCFSVAALTNNVAFQTVKPGNFNKDFY DFAVSKGFFKEGSSVELKHFFFAQDGNAAISDYDYRYNLPMTCDIRQLLFVVEVVVKYF DCYDGGCINANQVIVNNLDKSAGFPFNKWGKARLYYDSMSYEDQDALFAYTKRNVIPITIT QMNLKYAISAKNRARTVAGVSICSTMTNRQFHQKLLKSIAATRGATVVIGTSKFYGGWHN MLKTVYSDVENPHLMGWDYPKCDRAMPNMLRIMASLVLARKHTTCCSLSHRFYRLANCA</p>

QVLSEVMVMCGGSLYVKPGGTSSGDATTAYANSVFNICQAVTANVNALLSTDGNKIADKYV
RNLQHRLYECLYRNRDVDTDVNEFYAYLRKHFSMMILSDDAVVCFNSTYASQGLVASIK
NFKSVLYYQNNVFMSEAKCWTETDLTKGPHEFCSQHTMLVKQGDDYVYLPYDPDSRILGA
GCFVDDIVKTDGTLMIERFVSLAIDAYPLTKHPNQEYADVFLYLQYIRKLHDELTGHML
DMYSVMLTNDNTSRYWEPEFYEAMYPHTVLQ

>MERS| UniProt ID: K9N7C7 (Middle East respiratory syndrome-related coronavirus)
SKDSNFLKRVRGSIVNARIEPCSSGLSTDVVFRAFDICNYKAKVAGIGKYYKTNTCRFVE
LDDQGHHLDSYFVVKRHTMENYELEKHCYDLLRDCDAVAPHDFFIFDVDKVKTPHIVRQR
LTEYTMMDLVYALRHFQDNSEVLKAILVKYGCCDVTYFENKLWFDVFNPSVIGVYHKL
ERVRQAILNTVKFCDHMKAGLVGVLTLDNQDLNGKWYDFGDFVITQPGSGVAIVDSYYS
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NCTDDRCVLHCANFNVLFAMTMPKTCFGPIVRKIFVDGVPFVVSCGYHYKELGLVMNMDV
SLHRHRLSLKELMMYAADPAMHIASSNAFLDLRTSCFSVAALTTGLTFQTVRPGNFNQDF
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FEIYDGGCLNASEVVNNLDKSAGHPFNKFGKARVYYESMSYQEDEL FAMTKRNVIP TM
TQMNLYAISAKNRARTVAGVSILSTMTNRQYHQKMLKSMAATRGCATCIGTTKFGYGGWD
FMLKTLKYKDVDNPHLMGWDYPKCDRAMPNMCRIASLILARKHGTCCTTRDRFYRLANEC
AQVLSEYVLCGGGYVVKPGGTSSGDATTAYANSVFNILQATTANVSALMGANGNKIVDKE
VKDMQFDLYNVYRSTSPDPKFVDKYYAFLNKHFSMMILSDDGVVCYNSDYAAKGYIAGI
QNFKETLYYQNNVFMSEAKCWVETDLKKGPHEFCSQHTLYIKDGDDGYFLPYDPDSRILS
AGCFVDDIVKTDGTLMVERFVSLAIDAYPLTKHEDIEYQNVFWVYLQYIEKLYKDLTGHM
LDSYSVMLCGDNSAKFWEEAFYRDLYSSPTTLQ

>Rhinovirus| UniProt ID: P23008 (Human rhinovirus 1A (HRV-1A))
GQIKVNXHATECGLPTIHTPSKTKLQPSVFYDVFPGSKEPAVLTDNDPRLEVNFKEALFS
KYKGNVECNLNEHMEIAIAHYSACLMTLDIDSRPIALESVFGIEGLEALDLNTSAGFPY
VTMGIKKRDLINNKTKDISRLKEALDKYGVDLPMITFLKDELRRKKEISTGKTRVIEASS
INDTILFRITTFGNLFSKFHLNPGVVTGSAVGCDPETFWSKIPVMDGDCIMAFDYTNYDG
SIHPVWFQALKKVLENLSFQSNLIDRLCYSKHLFKSTYYEVAGGVPSGCSGTSIFNTMIN
NIIRTLVLDAYKNIDLDKLKIIAYGDDVIFS YKYTLDM EAIANEGKKYGLTITPADKSN
EFKKLDYSNVTF LKRGFKQDERHTFLIHPTFPVEEIHESIRWTKKPSQM QEHVLSLCHLM
WHNGRKVYEDFSSKIRSVSAGRALYIPPYDLLKHEWYEKF

>RSV_Strain_B| UniProt ID: O36635 (Human respiratory syncytial virus B (strain B1))

MDPIINGNSANVYLTD SYLKGVISFSECNALG SYLFNGPYLKNDYTNLISRQSP LLEHMN
LKKLTITQSLISRYHKGELKLEPTYFQSLLMTYKSMSSSEQIATTNLLKKIIRRAIEIS
DVKVYAILNKLGLKEKDRVKPNNSGDENSVLTTHKDDILSAVESNQSYTNSDKNHSVN
QNITIKTTLLKKLMCSMQHPPSWLIHWFNLYTKLNNILTQYRSNEVKSHGFILIDNQTLS
GFQFILNQYGCIVYHKGGLKITT TTYNQFLTWKDISLSRLNVCLITWISNCLNTLNKSLG
LRCGFNNVLSQLFLYGDCILKLFHNEGFIIEKEVEGFIMSLILNITEEDQFRKRFYNM
LNNITDAAIKAQKNLLSRVCHTLLDKTVSDNIINGKWIILLSKFLKLIKLAGDNNLNNLS
ELYFLFRIFGHPMVDERQAMDAVRINCNETKFYLLSSLSTLRGAFIYRIIKGFVNTYNRW
PTLRNAIVLPLRWLNYYKLNTPSLEITENDLIILSGLRFYREFHLPKKVDLEMIINDK
AISPPKDLIWTSPRNYMPSHIQNYIEHEKLFSESDRSRRVLEY YLRDNKFNECDLYNC
VVNQSYLNNNSNHVVSLTGKERELSVGRMFAMQPGMFRQIQILAEKMAENILQFFPESLT
RYGDLELQKILELKAGISNKS NRYNNDYNNYISKCSIITDLSKFNQAFRYETSCICSDVL
DELHGVQSLFSWLHLTIPLVTIICTYRHAPPFIKDHVVNLNEVDEQSGLYRYHMGGIEGW
CQKLWTIEAISLLDLISLKGKFSITALINGDNQSIDISKPVRLIEGQTHAQADYLLALNS
LKLLYKEYAGIGHKLKGTETYISRDMQFMSKTIQHNGVYYPASIKKVL RVGPWINTILDD
FKVSLESIGSLTQELEYRGESLLCSLIFRNWLYNQIALQLRNHALC NNKLYLDILKVLK
HLKTFFNLDSIDMALSLYMNLPMLFGGGDPNLLYRSFYRRTPDFLTEAIVHSVFVLSYYT
GHDLDQDKLQDLPDDRNLNKFLT CVITFDKNPNAEFVTLMRDPQALGSERQAKITSEINRLA
VTEVLSIAPNKIFS KSAQHYYTTTEIDLNDIMQNIPTYPHGLRVVYESLPFYKAEKIVNL
ISGTSITNILEKTS AIDTTDINRATDMMRKNITLLIRILPLDCNKDKRELLSLENLSIT
ELSKYVRERSWSLSNIVGVTSPSIMFTMDIKYTTSTIASGIIIEKYNVNSLTRGERGPTK
PWVGSSTQEKKTMPVYNRQVLT KKKQRDQIDLLAKLDWVYASIDNKDEFMEELSTGTLGLS
YEKAKKLFPQYLSVNYLHRLTVSSRPCEFPASIPAYRTTNYHFDTSPINHVLTEKYGDED
IDIVFQNCISFGLSLMSVVEQFTNICPNRIILIPKLNEIHLMKPPIFTGDVDIILKQVI
QKQHMFLPDKISLTQYVELFLSNKALKSGSNINSNLILVHKMSDYFHNAYILSTNLAGHW
ILIIQLMKDSKGIFEKDWGEGYITDHMFINLVFFNAYKTYLLCFHKGYGKAKLECDMNT
SDLLCVLELIDSSYWKSM SKVFLEQKVIKYIVNQDTS LHRIKGCHSFKLWFLKRLNNAKF
TVCPWVVNIDYHPT HMKAILS YIDLVRMGLINVDKLTIKNKNKFNDEFYTSNLFYISYNF
SDNTHLLTKQIRIANSELEDNYNKL YHPTPETLENISLIPVKSNN SNKPKFCISGNTESI
MMSTFSNKMHIKSSTVTTRFNYSKQDLYNLFPNVVIDRIIDHSGNTAKSNQLYITTSHQT
SLVRNSASLYCMLPW HHHVNRFN VFSSTGCKISIEYILKDLKIKDPSCIAFIGEGAGNLL
LRTVVELHPDIRYIYRSLKDCNDHSLPIEFLRLYNGHINIDYGENLTIPATDATNNIHWS

YLHIKFAEPISIFVCDAELPVTANWSKIIIEWSKHVRKCKYCSSVNRCLIAKYHAQDDI
DFKLDNITILKTYVCLGSKLKGSEVYLVLTIGPANILPVFDVVQNAKLIFSRTKNFIMPK
KTDKESIDANIKSLIPFLCYPITKKGIKTSLSKLKSVVNGDILSYSIAGRNEVFSNKLIN
HKHMNILKWLDHVLNFRSAELNYNHLYMIESTYPYLSELLNSLTTNELKKLIKITGSVLY
NLPNEQ

>RSV_Strain_A| UniProt ID: Q9IWW8 (Human respiratory syncytial virus A (strain Long))
MDPIINGNSANVYLTD SYLKGVISFSECNALGSYIFNGPYLKNDYTNLISRQNPLIEHMN
LKKLNITQSLISKYHKGEIKLEEPTYFQSLLMTYKSMTSLEQIATTNLLKKIIRRAIEIS
DVKVYAILNKLGLKEKDKIKSNNGQDEDNSVITTIKDDILSAVKDNQSHLKADKNHSTK
QKDTIKTTLLKKLMCSMQHPPSWLIHWFNLYTKLNNILTQYRSNEVKNHGFILIDNQTLS
GFQFILNQYGCIVYHKELKRITVTTYNQFLTWKDISLSRLNVCLITWISNCLNTLNKSLG
LRCGFNNVILTQLFLYGDCILKLFHNEGFIKEVEGFIMSLILNITEEDQFRKRFYNM
LNNITDAANKAQKNLLSRVCHTLDDKTVDNIINGRWIILLKFLKLIKLAGDNNLNNLS
ELYFLFRIFGHPMVDERQAMDAVKVNCNETKFYLLSSLSMLRGAFIYRIIKGFVNNYNRW
PTLRNAIVLPLRWLTYYKLNTYPSLLELTERDLIVLSGLRFYREFRLPKKVDLEMIINDK
AISPPKNLIWTSFPRNYMPSHIQNYIEHEKLKFSESDKSRRVLEYLRLDNKFNECDLYNC
VVNQSYLNNPNHVVS LTGKERELSVGRMFAMQPGMFRQVQILA EKMI AENILQFFPESLT
RYGDLELQKILELKAGISNKS NRYNDNYNNYISKCSIITDLSKFNAFRYETSCICSDVL
DELHGVQSLFSWLHLTIPHVTIICTYRHAPPYIRDHNVDLNNVDEQSGLYRYHMGGIEGW
CQKLWTIEAISLLDLISLKGKFSITALINGDNQSIDISKPVRLMEGQTHAQADYLLALNS
LKLLYKEYAGIGHKLKGTETYISRDMQFMSKTIQHNGVYYPASIKKVL RVGPWINTILDD
FKVSLESIGSLTQELEYRGESLLCSLIFRNWLYNQIALQLKNHALC NKNLYLDILKVLK
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NHDLDKDLQDLSDDR LNKFLTCHITFDKNPNAEFVTLMRDPQALG SERQAKITSEINRLA
VTEVLSTAPNKIFS KSAQH YTTTEIDLNDIMQNI EPTYPHGLRVVYESLPFYKA EKIVNL
ISGTKSITNILEKTS AIDLTDIDRAT EMMRKNITLLIRILPLDCNRDKREILSMENLSIT
ELSKYVRERSWSLSNIVGVTSPSIMYTMDIKYTTSTIASGIIIEKYNVNSLTRGERGPTK
PWVGSSTQEKKTMPVYNRQVLTKKQRDQIDLLAKLDWVYASIDNKDEFMEELSIGTLGLT
YEKAKKLFPQYLSVNYLHRLTVSSRPCEFPASIPAYRTTNYHFDTSPINRILTEKYGDED
IDIVFQNCISFGLSLMSVVEQFTNVCPNRIILIPKLNEIHLMKPPIFTGDVDIHKLKQVI
QKQHMFLPDKISLTQYVELFLSNKTLKSGSHVNSNLILAHKISDYFHNTYILSTNLAGHW
ILIIQLMKDSKGIFEKDWGEGYITDHMFINKVFFNAYKTYLLCFHKGYGKAKLECDMNT

SDLLCVLELIDSSYWKSMSKVLFLEQKVIKYILSQDASLHRVKGCHSFKLWFLKRLNVAEF
TVCPWVVNIDYHPHTMKAILTYIDLVRMLINIDRIHIKNKHKFNDEFYTSNLFYINYNF
SDNTHLLTKHIRIANSELENNYNKLYHPTPETLENILANPIKSNDKKTLDYCYGKNVDS
IMLPLLSNKKLVKSSAMIRTNYSKQDLYNLFPTVVIDRIIDHSGNTAKYNQLYTTTSHQI
SLVHNSTSLYCMLPWHHINRFNFVFSSTGCKISIEYILKDLKIKDPNCIAFIGEGAGNLL
LRTVVELHPDIRYIYRSLKDCNDHSLPIEFLRLYNGHINIDYGENLTIPATDATNNIHWS
YLHIKFAEPISLFVCDAELPVTVNWSKIIIEWSKHVRKCKYCSSLVNKCTLIVKYHAQDDI
DFKLDNITILKTYVCLGSKLKGSEVYLVLTIGPANIFPVFNVVQNAKLILSRKTNFIMPK
KADKESIDANIKSLIPFLCYPITKKGINTALSKLKSVVSGDILSYSIAGRNEVFSNKLIN
HKHMNILKWFNHLNFRSTELNYNHLVMVESTYPYLSELLNSLTTELKLIKITGSLLY
NFHNE

Table S4. Molecular docking results of Comp-1 and EMC-1 with other available SARS-CoV-2 non-structural proteins.

Protein/Ligand	EMC-1		Comp-1		TBP-2		TPP-1	
PDB ID_Protein Name	Affinity	Total Energy	Affinity	Total Energy	Affinity	Total Energy	Affinity	Total Energy
5rhb_MPro	-6.739	-1.884	-6.031	-5.596	-5.923	-6.512	-6.674	-0.538
5rlj_Helicase	-7.545	-4.596	-6.475	-8.296	-6.112	-9.81	-6.963	-6.035
6wtc_NSP8	-6.474	1.683	-6.689	-5.693	-6.249	-6.705	-6.462	0.056
7cz4_NSP3	-8.359	-5.425	-6.996	-7.21	-6.208	-6.488	-7.043	-3.45
7k7p_NSP1	-6.769	-0.568	-6.508	-4.72	-6.285	-5.569	-6.57	-2.187
7keh_NSP15	-7.332	-2.183	-6.887	-13.277	-6.444	-9.075	-6.667	-3.873
7msx_NSP2	-7.607	-1.233	-6.69	-7.684	-6.274	-6.048	-7.295	-6.405

All energies are in kcal/mol. Colour fill indicates the best energies of docked complex.

Table S5. Molecular docking results of drugs studied against mutated SARS-CoV-2 RdRp (P323L).

Ligand	Affinity	Total Energy
REM	-7.589	-31.368
Comp-1	-6.195	-7.928
EMC-1	-6.074	-5.247
FAV	-5.901	-4.163
TPP	-6.456	-3.135

All energies are in kcal/mol. Colour fill indicates the best energies of docked complex.

EMC-1 = Essramycin
Comp-1 = Monomethylated triazolopyrimidine
TBP-2 = MTP stereoisomer
TPP-1 = Triazolopyrimidine
REM = Remdesivir
FAV = Favipiravir

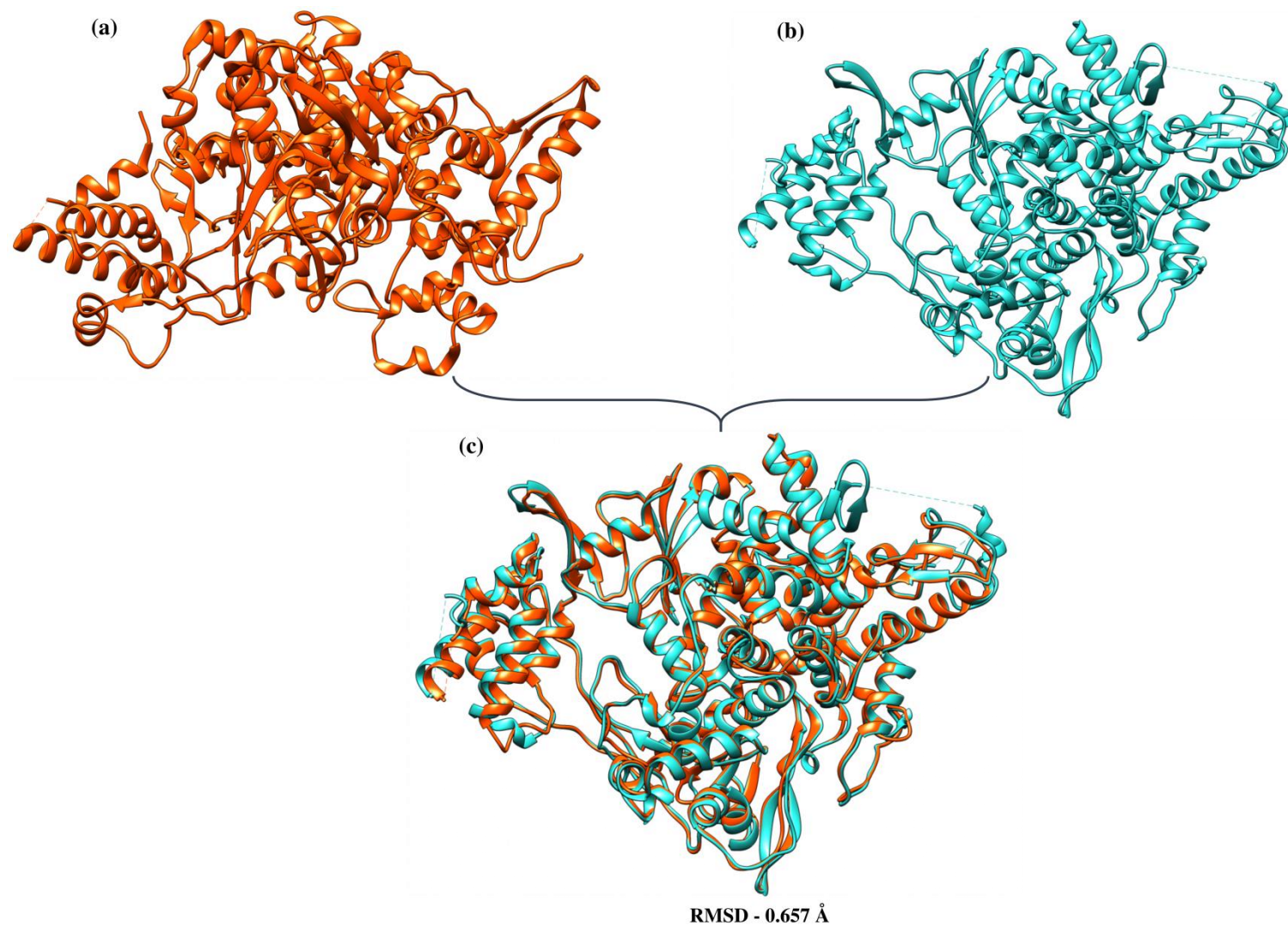


Figure S1(A). Superimposed structures of SARS-CoV-2 and SARS-CoV RdRp. (a) 3D structure of SARS-CoV, (b) 3D structure of SARS-CoV-2 and (c) superimposed conformation of SARS-CoV & SARS-CoV-2 RdRp.

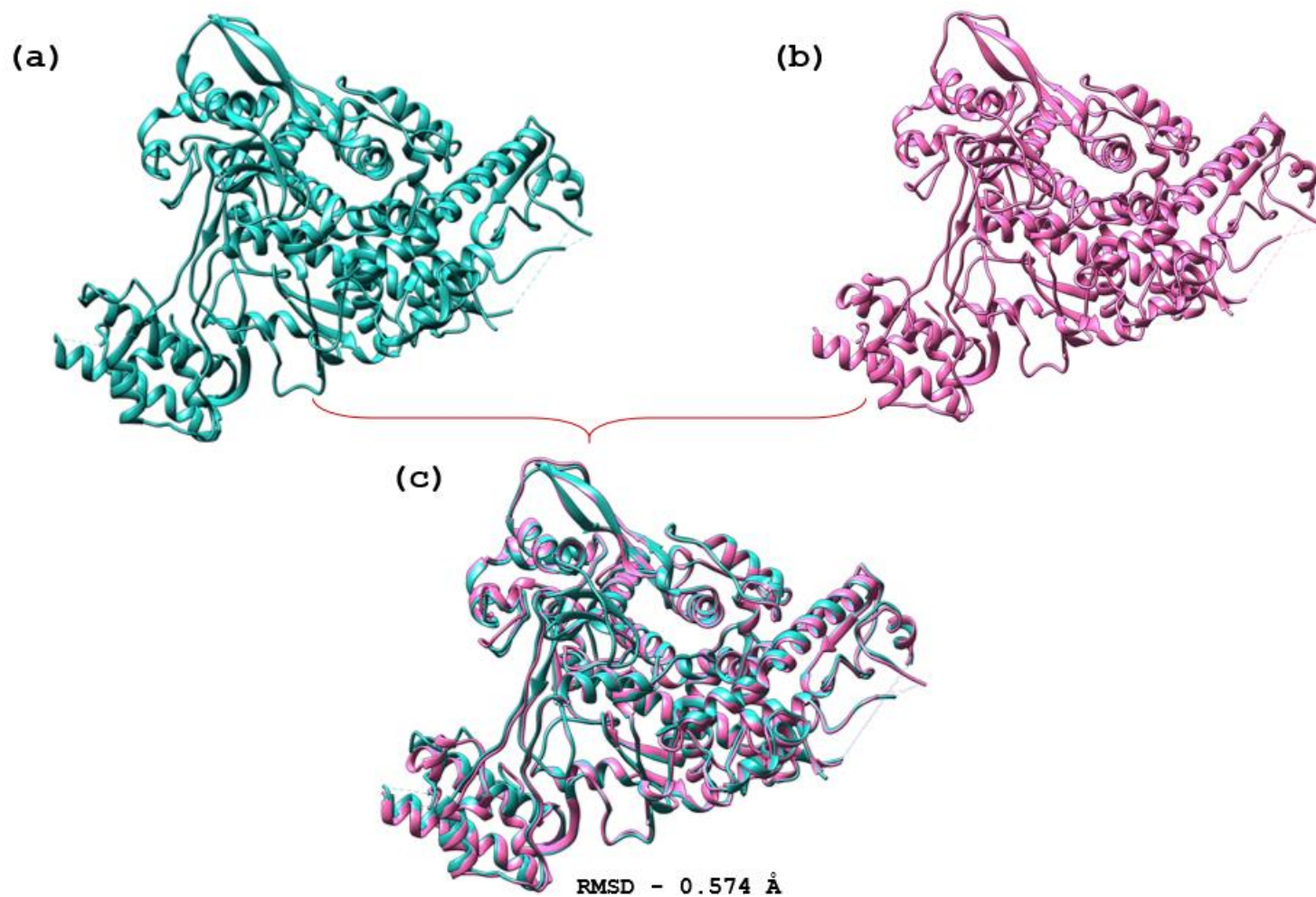
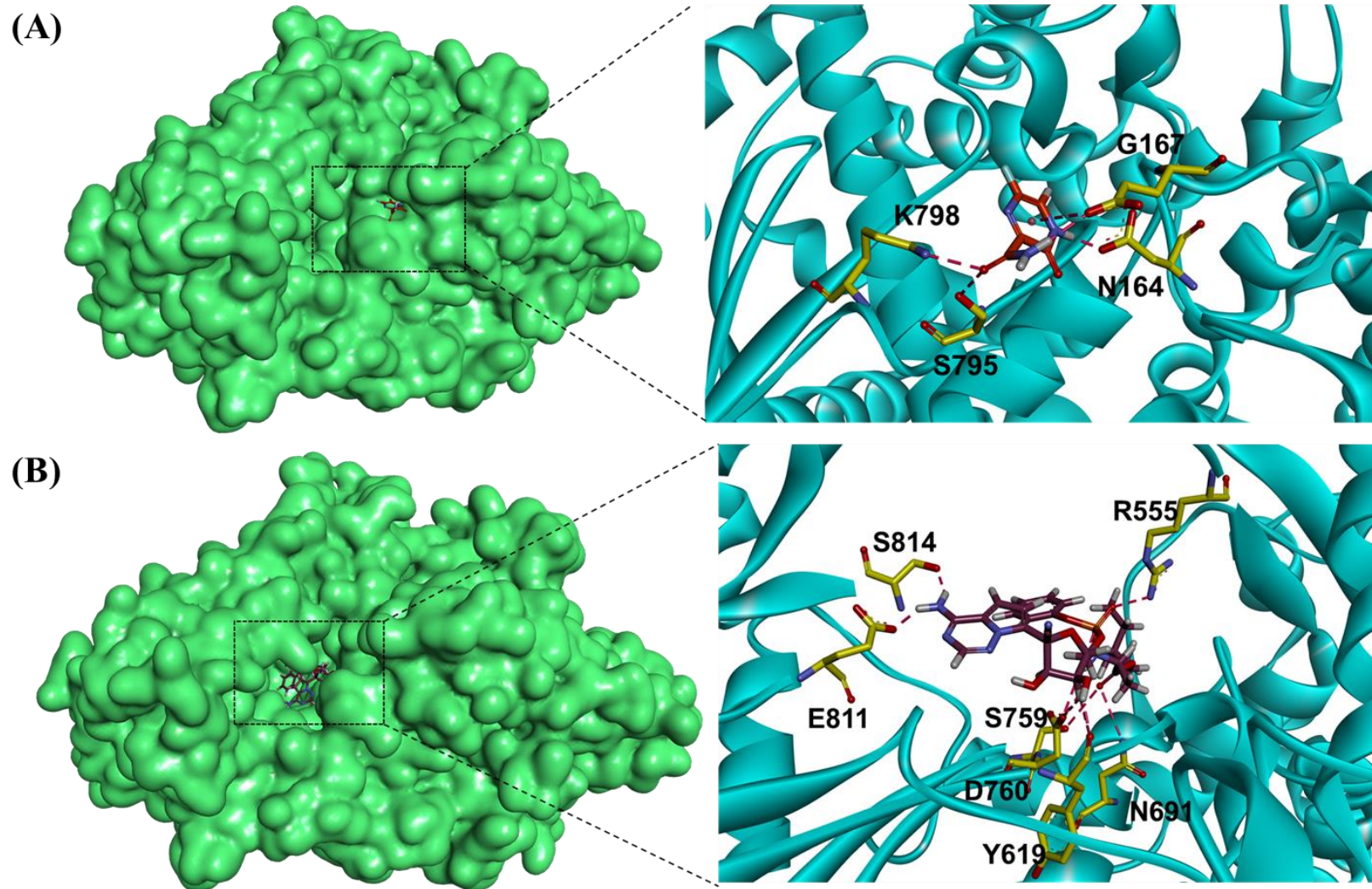


Figure S1 (B). Superimposed conformation of 7bv1 and 7bv2 RdRp protein of SARS-CoV-2. (a) Showing the apo RdRp (7bv1), (b) represent the complex RdRp (7bv2) and (c) superimposed structure of both protein



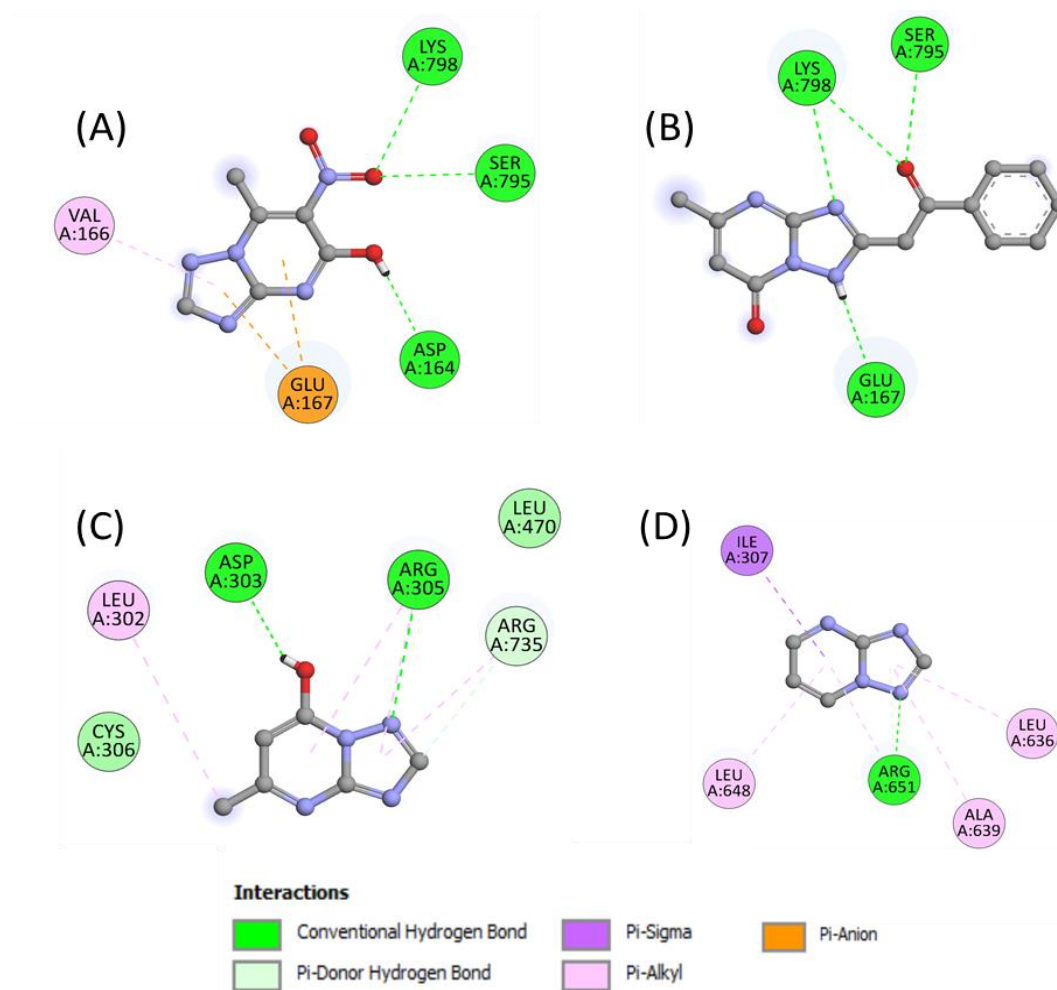


Figure S3. 2D representation of ligand interactions with SARS-CoV-2 RdRp. (A) Comp-1 (B) EMC-1 (C) TBP-2 (D) TPP-1.

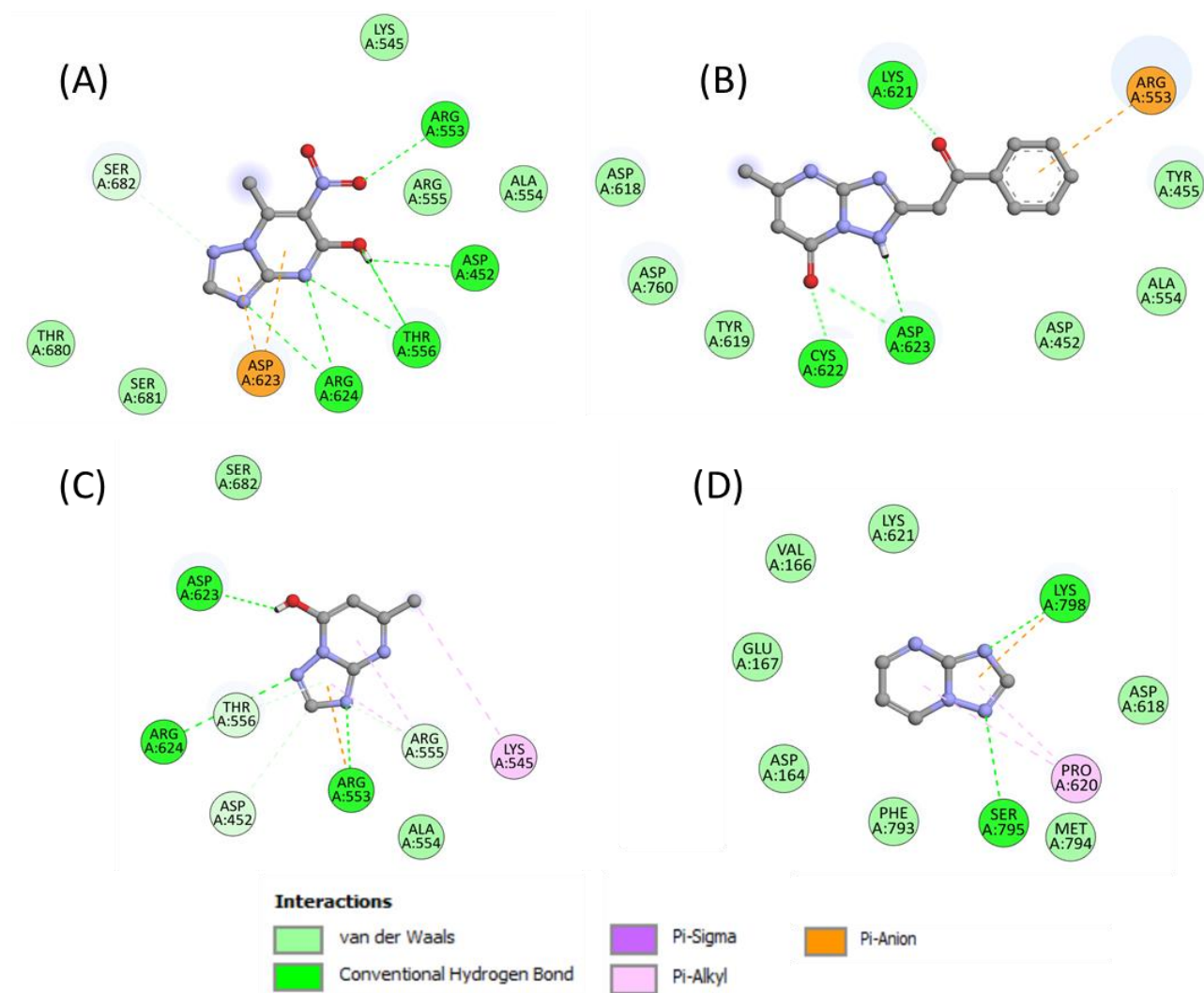


Figure S4. 2D representation of ligand interactions with SARS-CoV RdRp. (A) Comp-1 (B) EMC-1 (C) TBP-2 (D) TPP-1.

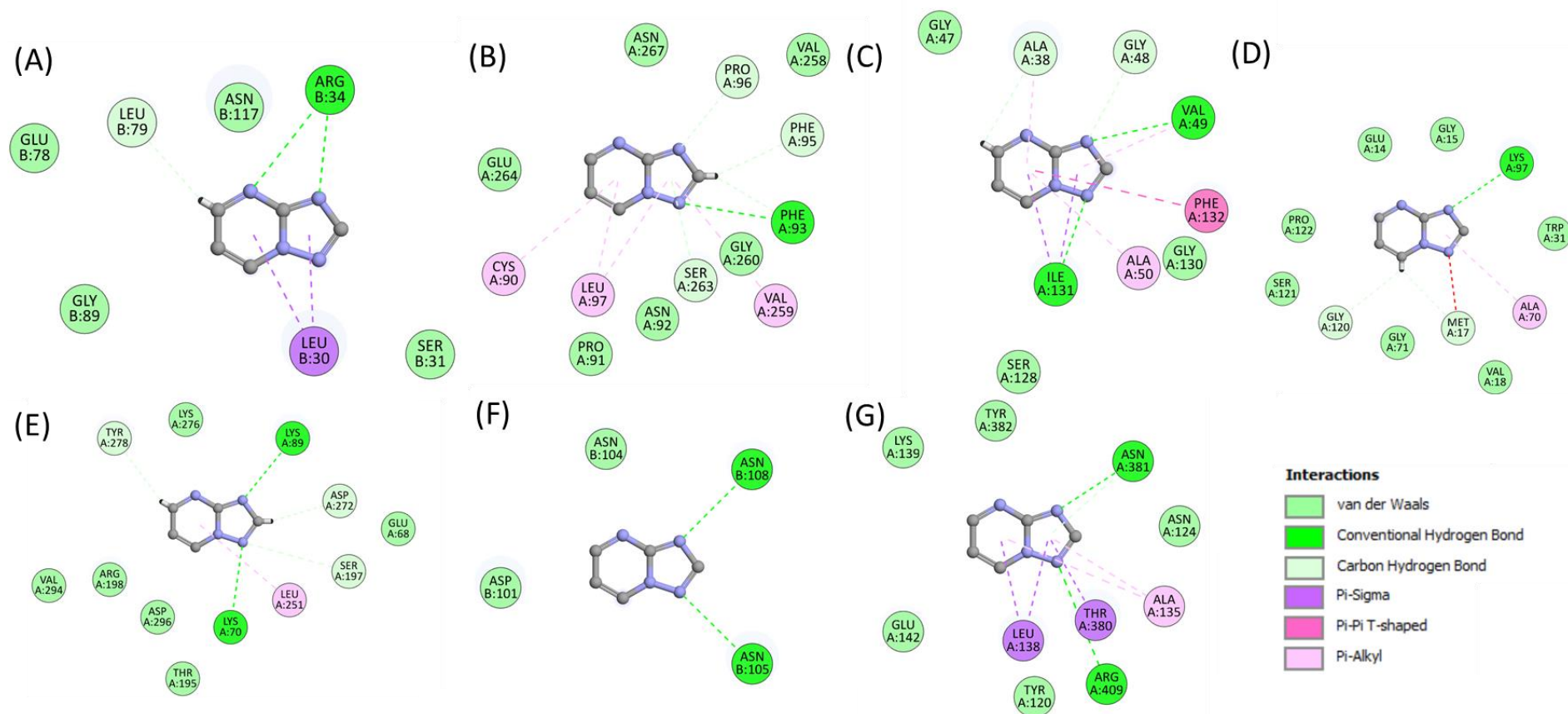


Figure S5. 2D representation of Comp-1 interactions with SARS-CoV-2 NSPs. (A) NSP1 (B) NSP2 (C) NSP3 (D) NSP5 (E) NSP8 (F) NSP13 (G) NSP15.

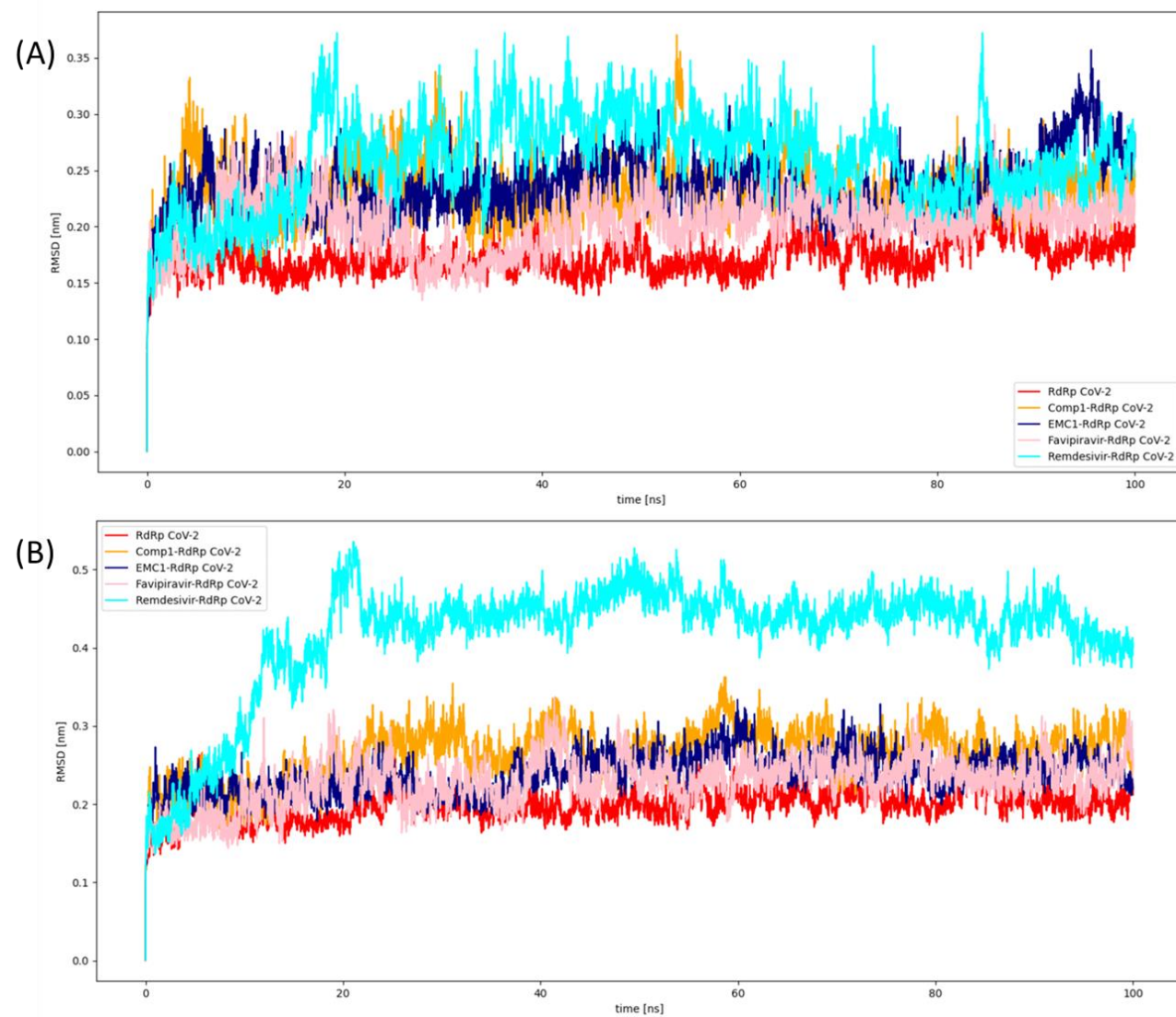


Figure S6. RMSD values of SARS-CoV-2 RdRp and complexes at (A) set random velocity of -1 (B) set random velocity of -2 during 100 ns MD simulation.

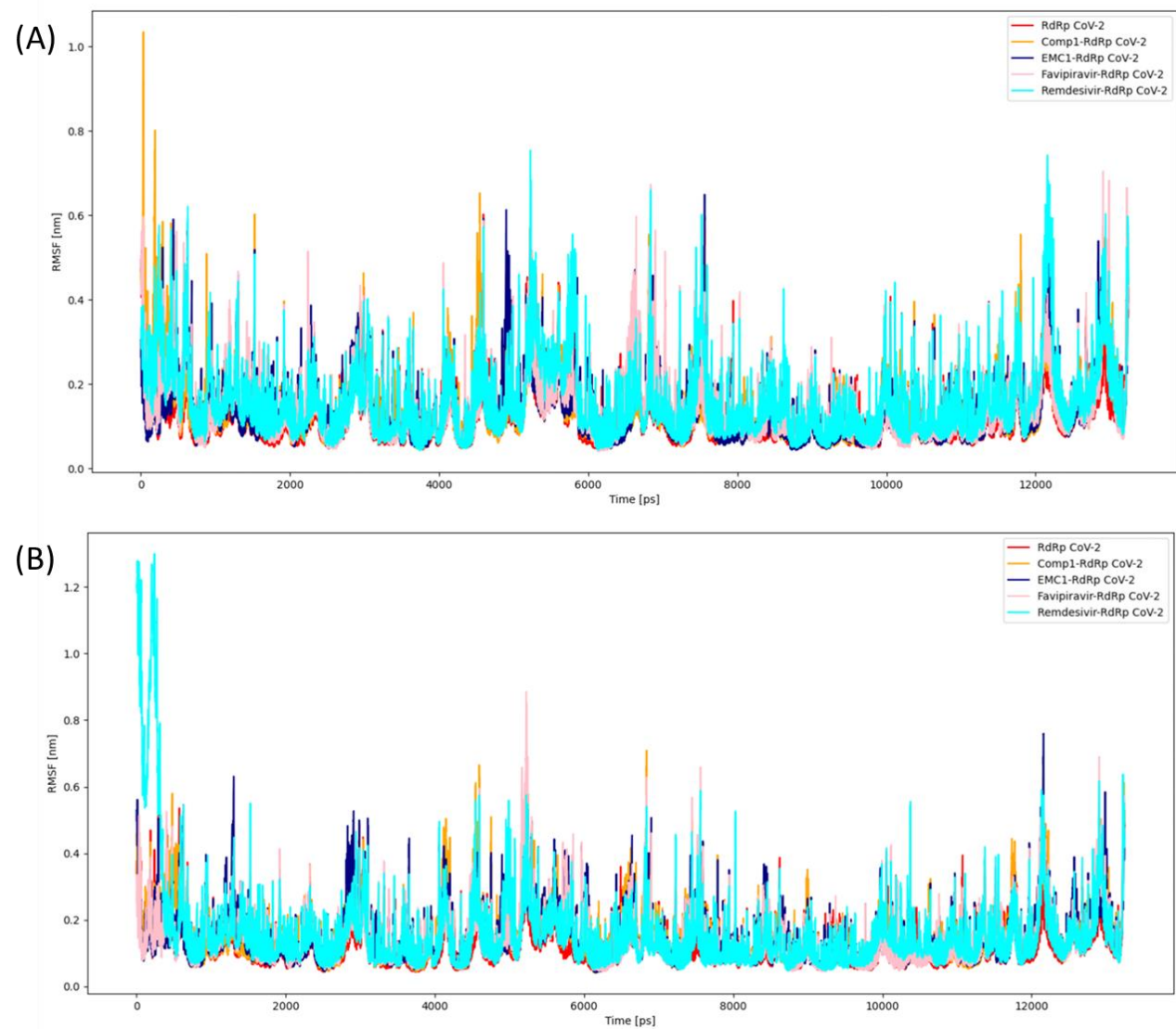


Figure S7. RMSF values of SARS-CoV-2 RdRp and complexes at (A) set random velocity of -1 (B) set random velocity of -2 during 100 ns MD simulation.

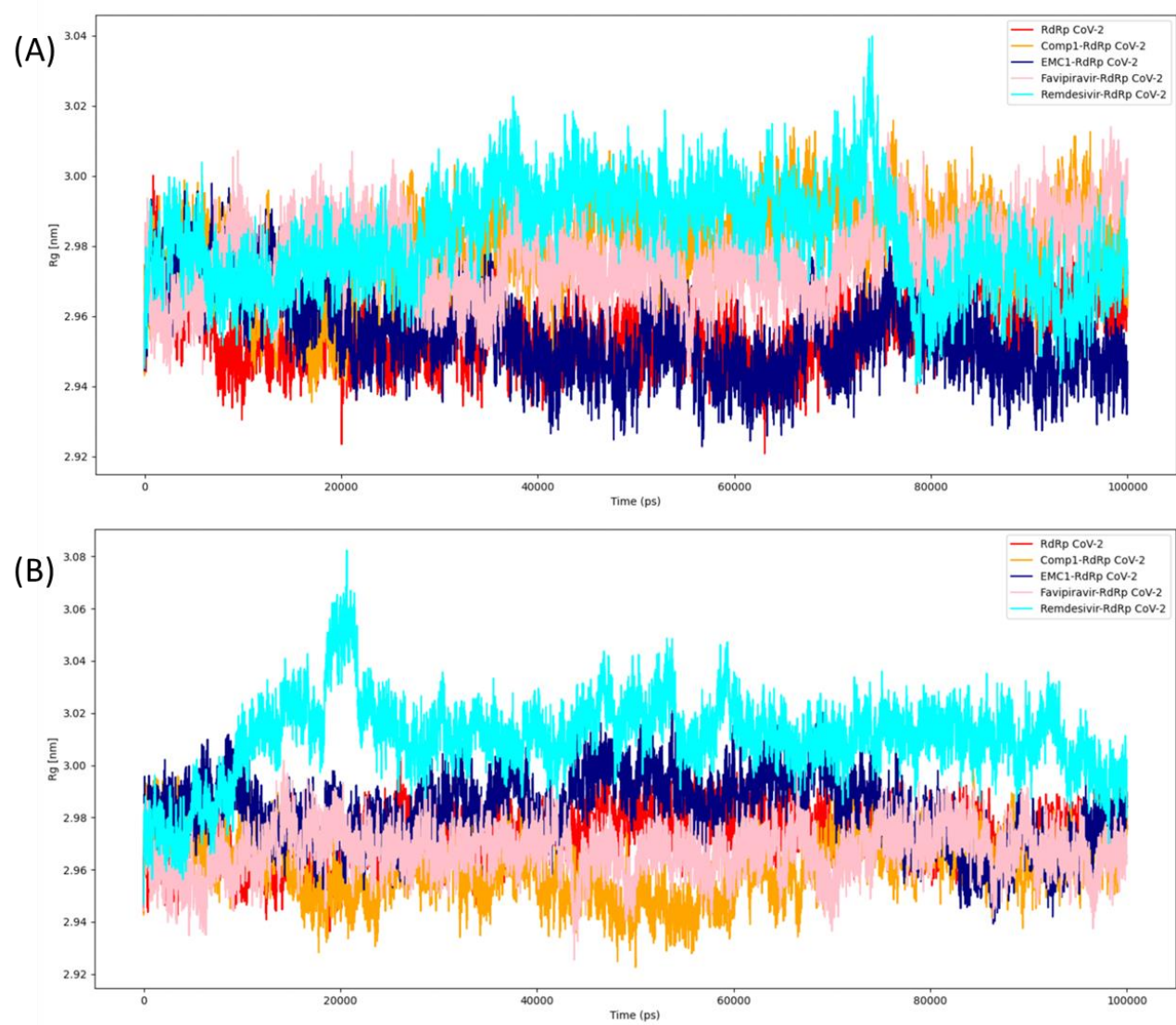


Figure S8. R_g values of SARS-CoV-2 RdRp and complexes at (A) set random velocity of -1 (B) set random velocity of -2 during 100 ns MD simulation.

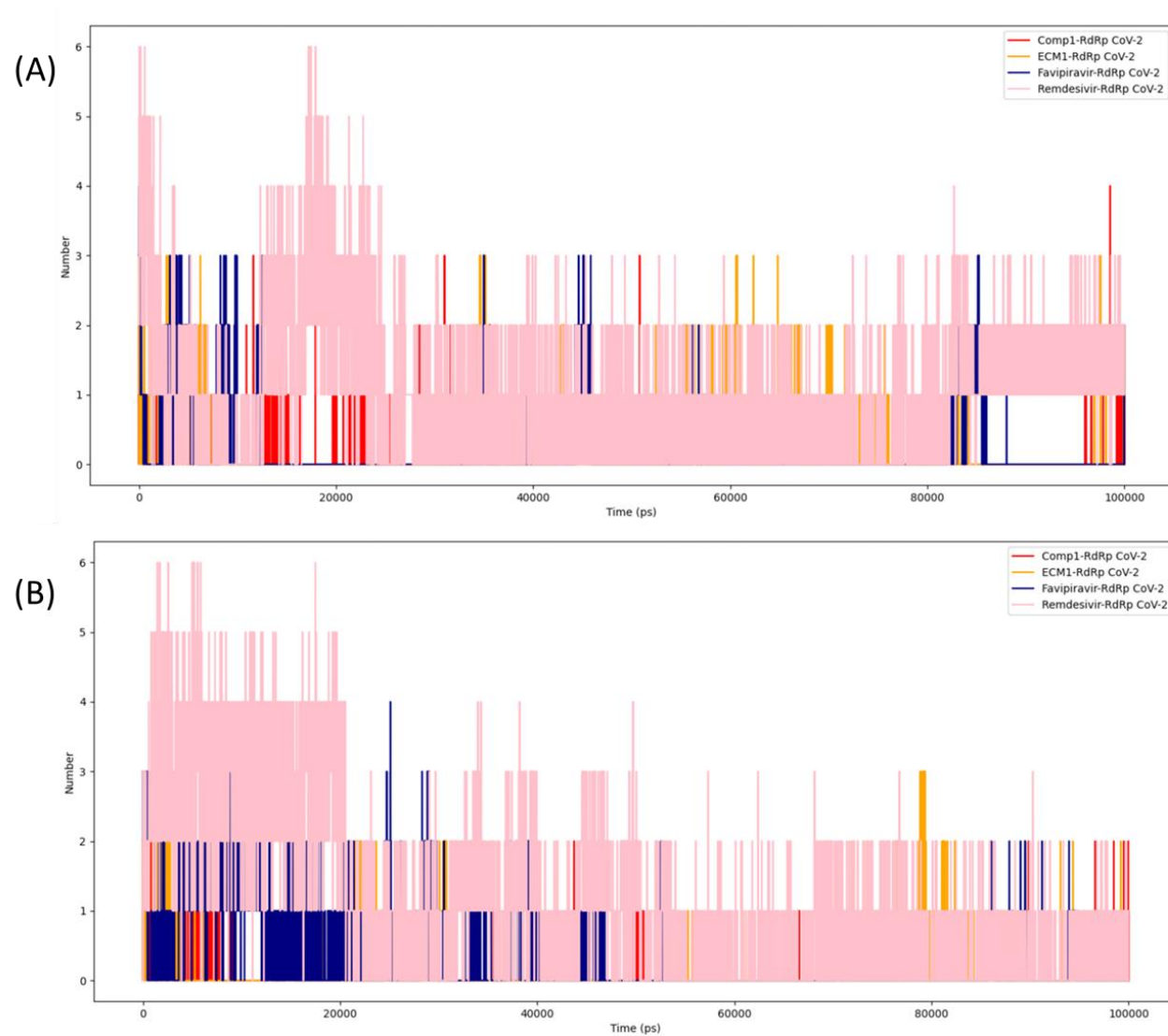


Figure S9. Number of H-bonds formed by SARS-CoV-2 RdRp-ligand complexes at (A) set random velocity of -1 (B) set random velocity of -2 during 100 ns MD simulation.

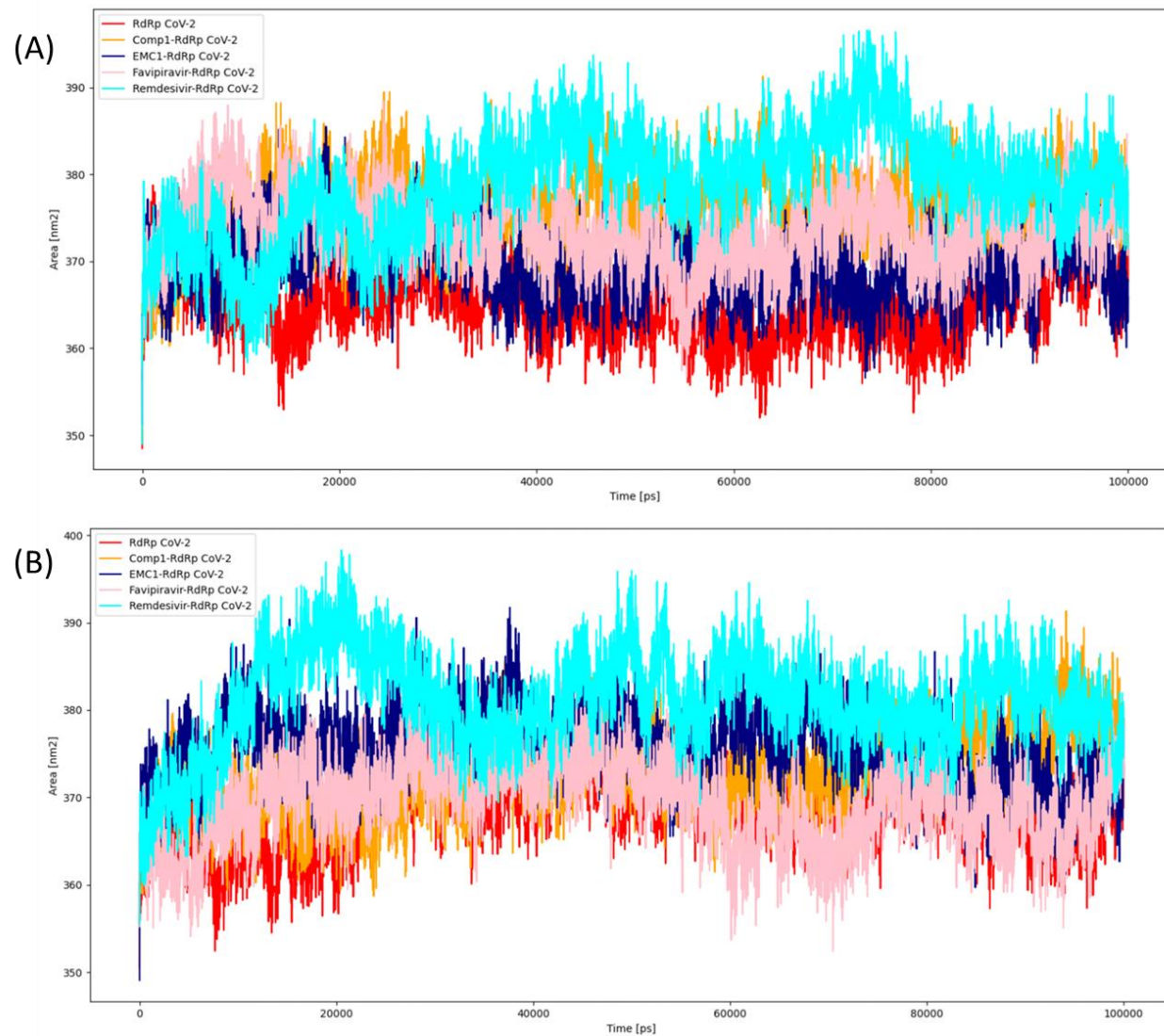


Figure S10. Solvent accessible surface area of SARS-CoV-2 RdRp and complexes at (A) set random velocity of -1 (B) set random velocity of -2 during 100 ns MD simulation.