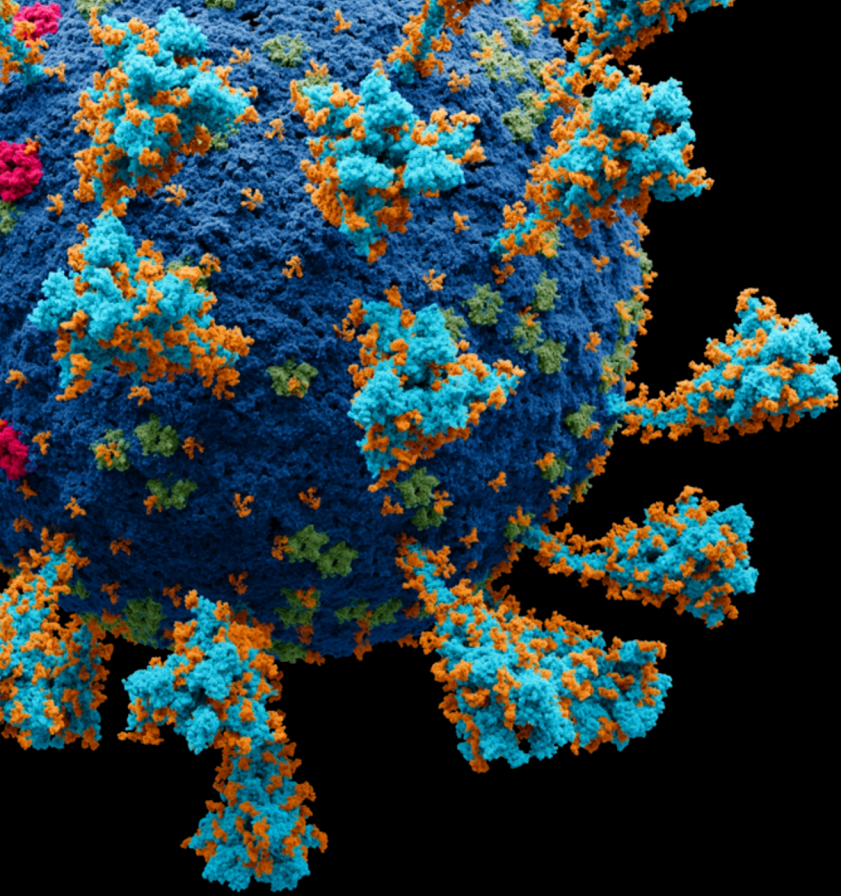




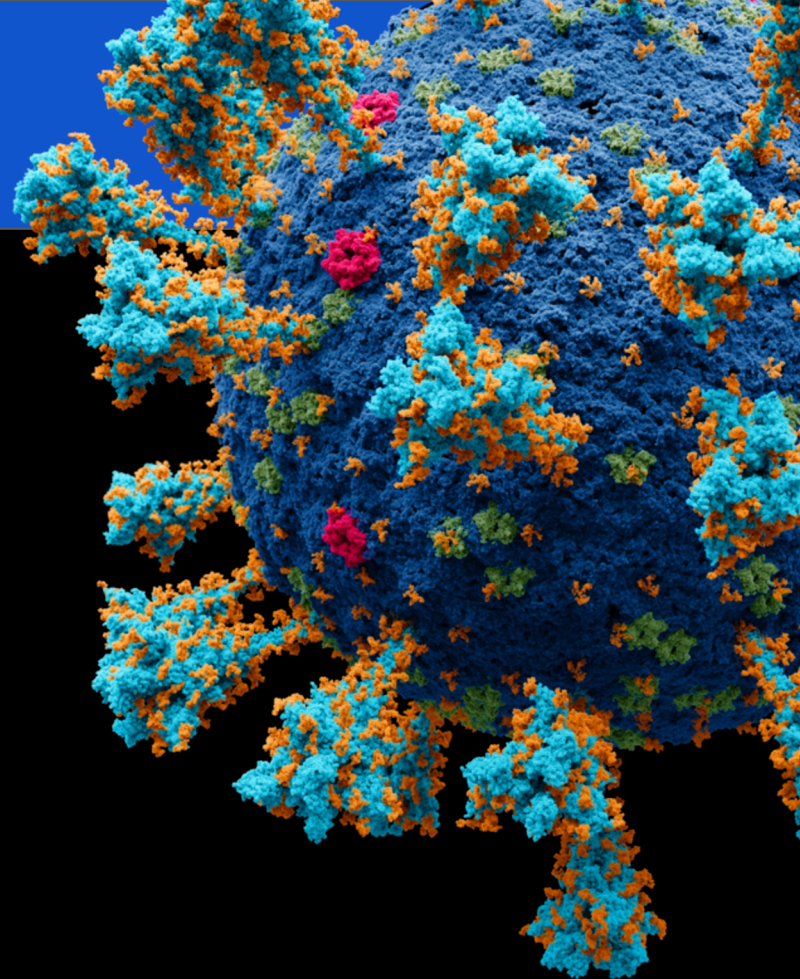
SARS-COV-2

Pau Bosch, Anna Fustero,
Gisela Juliachs
4t Biologia Humana, 2024

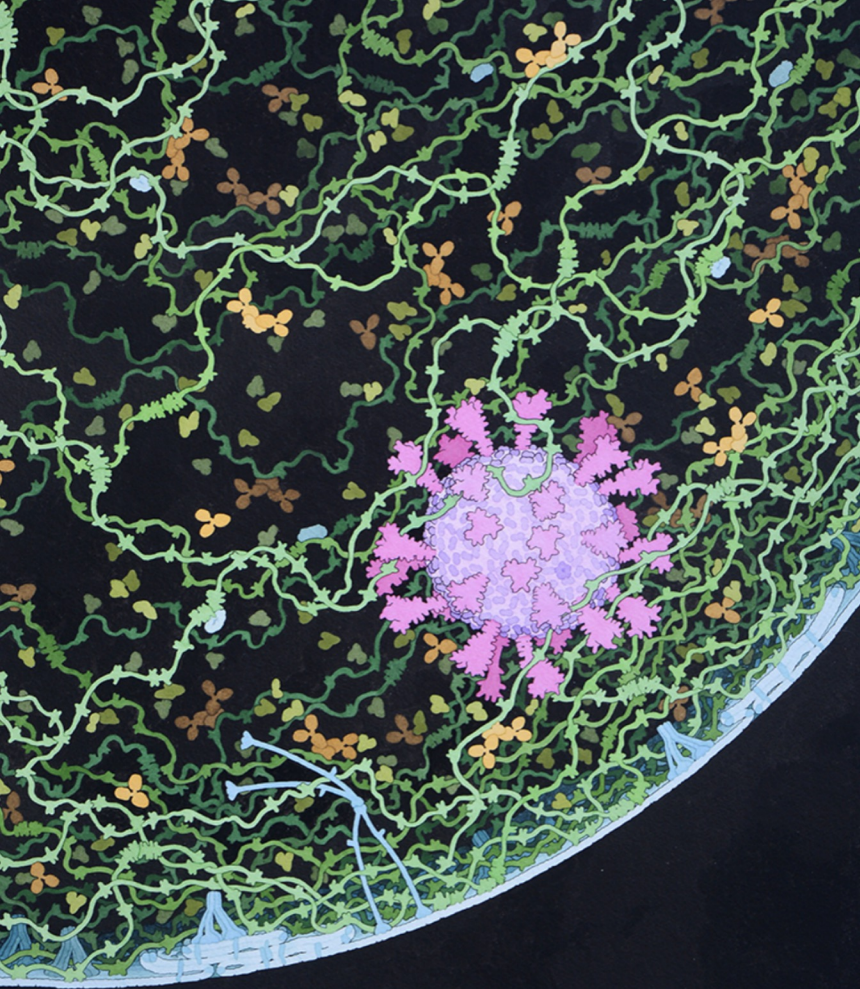
Scientifically accurate atomic model of the external structure of
SARS-covid. Global Service Center, 2024

INDEX

- 1 INTRODUCTION
- 2 STRUCTURAL PROTEINS
- 3 STRUCTURE DOMAIN ANALYSIS
- 4 CONCLUSION AND
SUPPLEMENTARY MATERIAL



Scientifically accurate atomic model of the external structure of SARS-covid. Global Service Center, 2024



INTRODUCTION

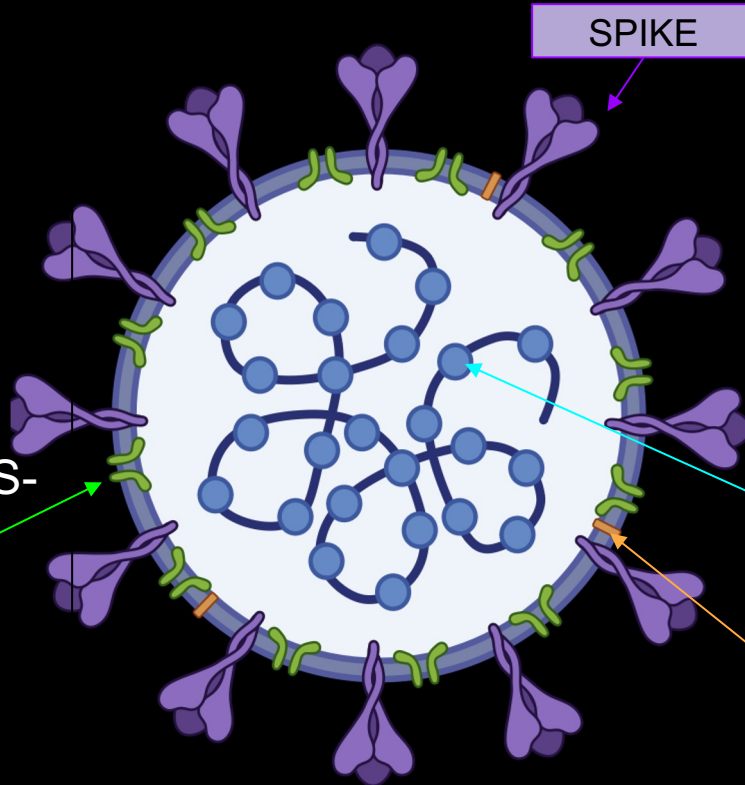
GENERAL DESCRIPTION

SARS-CoV2

CHARACTERISTICS

- Positive single strand RNA virus
- Acute severe respiratory syndrome
- Pathogenic Cov like MERS-CoV and SARS-CoV

M PROTEIN
(MEMBRANE)



STRUCTURE

- Helicoidal nucleocapsid
- Spherical Envelope
- 4 Major Structural proteins

NUCLEOCAPSID

E PROTEIN
(ENVELOPE)

PHYLOGENY



Realm

Phylum

Order

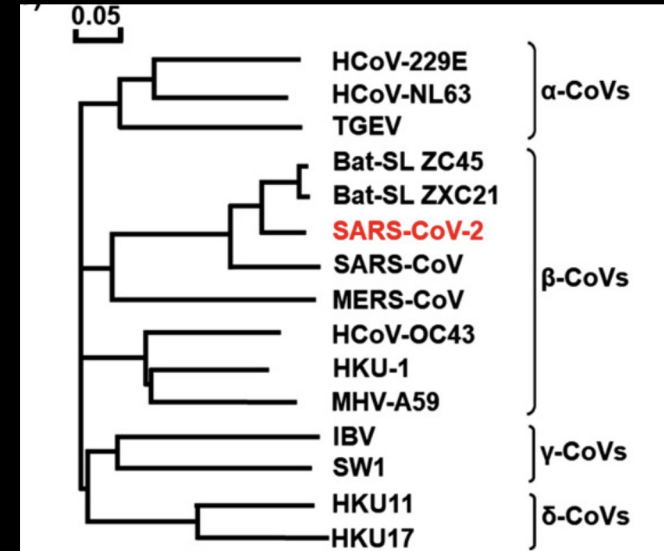
Family

Subfamily

Genera

Subgenera

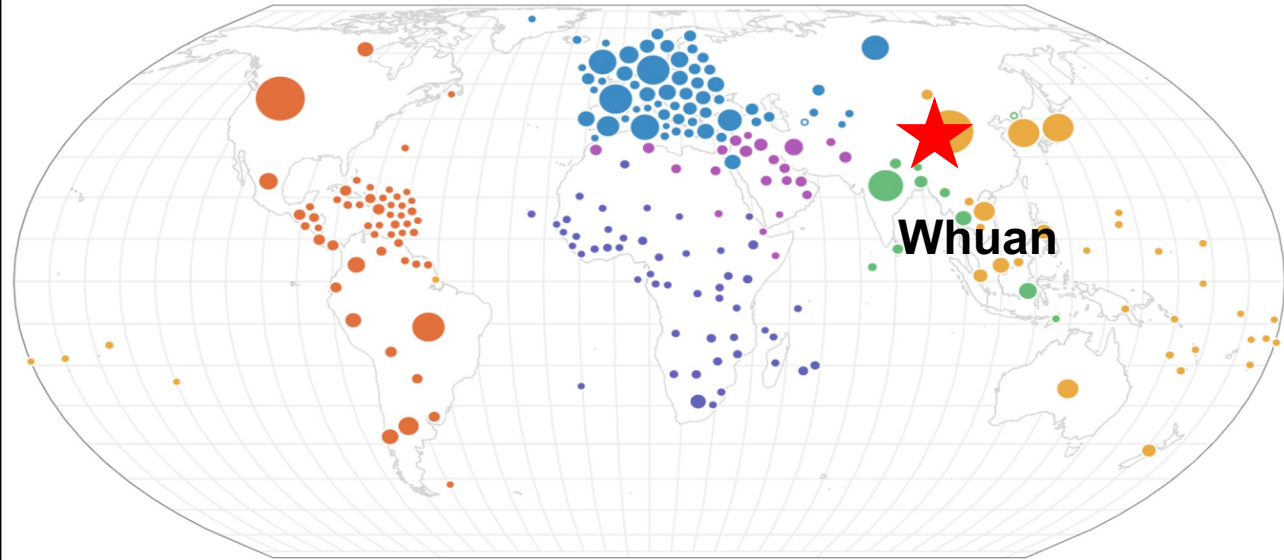
Strain



From SARS to SARS-CoV-2, insights on structure, pathogenicity and immunity aspects of pandemic human coronaviruses. *Infection, Genetics and Evolution*, Kirtipal, N. et al.2020

EPIDEMIOLOGY

- Emerged in Wuhan, China in 2019
- 703.584.660 cases
- 6.085447 death
- Zoonotic pathogen
- Incubation period 2-14 days
- High variance and efficient spreading capacity.
- R_0 (2-3)



WHO Regions

■ Africa

■ Americas

■ Eastern Mediterranean

■ Europe

■ South-East Asia

■ Western Pacific

EPIDEMIOLOGY

SYMPTOMS

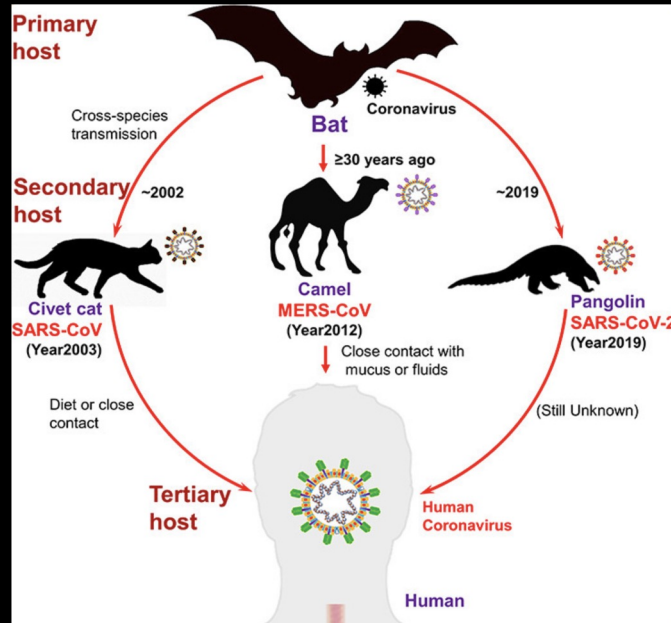
Main

- Fever
- Myalgia
- Headache
- Loss of taste and smell

Complex

- Hepatic necrosis
- Myocardial Infarction
- Lymphatic endothelitis
- ARDS

HOSTS



From SARS to SARS-CoV-2: insights on structure, pathogenicity and immunity aspects of pandemic human coronaviruses. *Infection, Genetics and Evolution*, Kirtipal, N. et al.2020

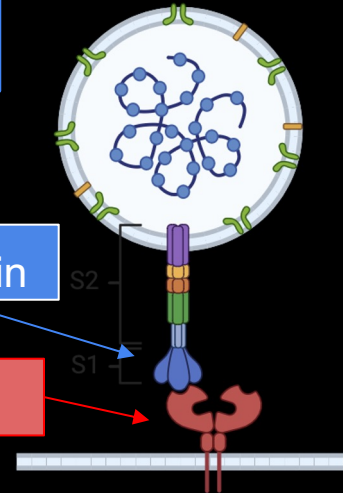
TRANSMISSION

Droplets and aerosols

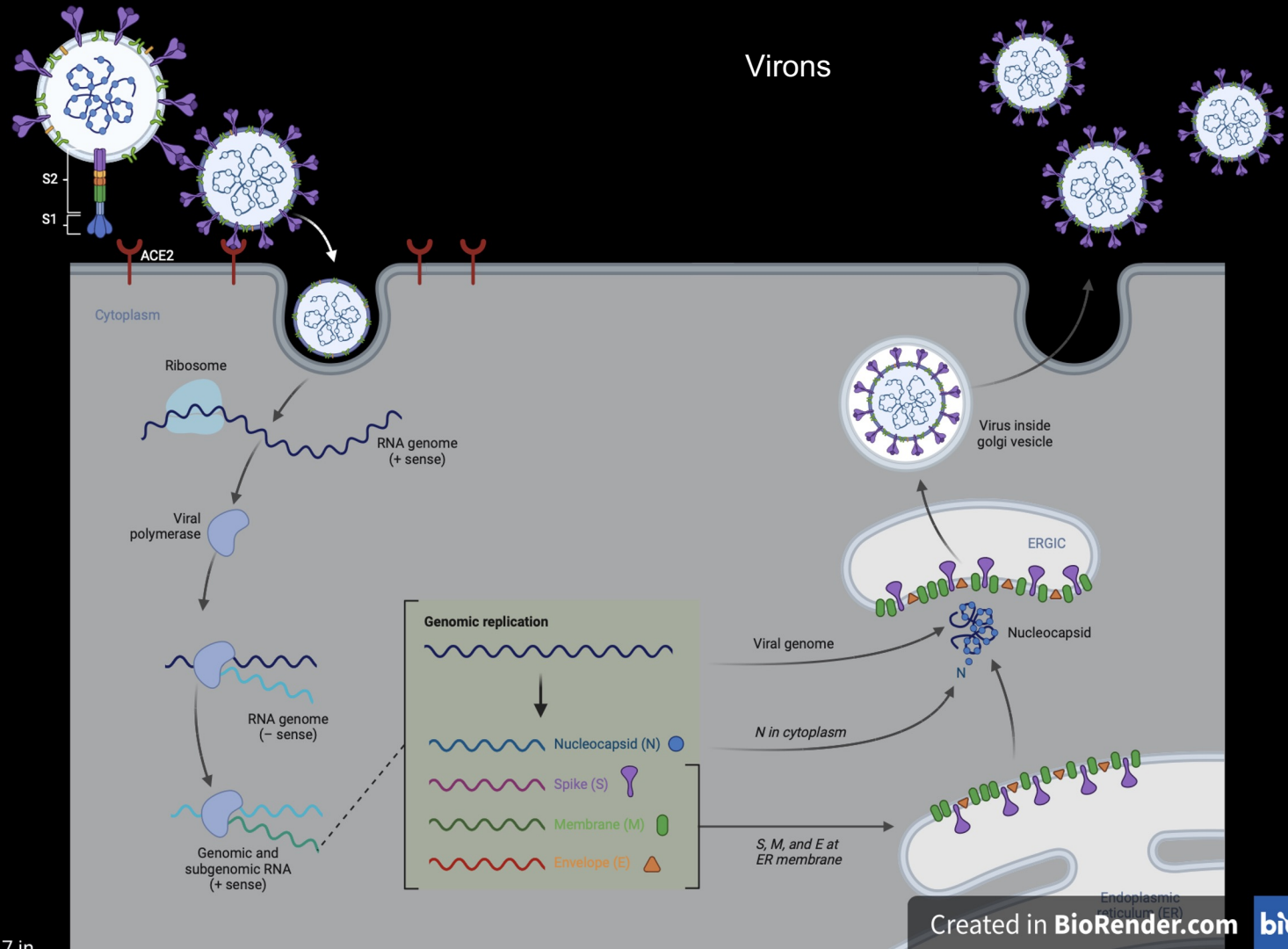
URT

S protein

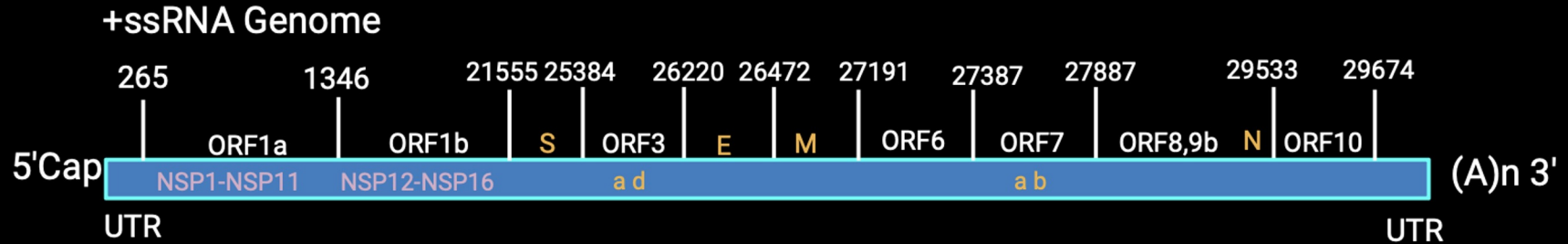
ACE2



VIRAL CYCLE

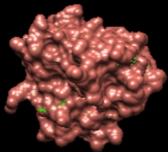


GENOME

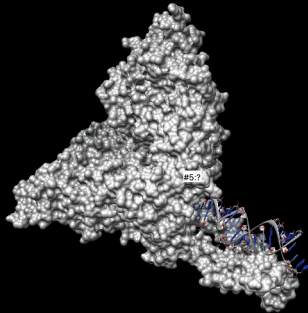


Non-Structural proteins

Structural and Accessory proteins



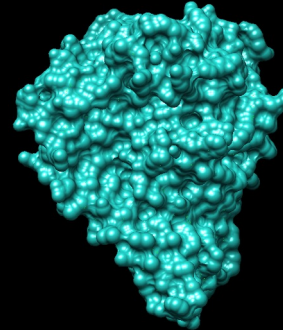
NSP1
PDB:7K3N



NSP12
PDB:6YYT



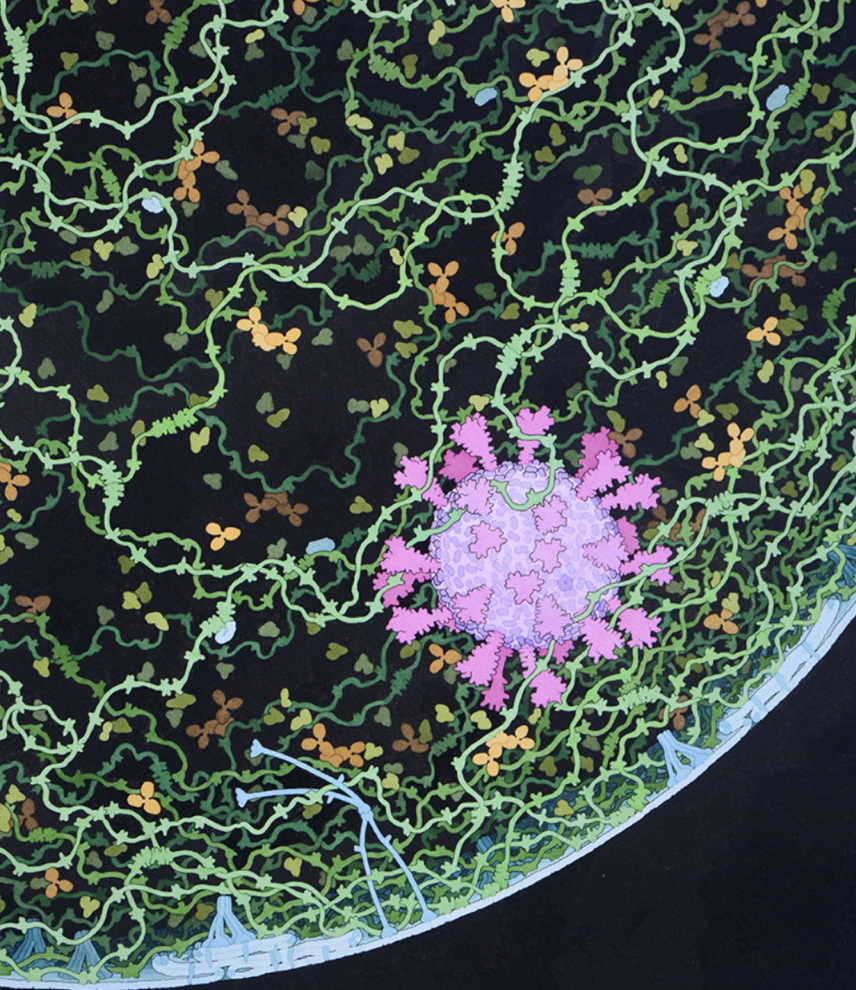
SPIKE PROTEIN
PDB:6VYB



M PROTEIN
PDB:8CTK



N PROTEIN
PDB:8FD5



STRUCTURAL PROTEINS

N PROTEIN



PDB: 8FD5

N PROTEIN NTD

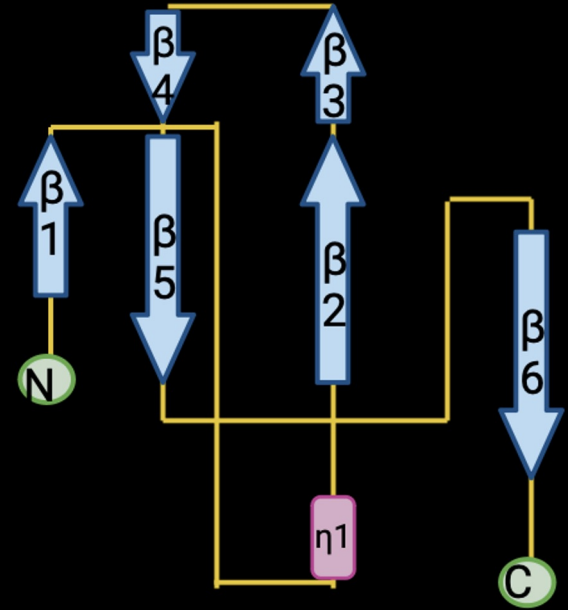


β antiparallel strand

- $\beta 1$
- $\beta 2$
- $\beta 3$
- $\beta 4$
- $\beta 5$
- $\beta 6$

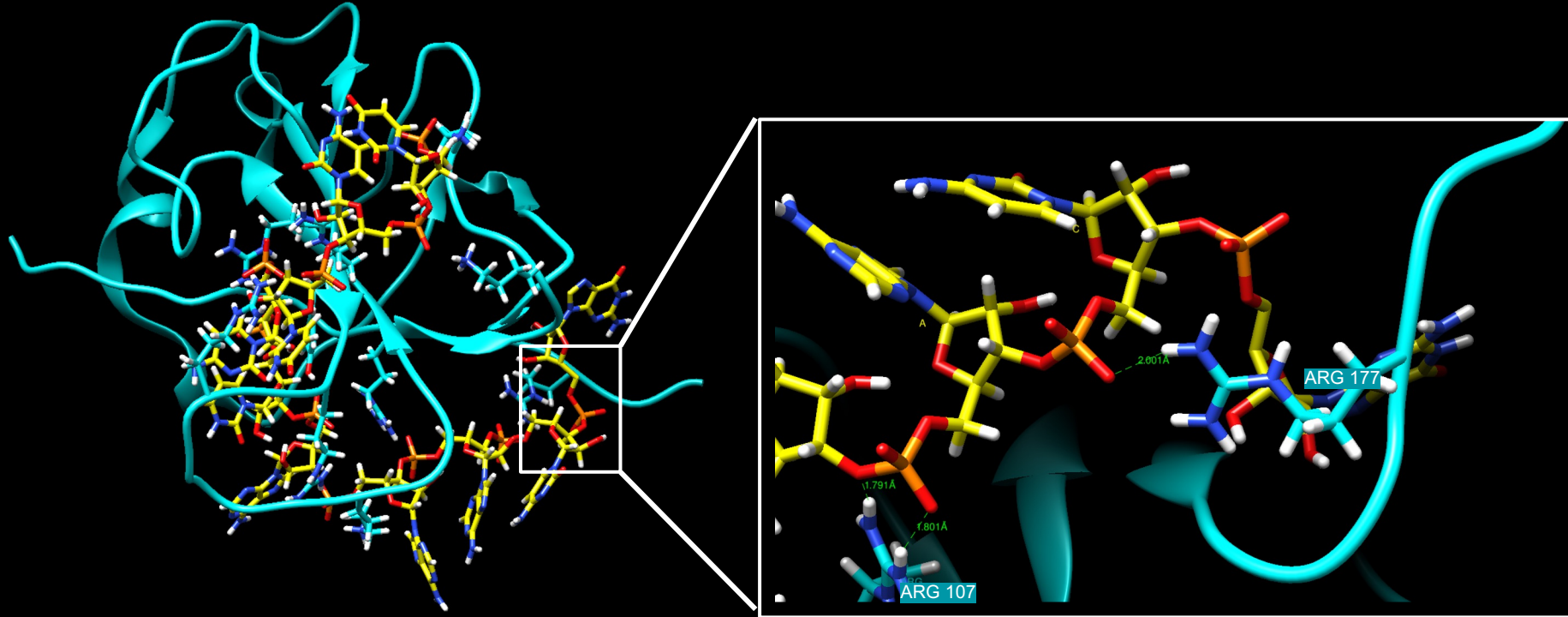
3_{10} Helix

• $\eta 1$



PDB: 7CDZ

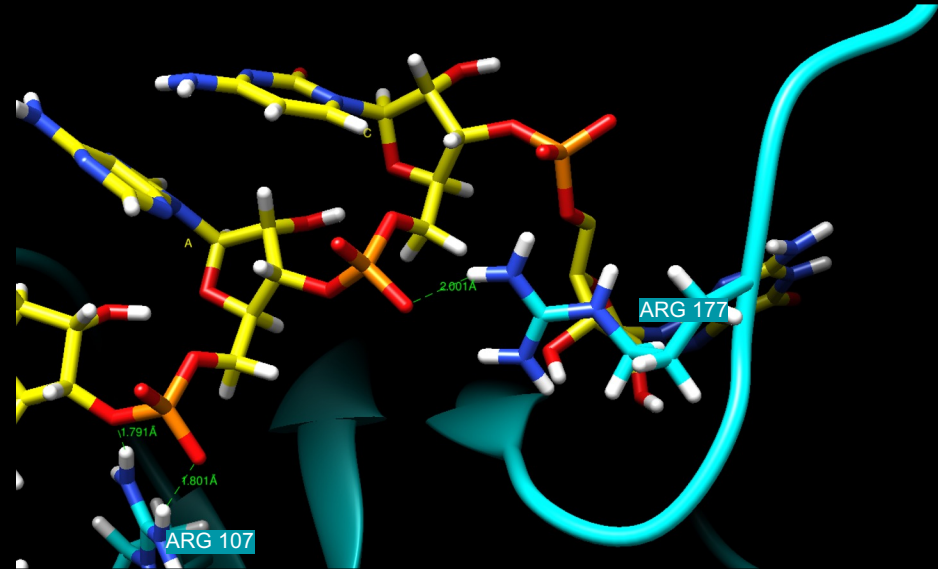
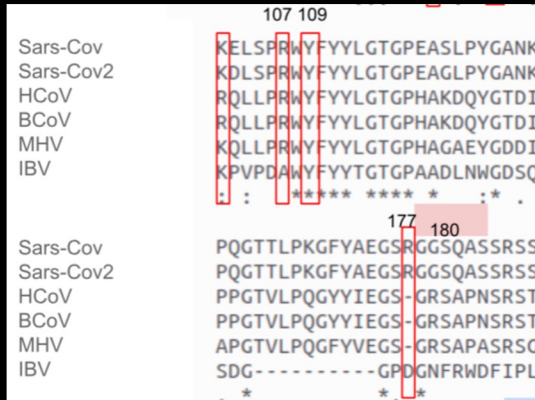
N-NTD/ssRNA INTERACTIONS



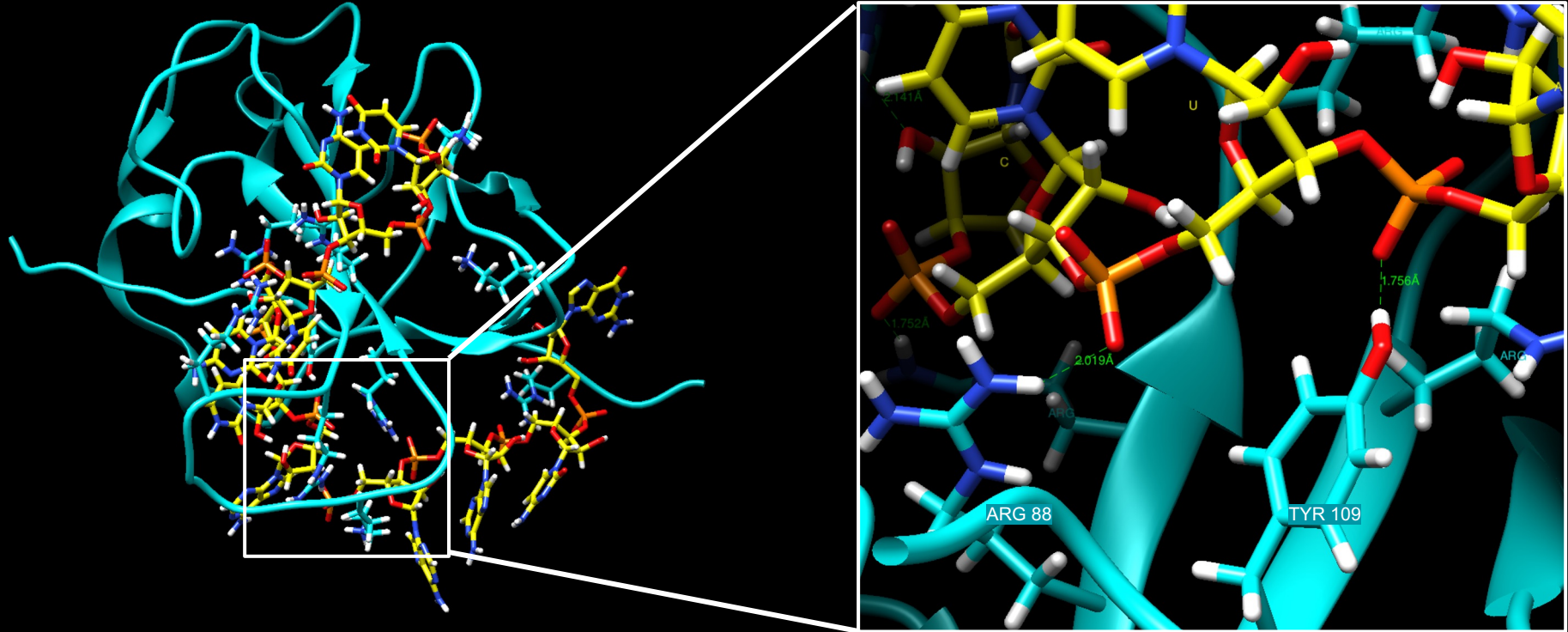
PDB: 7ACT

N-NTD/ssRNA INTERACTIONS

Protein residue	Atom	ssRNA nucleotide
ARG 177	N	C 9 [OP1]
ARG 107	N	A 7 [O3']
ARG 107	N	A 8 [OP1]



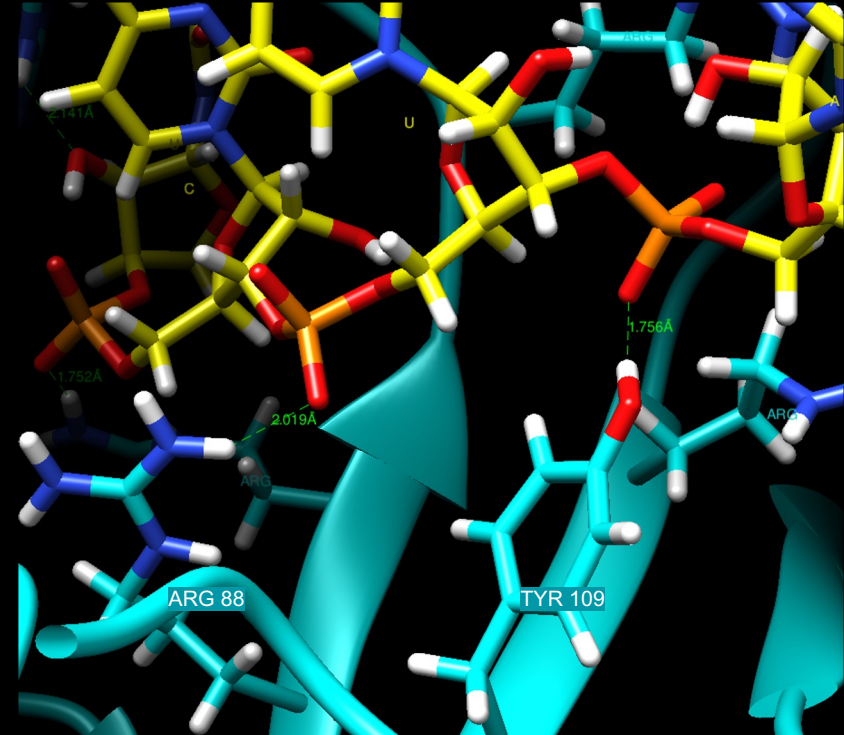
N-NTD/ssRNA INTERACTIONS



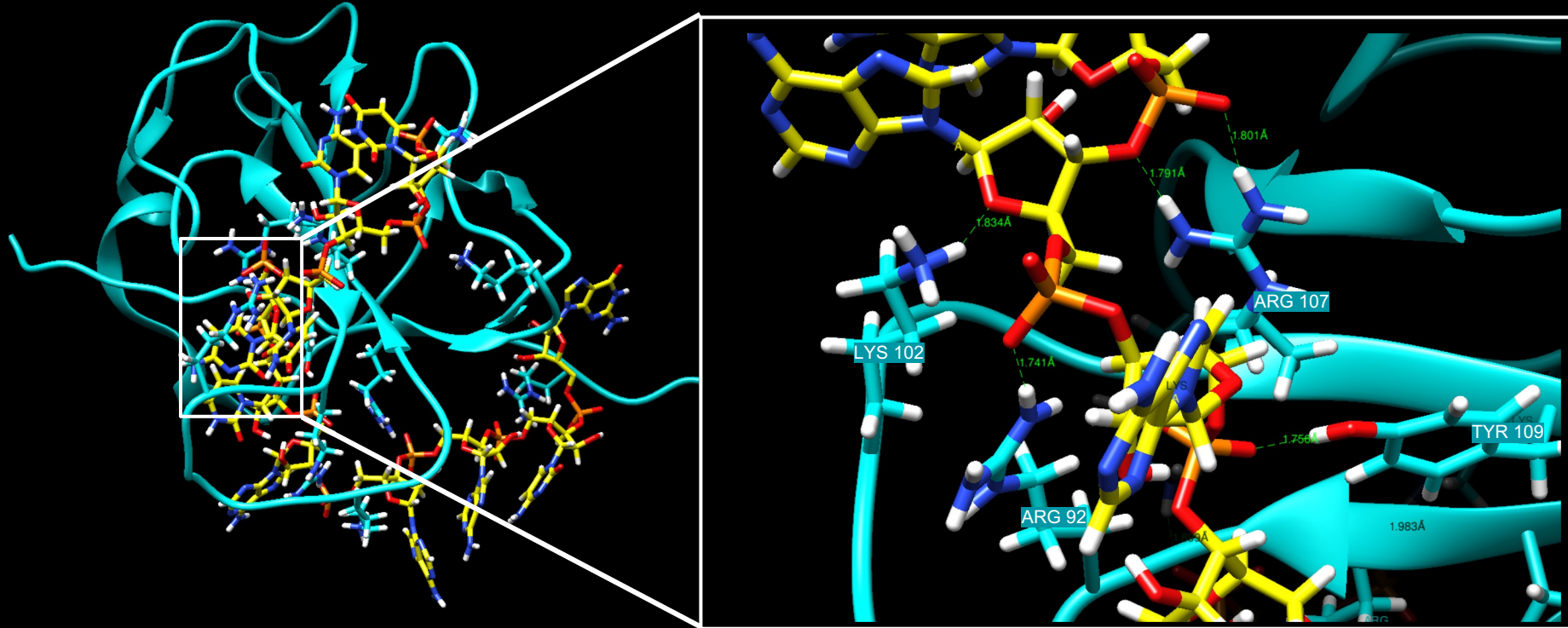
N-NTD/ssRNA INTERACTIONS

Protein residue	Atom	ssRNA nucleotide
ARG 88	N	U 5 [OP1]
TYR 109	OH	A 6 [OP2]

	88 89
Sars-Cov	GYRRAT
Sars-Cov2	GYRRAT
HCoV	GYWYRH
BCoV	GYWYRH
MHV	GYWYRH
IBV	GYWRR -
	** : *

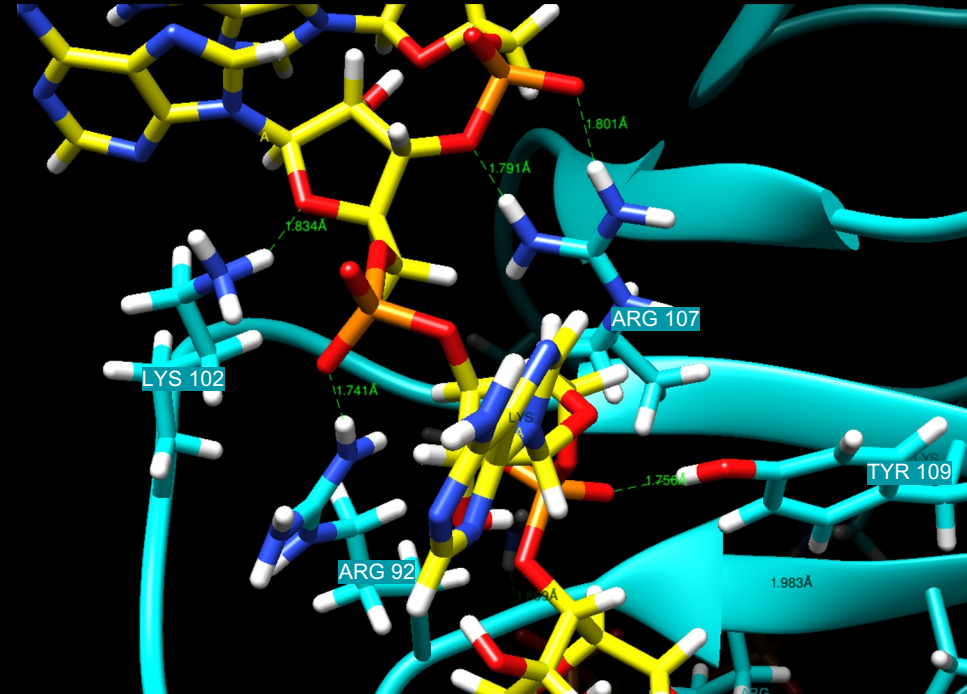


N-NTD/ssRNA INTERACTIONS



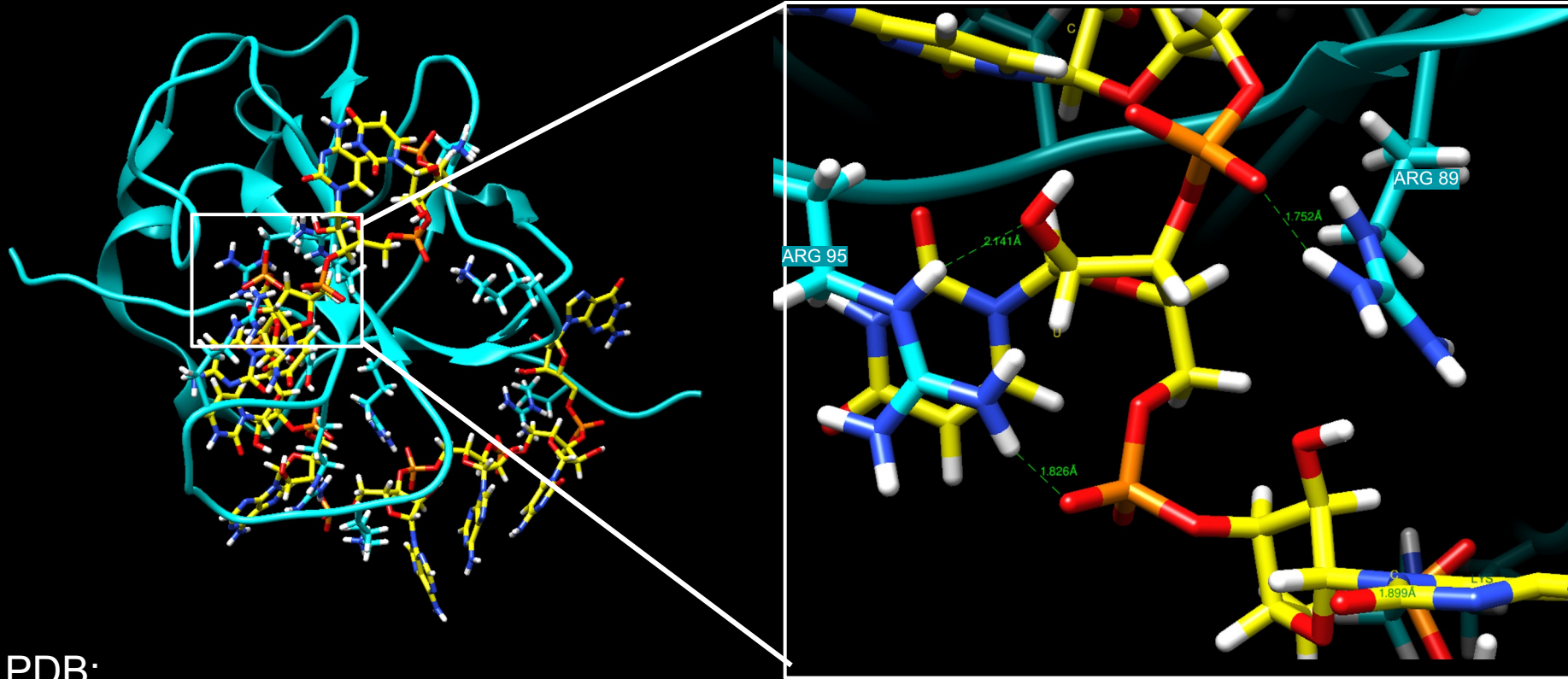
N-NTD/ssRNA INTERACTIONS

Protein residue	Atom	ssRNA nucleotide
LYS 102	N	A 7 [O4']
ARG 107	N	A 7 [O3']
ARG 107	N	A 8 [OP1]
ARG 92	N	A 7 [OP2]
TYR 109	OH	A 6 [OP2]



	88	89	92	95	102	107	109
Sars-Cov	Y	R	R	A	T	R	R
Sars-Cov2	Y	R	R	A	T	R	R
HCoV	Y	W	R	H	N	R	G
BCoV	Y	W	R	H	N	R	R
MHV	Y	W	R	H	N	R	R
IBV	Y	W	R	R	-	-	-
	*	*	*	*	*	*	*

N-NTD/ssRNA INTERACTIONS

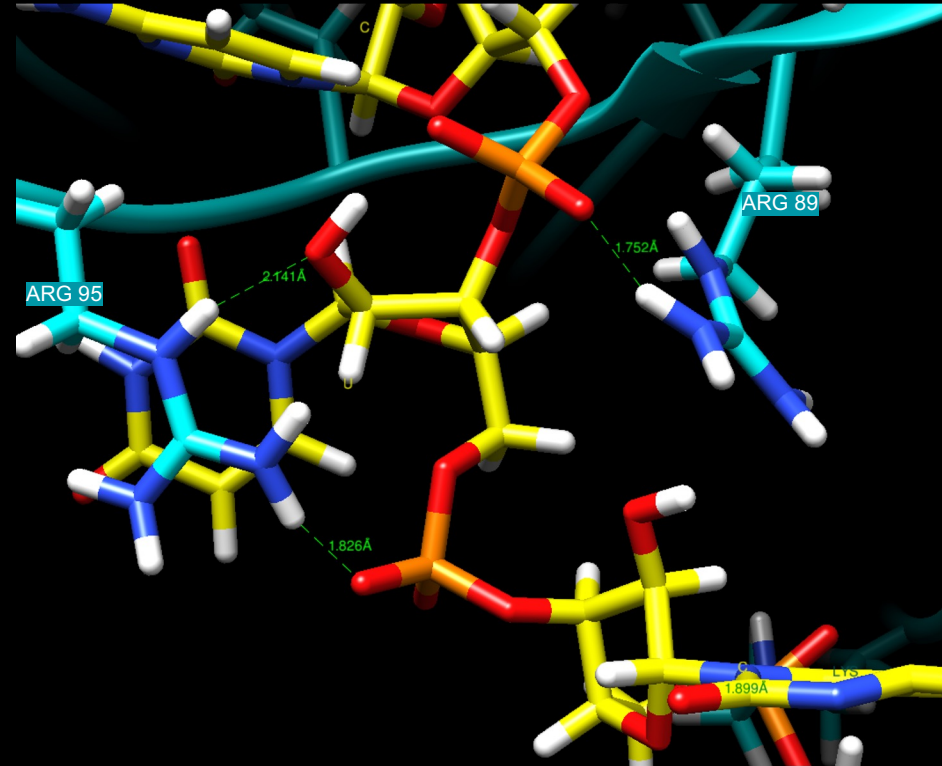


PDB:

N-NTD/ssRNA INTERACTIONS

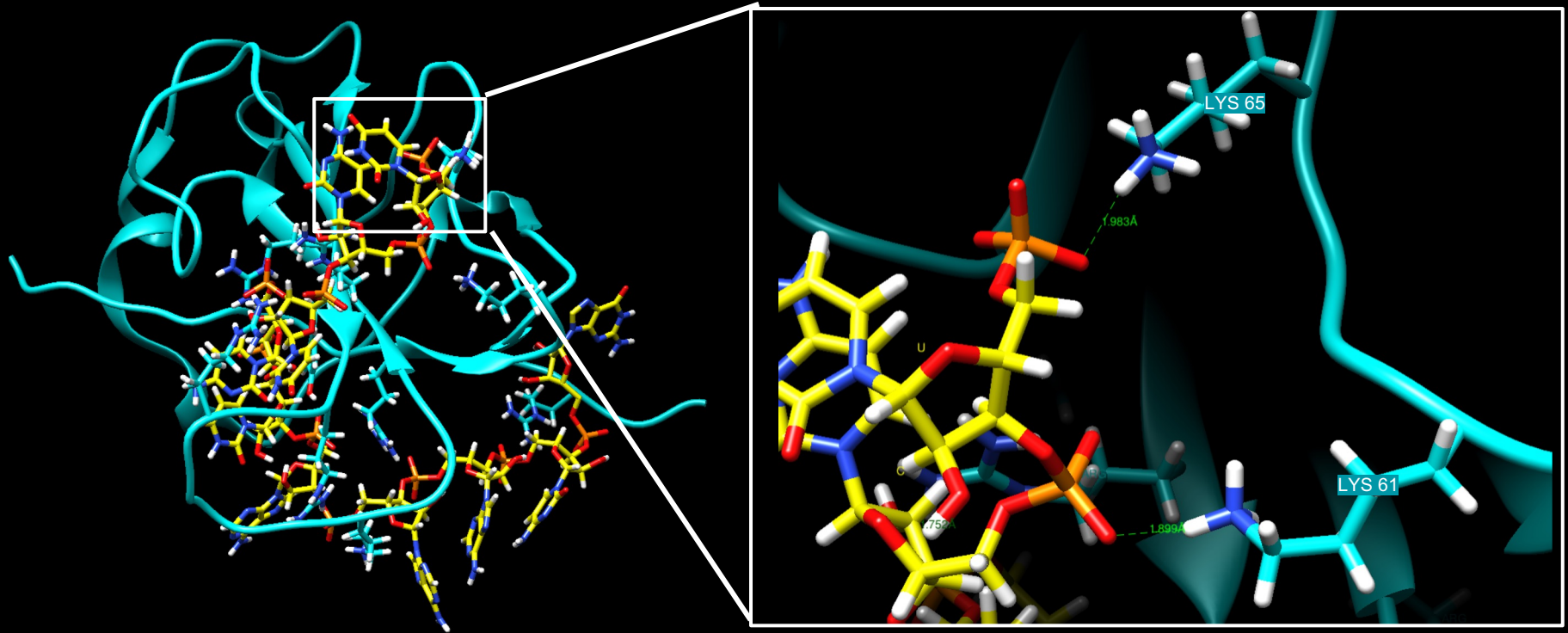
Protein residue	Atom	ssRNA nucleotide
ARG 95	N	U 3[O2']
ARG 95	N	U 3[OP1]
ARG 89	N	C 4[OP1]

	88	89	92	95
Sars-Cov	I	G	Y	R
Sars-Cov2	I	G	Y	R
HCoV	C	G	Y	R
BCoV	C	G	Y	R
MHV	C	G	Y	R
IBV	I	G	Y	R
	**	:	*	:



PDB:

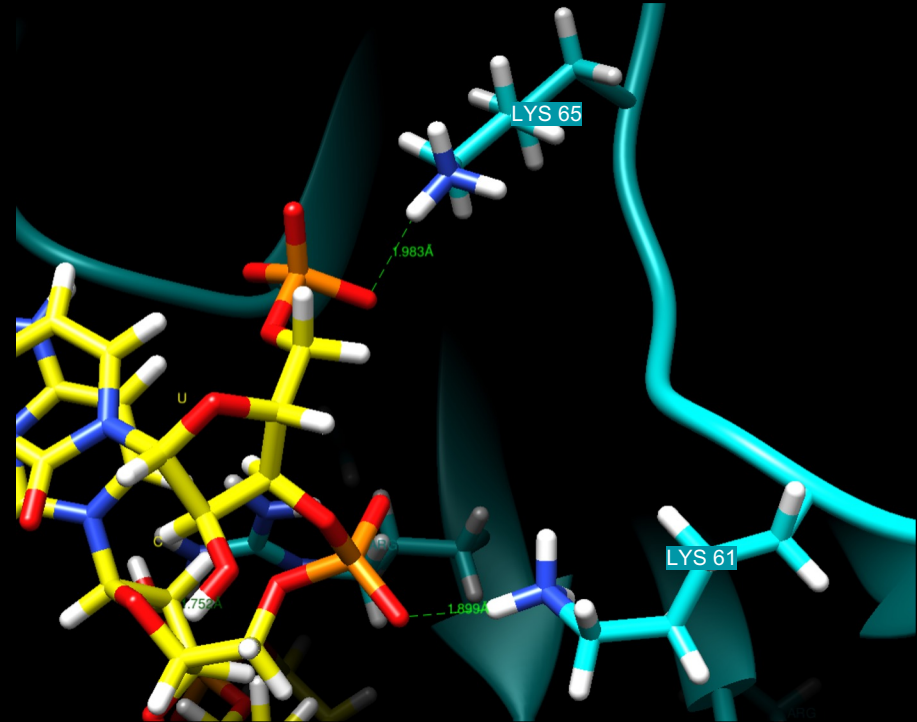
N-NTD/ssRNA INTERACTIONS



N-NTD/ssRNA INTERACTIONS

Protein residue	Atom	ssRNA nucleotide
LYS 61	N	C 2[OP1]
LYS 65	N	U 1[OP1]

	61	65
Sars-Cov	T-----ASWFTALTQHCK-EELRFPRG	
Sars-Cov2	T-----ASWFTALTQHCK-EDLKFP	
HCoV	GNVVPYYSWFSGITQFQKGKEFEFVEG	
BCoV	GNVVPYYSWFSGITQFQKGKEFEFAEG	
MHV	GSVVPHYSWFSGITQFQKGKEFQFAQG	
IBV	GN-----ASWFQAIKAKKLNSPQPKFEG	
	*** ..	*



N PROTEIN



PDB: 8FD5

N PROTEIN CTD

Monomer



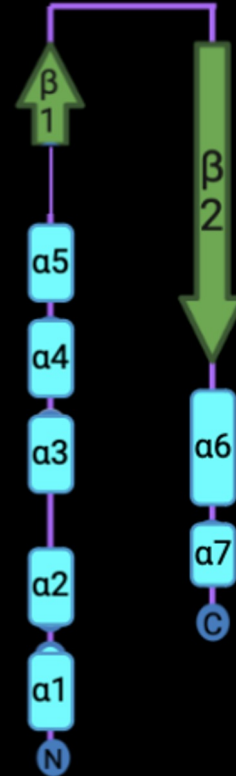
PDB:7CE0

α -helix / β_{10} Helix

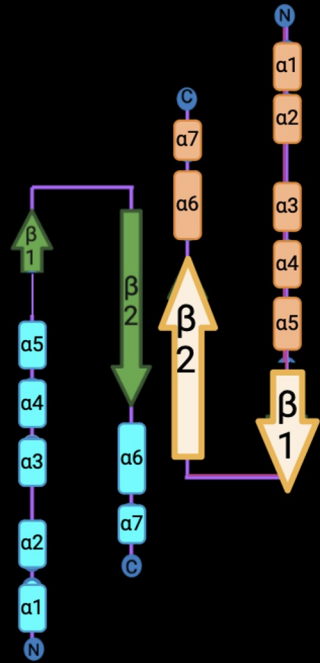
- $\alpha 1$
- $\alpha 2$
- $\alpha 3$
- $\alpha 4$
- $\alpha 5$
- $\alpha 6$
- $\alpha 7$

β antiparallel strand

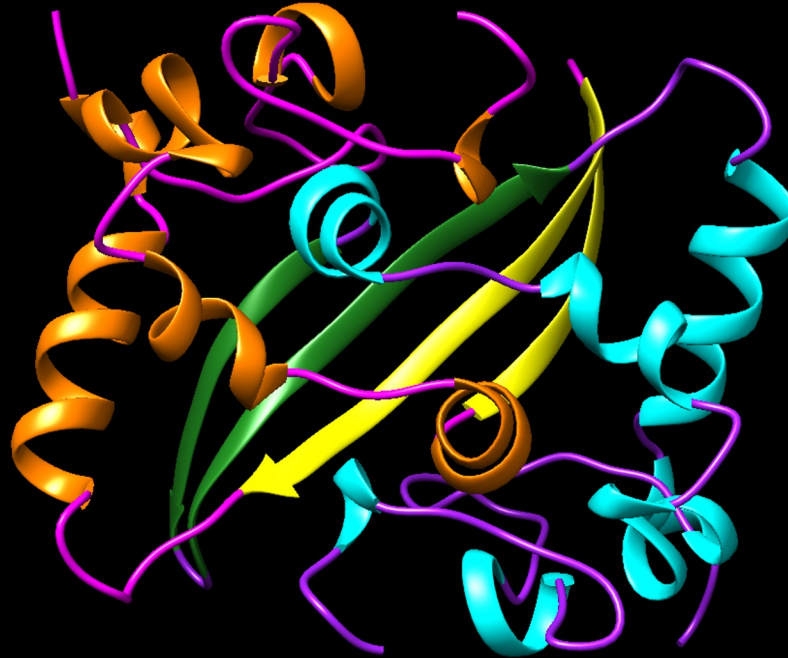
- $\beta 1$
- $\beta 2$



N PROTEIN CTD



Dimer



PDB: 7CE0

N-CTD CLASSIFICATION

N-CTD

Class 1000001
Alpha and beta proteins (a+b)

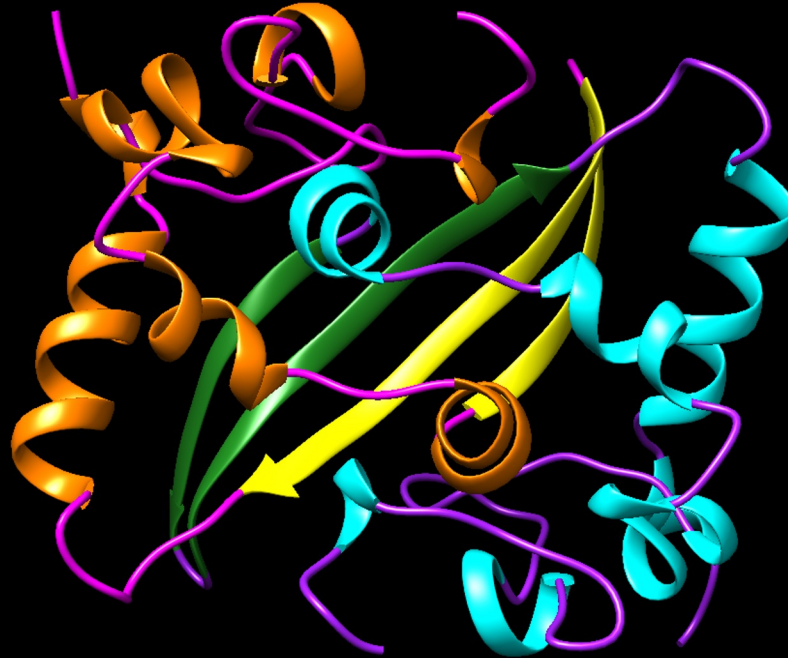
Fold 2000348
Nucleocapsid protein dimerization domain

Superfamily 3000498
Nucleocapsid protein dimerization domain

Family 3000498
Coronavirus nucleocapsid protein dimerization domain

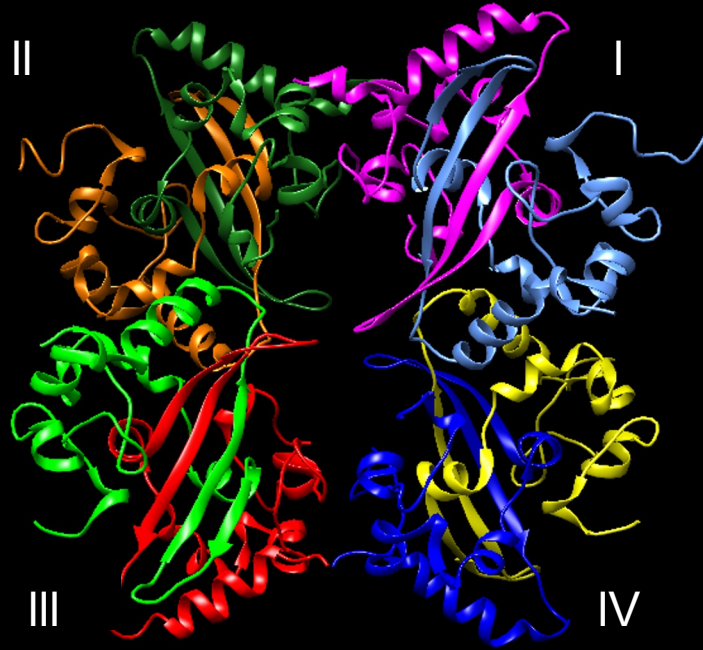
domain 8092432

Dimer



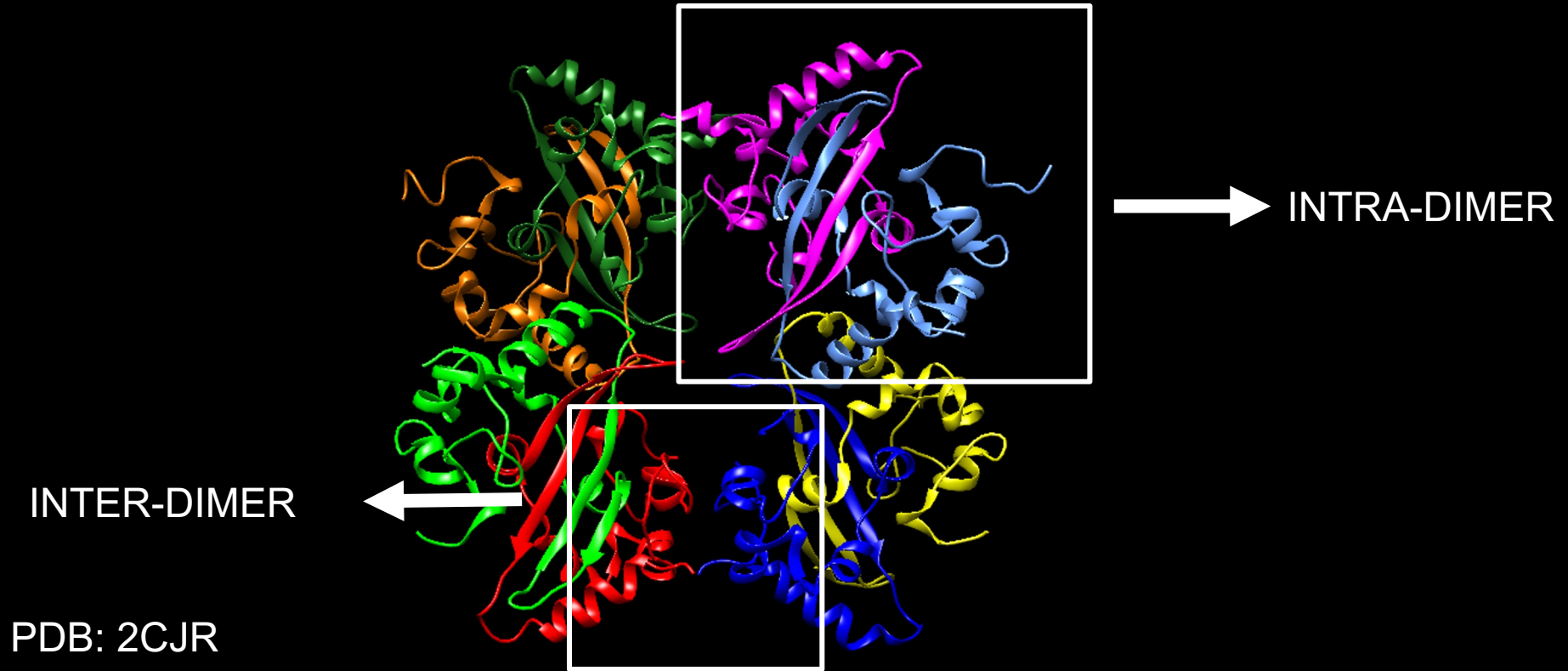
PDB: 7CE0

N-CTD INTERACTIONS AND SYMMETRY



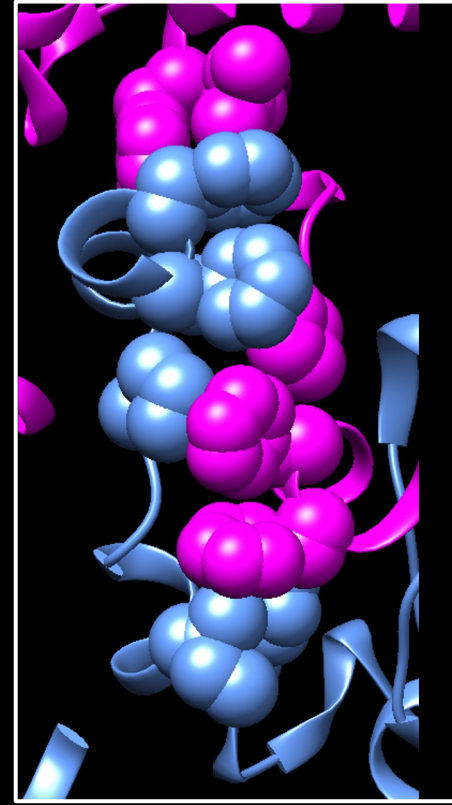
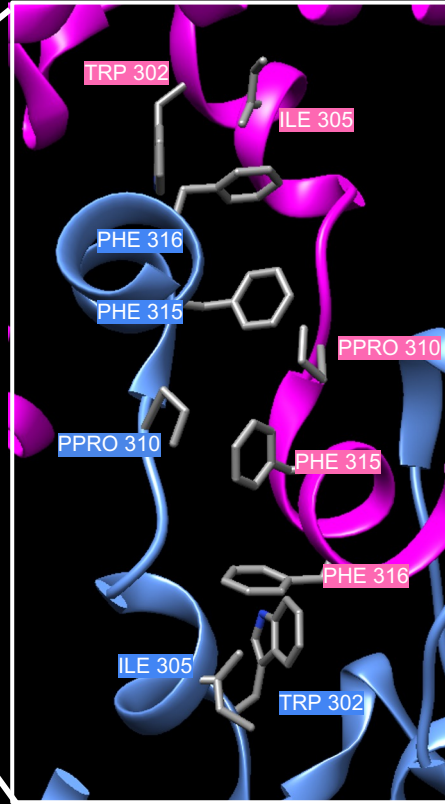
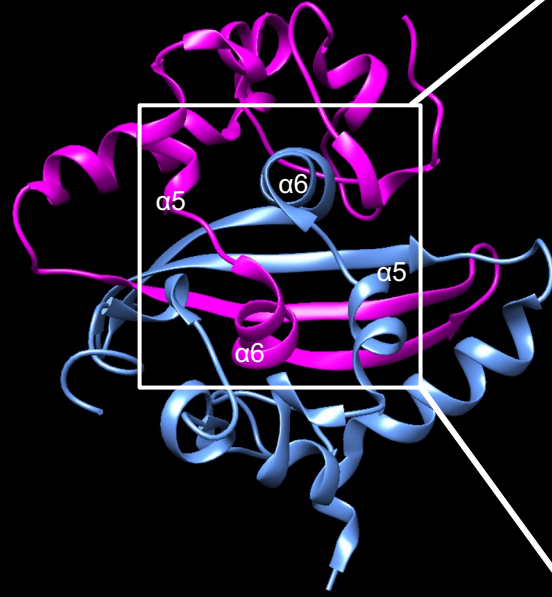
PDB: 2CJR

N-CTD INTERACTIONS AND SYMMETRY



N-CTD INTERACTIONS AND SYMMETRY

INTRA-DIMER

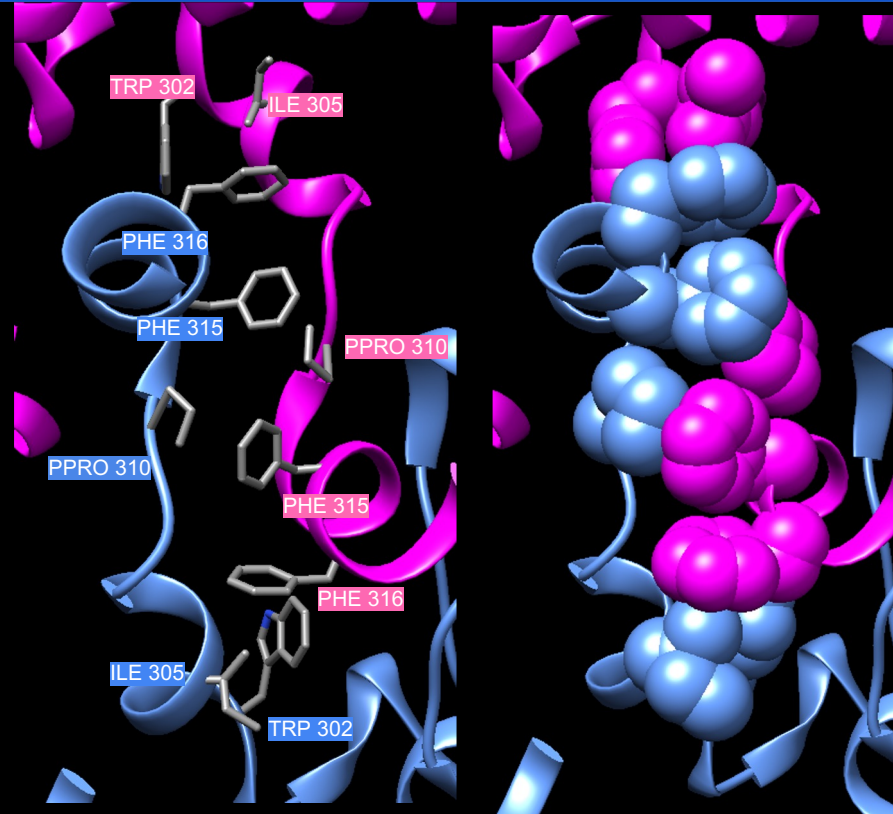


N-CTD

INTERACTIONS AND SYMMETRY

INTRA-DIMER

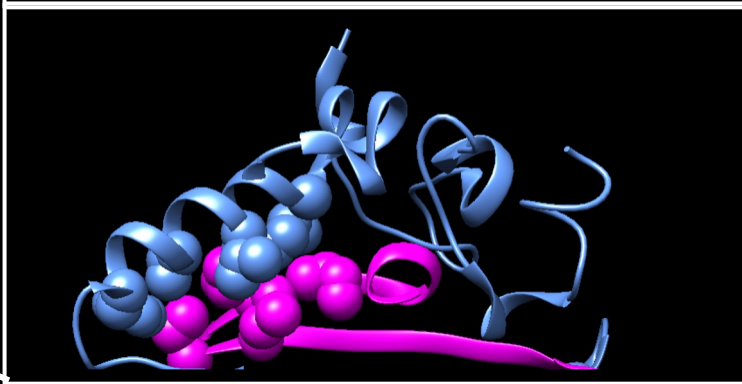
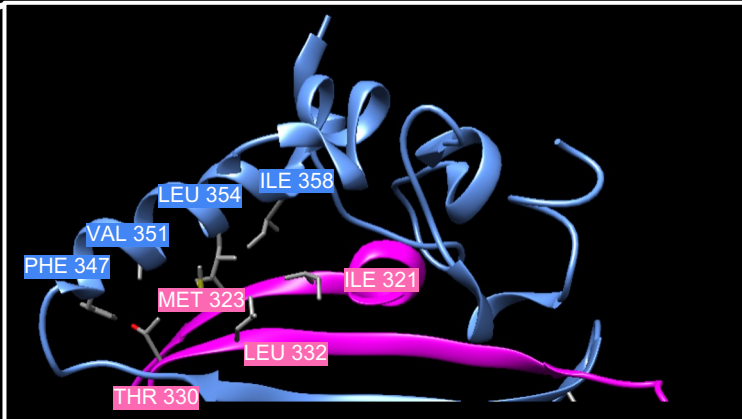
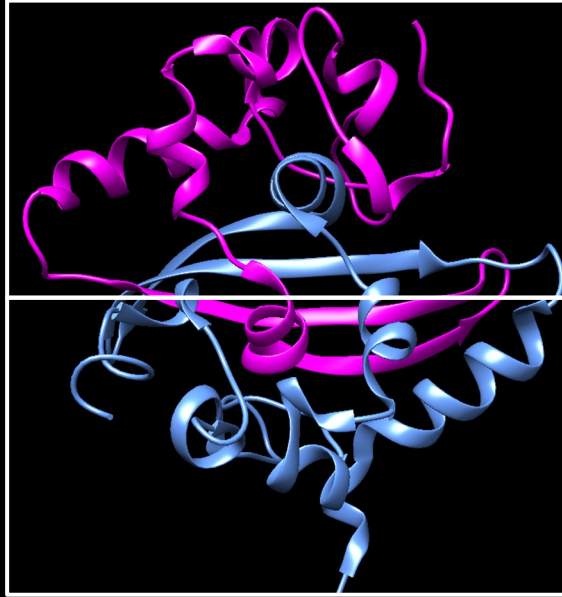
	290	294	297/8	302	305	310/11	315/16	
Sars-CoV	TQGNFGD	QDL	TRQGT	DYKHWP	QIAQFAPS	SASAFFGMS		
Sars-CoV 2	TQGNFGD	QEL	TRQGT	DYKHWP	QIAQFAPS	SASAFFGMS		
HCoV	---	NFGG	GEM	LKLG	TSDP	QFPILAELAPT	AGAFFGMS	
BCoV	---	NFGG	GEM	LKLG	TSDP	QFPILAELAPT	AGAFFGMS	
MHV	---	NFGG	SEM	LKLG	TSDP	QFPILAELAPT	PSAFFGMS	
IBV	-EGNFGD	DKMNE	EGLK	DGRVT	AMLNLV	PSSHACL	FMS	
	***	.	.	.	*	:	:	*



N-CTD

INTERACTIONS AND SYMMETRY

INTRA-DIMER



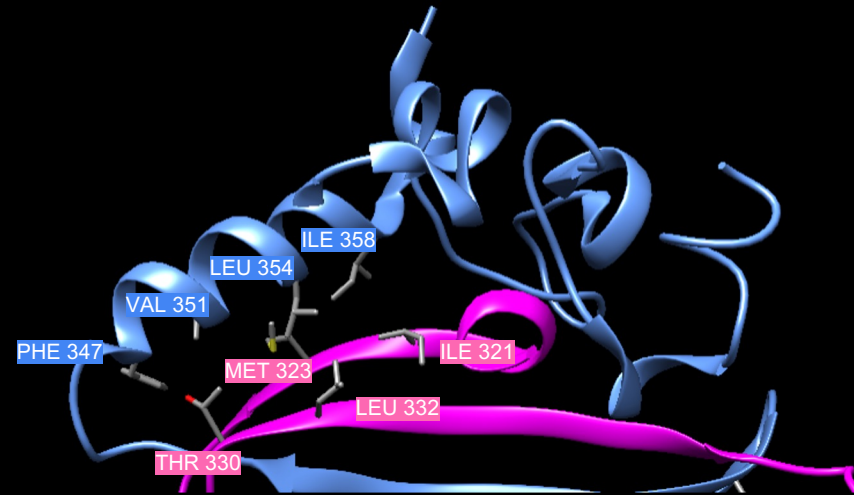
N-CTD

INTERACTIONS AND SYMMETRY

INTRA-DIMER

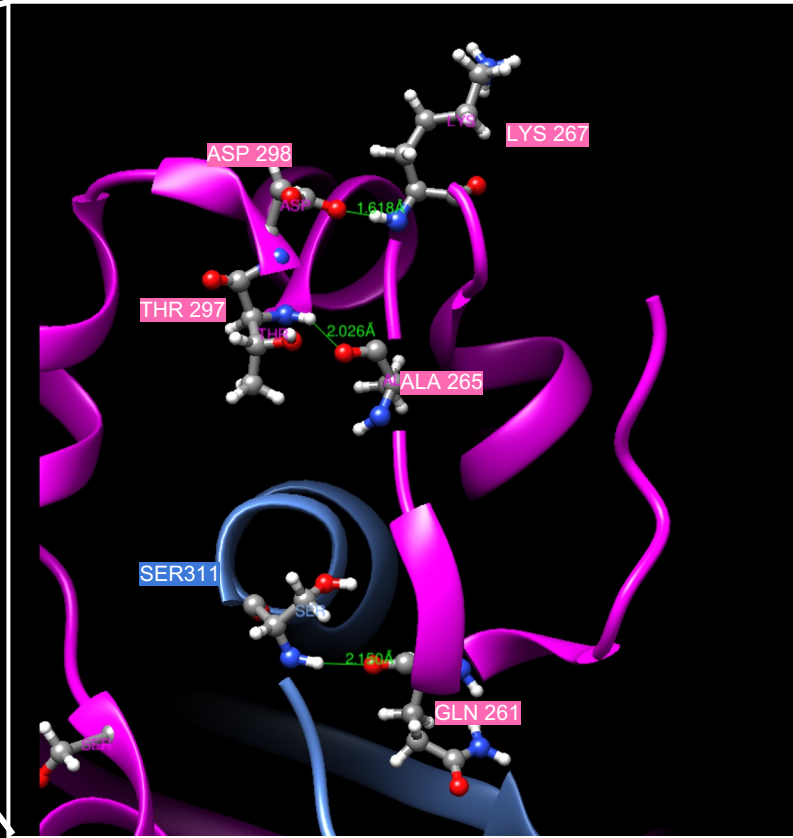
	290	294	297/8	302	305	310/11	315/16	321/23	330
Sars-CoV	TQGNFGDQDLIRQCTDYKHWPCIAQFAPSASAFFGMSRIGMEVTP-----								SGTW
Sars-CoV 2	TQGNFGDQDLIRQCTDYKHWPCIAQFAPSASAFFGMSRIGMEVTP-----								SGTW
HCoV	---NFGGSEMCLKLGTSDPQFPILAEAPTAGAFFFGSRLELAKVQNLSGNPDEPQKDVE								
BCoV	---NFGGSEMCLKLGTSDPQFPILAEAPTAGAFFFGSRLELAKVQNLSGNLDEPQKDVE								
MHV	---NFGGSEMCLKLGTSDPQFPILAEAPTASAFFFGSKLELVKKN--SGGADDPQKDVE								
IBV	-EGNFGDDKMNEECIKDGRVTAMNLVPSHACLFGRVTPKLQP-----DGLH								
	***	::	.	*	:	:	:	*	:

	332	347	351	354	358
Sars-CoV	LTYHGAIKLDDKDPQFKDNVILLNKHIDAYKT				
Sars-CoV 2	LTYTGAIKLDDKDPNFKDQVILLNKHIDAYKT				
HCoV	LRYNGAIRFDSTLSQFETIMKVLNENLNAYQQ				
BCoV	LRYNGAIRFDSTLSQFETIMKVLNENLNAYQQ				
MHV	LQYSGAIRFDSTLPGFETIMKVLNENLNAYQD				
IBV	LKFEFTTVVPRDDPQFDNYVKICDQCVDGVGT				
	*	:	:	.	*



N-CTD INTERACTIONS AND SYMMETRY

INTRA-DIMER

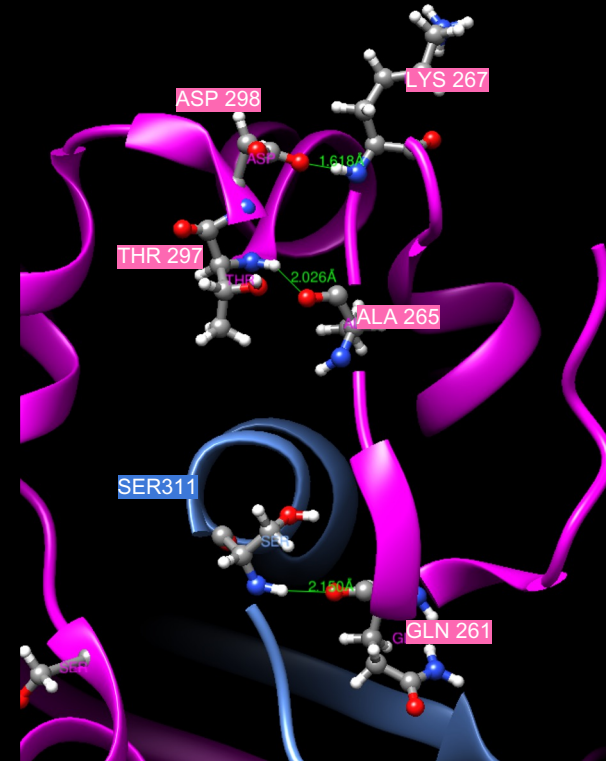


N-CTD

INTERACTIONS AND SYMMETRY

INTRA-DIMER

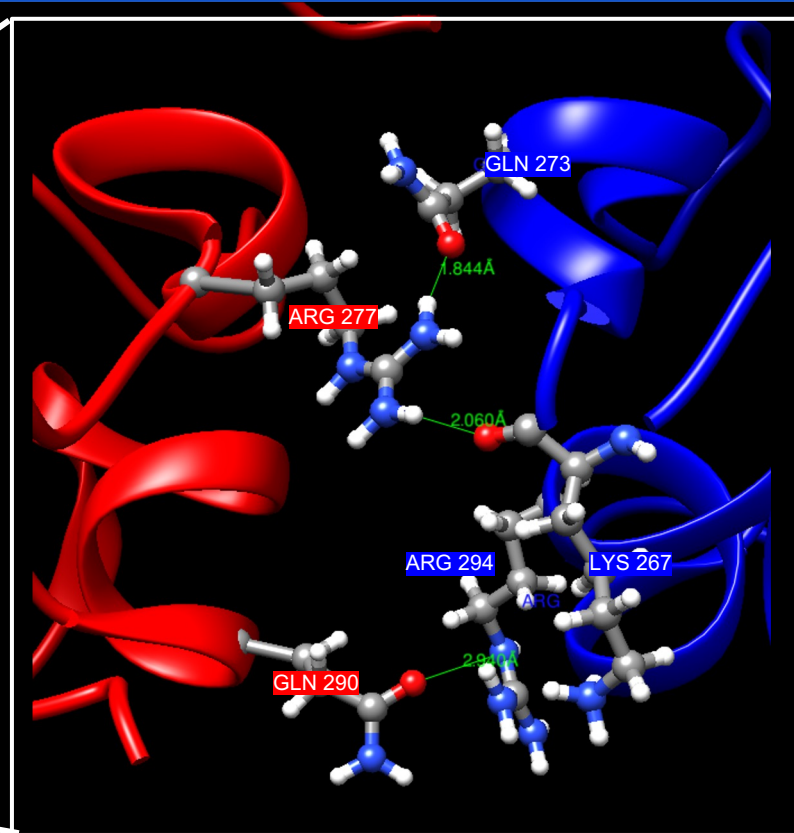
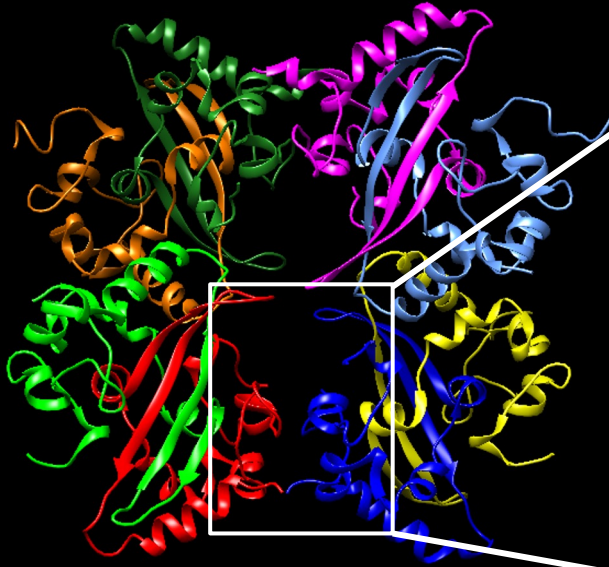
Protein residue 1	Atom 1	Atom 2	Protein residue 2
ALA 265	O	N	THR 297
LYS 267	N	O	ASP 298
GLN 261	O	N	SER 311



	261	265/67	273	277		290	294	297/8	302	305	310/11
Sars-Cov	RQ	KRTAT	KQYNVTQ	AF	CRRGPEQ	TQGNFGDQDL	IRQ	CTDYKHWP	QIAQFAPSAS		
Sars-Cov2	RQ	KRTAT	KAYNVTQ	AF	CRRGPEQ	TQGNFGDQEL	IRQ	CTDYKHWP	QIAQFAPSAS		
HCoV	RQ	KRSPNKQ	CTVQQ	CF	CKRGPNQ	---	NFGG	GEMCLKL	GTSDPQFP	ILAE	LAPTAG
BCoV	RQ	KRSPNKQ	CTVQQ	CF	CKRGPNQ	---	NFGG	GEMCLKL	GTSDPQFP	ILAE	LAPTAG
MHV	RQ	KRTPNKQ	CPVQQ	CF	CKRGPNQ	---	NFGG	SEMCLKL	GTSDPQFP	ILAE	LAPT
IBV	YCKRT	IPPGYKVDQ	VF	CP	RTKGK	-	EGNFGD	DKMNEEG	IKDGRV	TAMLNL	VPSSH
						***	.	.	.	.	.

N-CTD INTERACTIONS AND SYMMETRY

INTER-DIMER



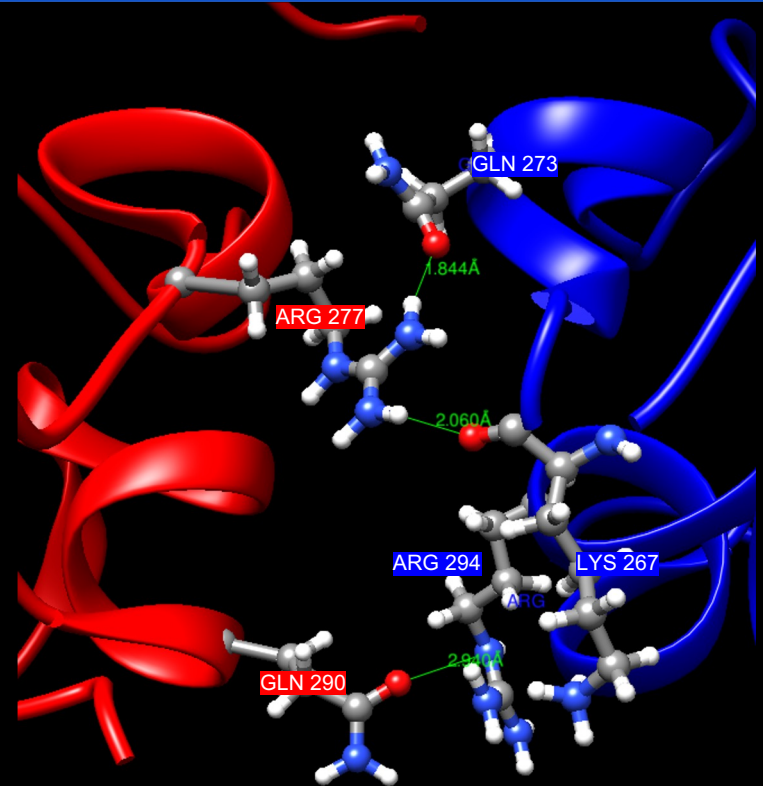
N-CTD

INTERACTIONS AND SYMMETRY

INTER-DIMER

Protein residue 1	Atom 1	Atom 2	Protein residue 2
LYS 267	O	N	ARG 277
GLN 273	O	N	ARG 277
GLN 290	O	N	ARG 294

	265/67	273	277	290	294
Sars-Cov	RTATKQYNVTQAF	CRRGPEQ	TQGNFGDQDLIRQ		
Sars-Cov2	RTATKAYNVTQAF	CRRGPEQ	TQGNFGDQELIRQ		
HCoV	RSPNKQCTVQOC	FCGRGPNQ	---NFGGGEMLKL		
BCoV	RSPNKQCTVQOC	FCGRGPNQ	---NFGGGEMLKL		
MHV	RTPNKQCPVQOC	FCGRGPNQ	---NFGGSEMLKL		
IBV	RTIPPGYKVDQV	FCPRTKGK	-EGNFGDDKMNEE		
	***	...	...		



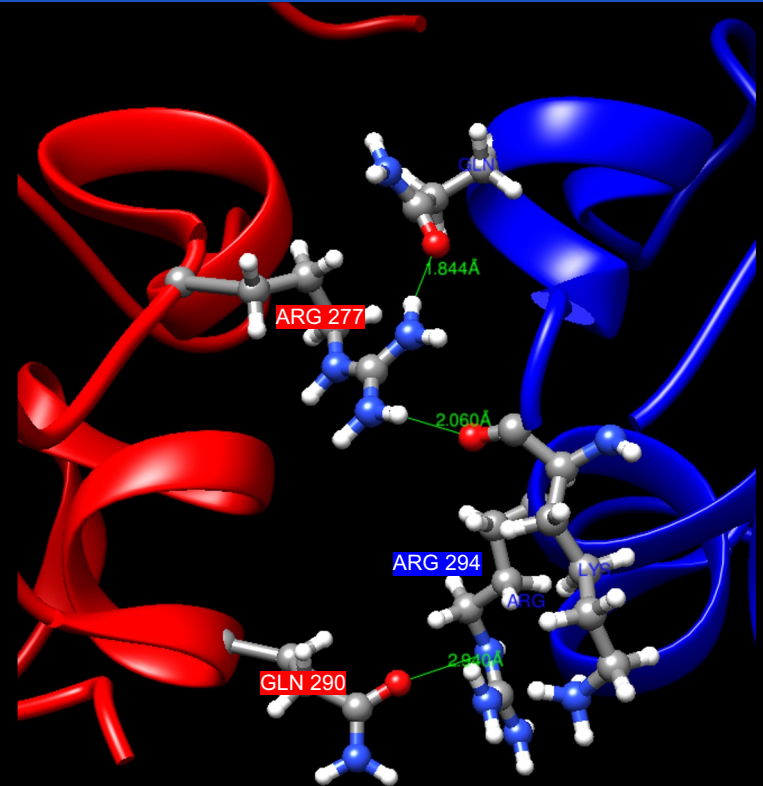
N-CTD INTERACTIONS AND SYMMETRY

INTER-DIMER

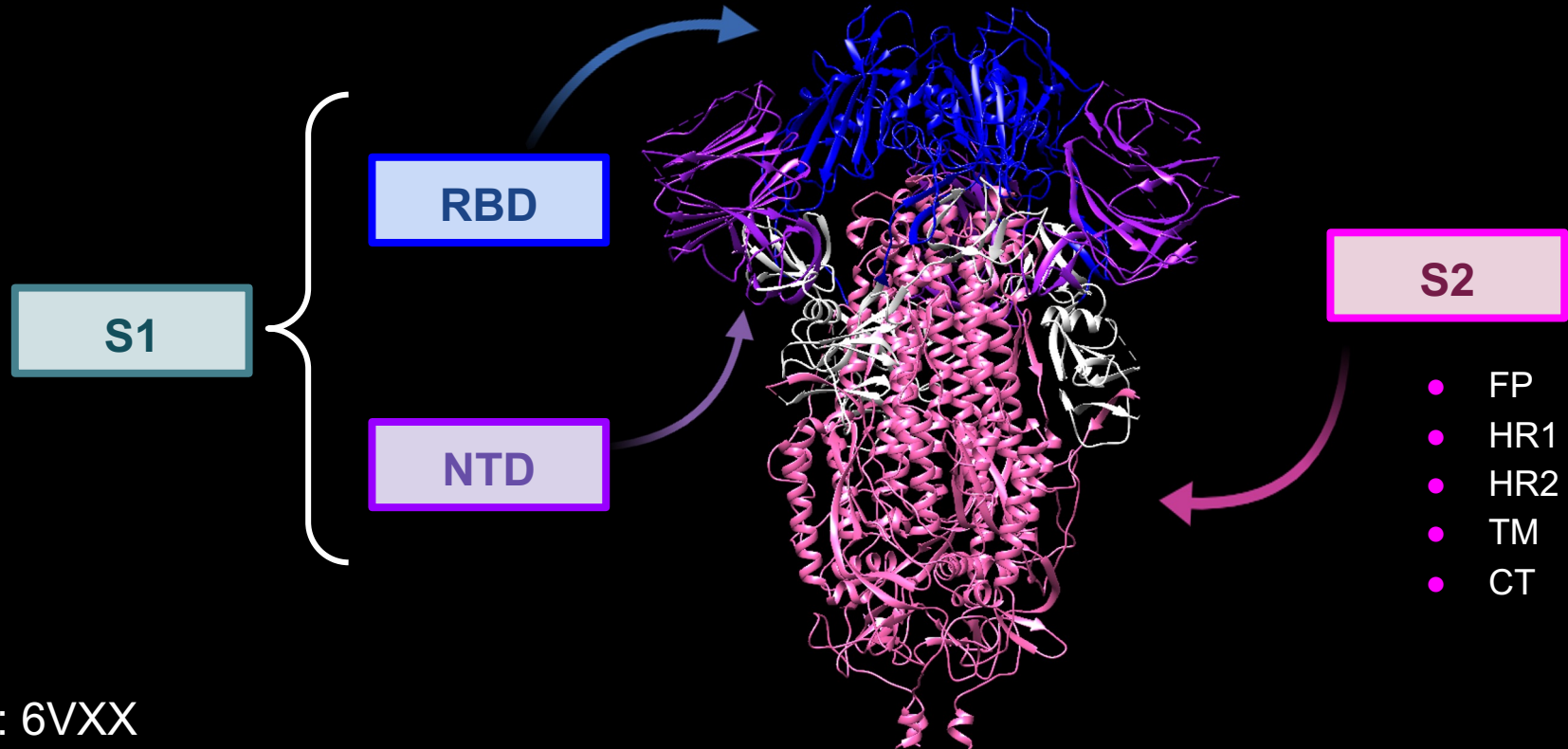
		277
36 Sars-Cov2	LLLDRLNQLLESKVSGKGQQQQGQTVTKKSAEEASKKPRQKRTATKQYNVTQAFQRRGPEQ	R
37 Sars-Cov	LLLDRLNQLLESKMSGKGQQQQGQTVTKKSAEEASKKPRQKRTATKAYNVTQAFQRRGPEQ	
38 HCoV	QIASLVLA LK GK DATK - PQQVT KHTAKEVRQKILNKPRQKRSPNKQCTVQQCFQKRGPNQ	
39 BCoV	QIASLVLA LK GK DATK - PQQVT KHTAKEIRQKILNKPRQKRSPNKQCTVQQCFQKRGPNQ	
40 MHV	EIAALVLA LK GK DAGQ - PKQVT KQSAKEVRQKILNKPRQKRTPNKQCPVQQCFQKRGPNQ	
41 IBV	DLIARA A K I I Q D Q Q K K - - - - GSRIT KAKADEMAHRRYCKRTIPP GYKVDQVFQPTKGK	
42	: . : . : *	* * * *

		290
44 Sars-Cov2	TQGNFGDQDLIRQGT DYKHWPQIAQFAPSASAFFGMSRIGMEVTP-----SGTW	R
45 Sars-Cov	TQGNFGDQDLIRQGT DYKHWPQIAQFAPSASAFFGMSRIGMEVTP-----SGTW	
46 HCoV	---NFGGGEM LK L G TSDPQFPILAELAPTAGAFFGSRLELAKVQNL SGNPDEPKD VYE	
47 BCoV	---NFGGGEM LK L G TSDPQFPILAELAPTAGAFFGSRLELAKVQNL SGNLDEPKD VYE	
48 MHV	---NFGGGEM LK L G TSDPQFPILAELAPTPSAFFGSKLELVKKN--SGGADDP TKD VYE	
49 IBV	-EGNFGDDKMNEEGIKDGRVTAMNLVPSSHACLF GSRVTPKLQP-----DGLH	
50	***. : . * . : . : : * . : * : * :	.
51		

		294
44 Sars-Cov2	TQGNFGDQDLIRQGT DYKHWPQIAQFAPSASAFFGMSRIGMEVTP-----SGTW	R
45 Sars-Cov	TQGNFGDQDLIRQGT DYKHWPQIAQFAPSASAFFGMSRIGMEVTP-----SGTW	
46 HCoV	---NFGGGEM LK L G TSDPQFPILAELAPTAGAFFGSRLELAKVQNL SGNPDEPKD VYE	
47 BCoV	---NFGGGEM LK L G TSDPQFPILAELAPTAGAFFGSRLELAKVQNL SGNLDEPKD VYE	
48 MHV	---NFGGGEM LK L G TSDPQFPILAELAPTPSAFFGSKLELVKKN--SGGADDP TKD VYE	
49 IBV	-EGNFGDDKMNEEGIKDGRVTAMNLVPSSHACLF GSRVTPKLQP-----DGLH	
50	***. : . * . : . : : * . : * : * :	.
51		

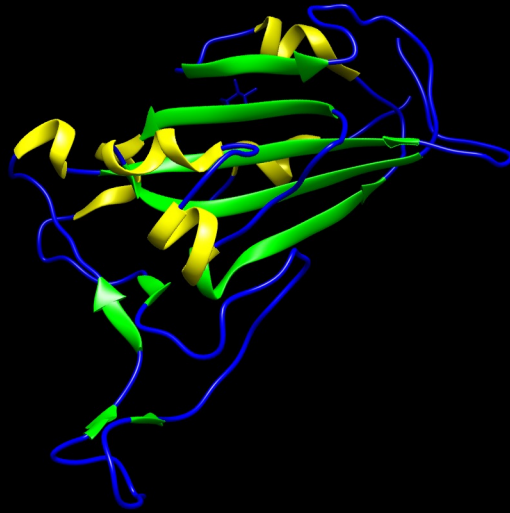


S PROTEIN



PDB: 6VXX

S PROTEIN CTD Domain



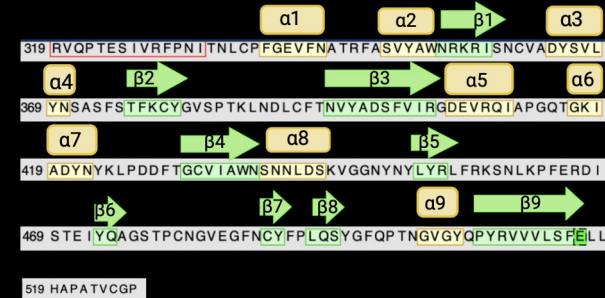
Class 1000003
Alpha and Beta proteins (a+b)

Fold 2001044
SARS coronavirus receptor-binding domain-like

Superfamily 3001706
SARS coronavirus receptor-binding domain-like

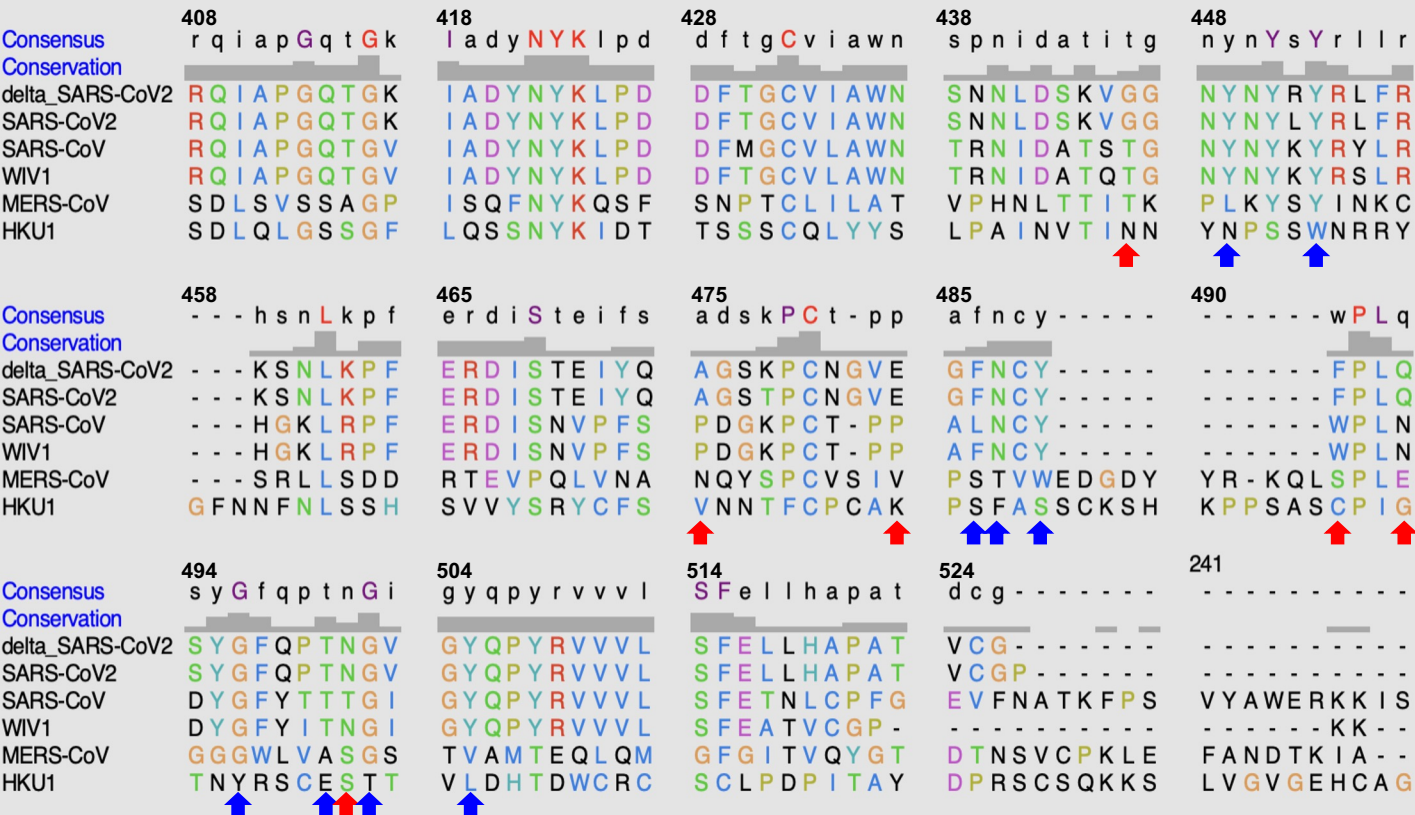
family 4003874
SARS coronavirus receptor-binding domain-like

Domain 8092466



PDB: 6LZG

INTERACTIONS RBD-ACE2



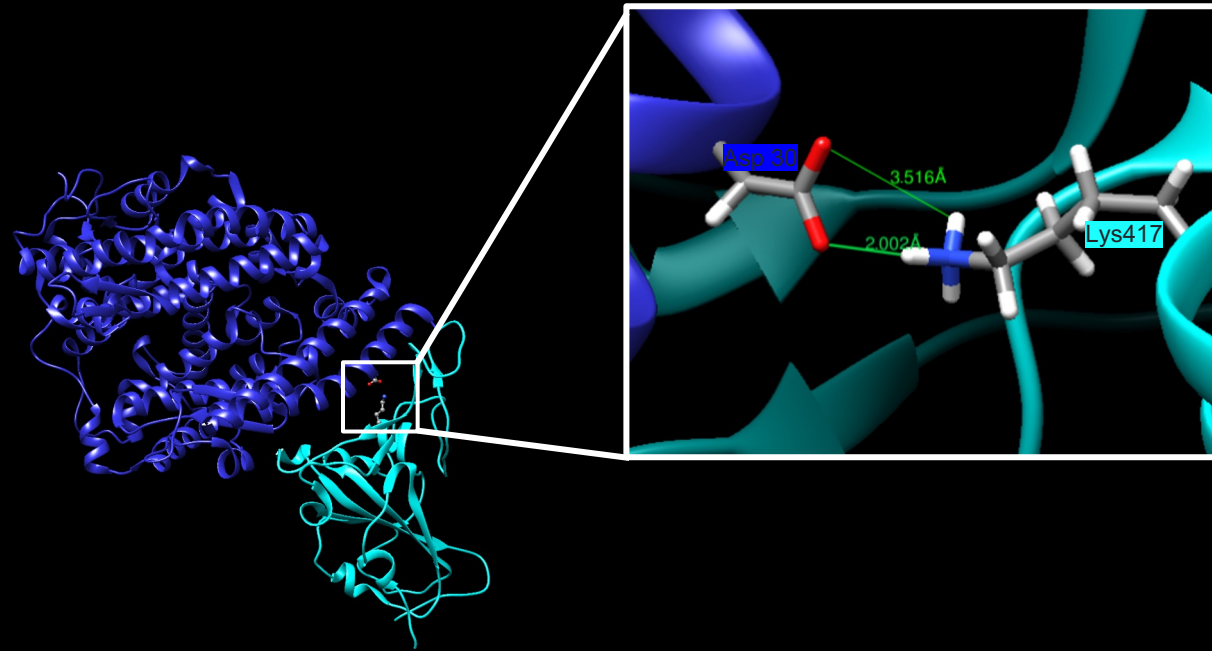
↑ SARS-CoV-2 residues interacting with ACE2

↑ Shared interaction SARS-CoV-2 and SARS-CoV

9/16 interactions are conserved

INTERACTIONS RBD-ACE2

SALT BRIDGE K417-D30



Protein residue	SARS-CoV-2 atom	ACE2 atom
LYS 417	N	O
LYS 417	N	O

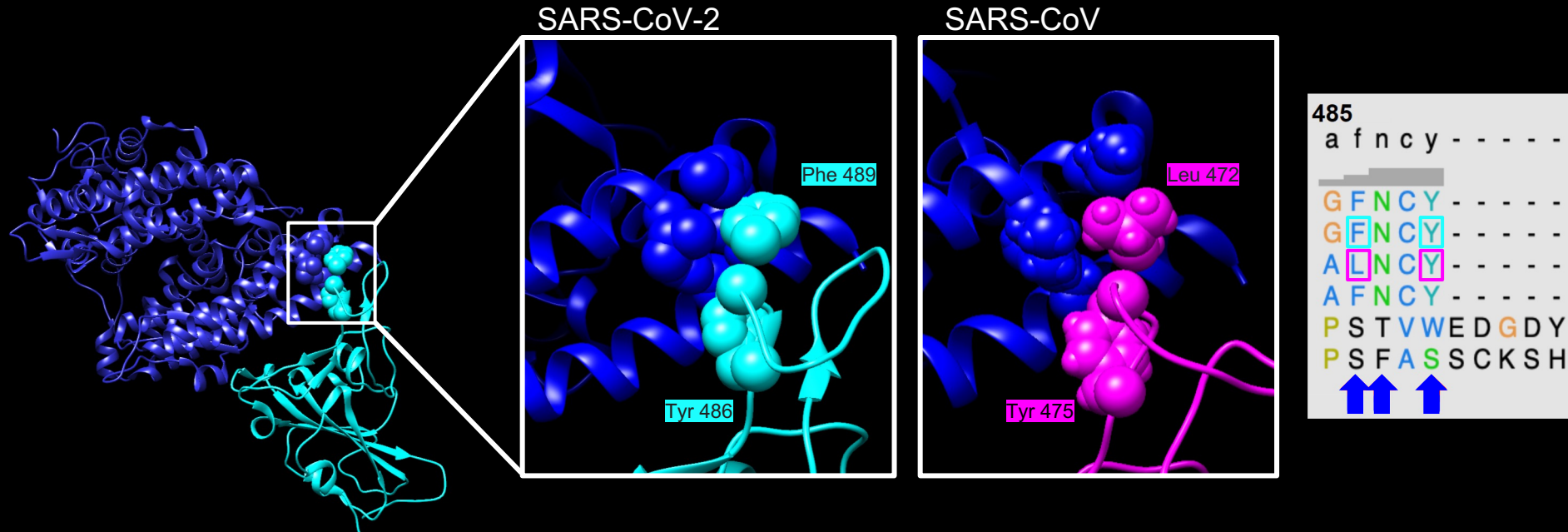
408	r	q	i	a	p	G	q	t	G	k
	R	Q	I	A	P	G	Q	T	G	K
	R	Q	I	A	P	G	Q	T	G	K
	R	Q	I	A	P	G	Q	T	G	V
	R	Q	I	A	P	G	Q	T	G	V
	S	D	L	S	V	S	S	A	G	P
	S	D	L	Q	L	G	S	S	G	F



INTERACTIONS RBD-ACE2

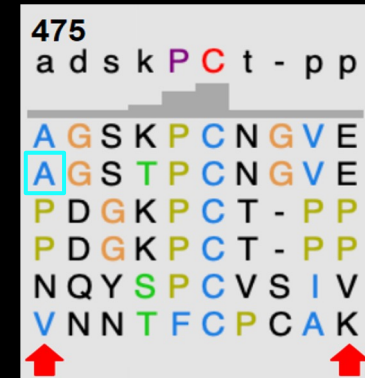
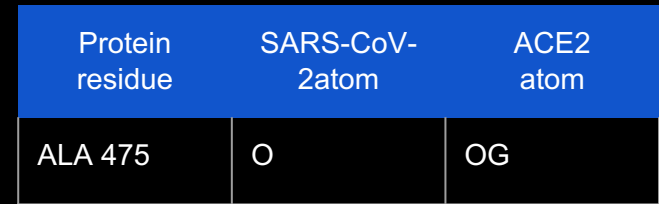
HYDROPHOBIC INTERACTIONS

Y486, F489 - F28, L79, M82, Y8



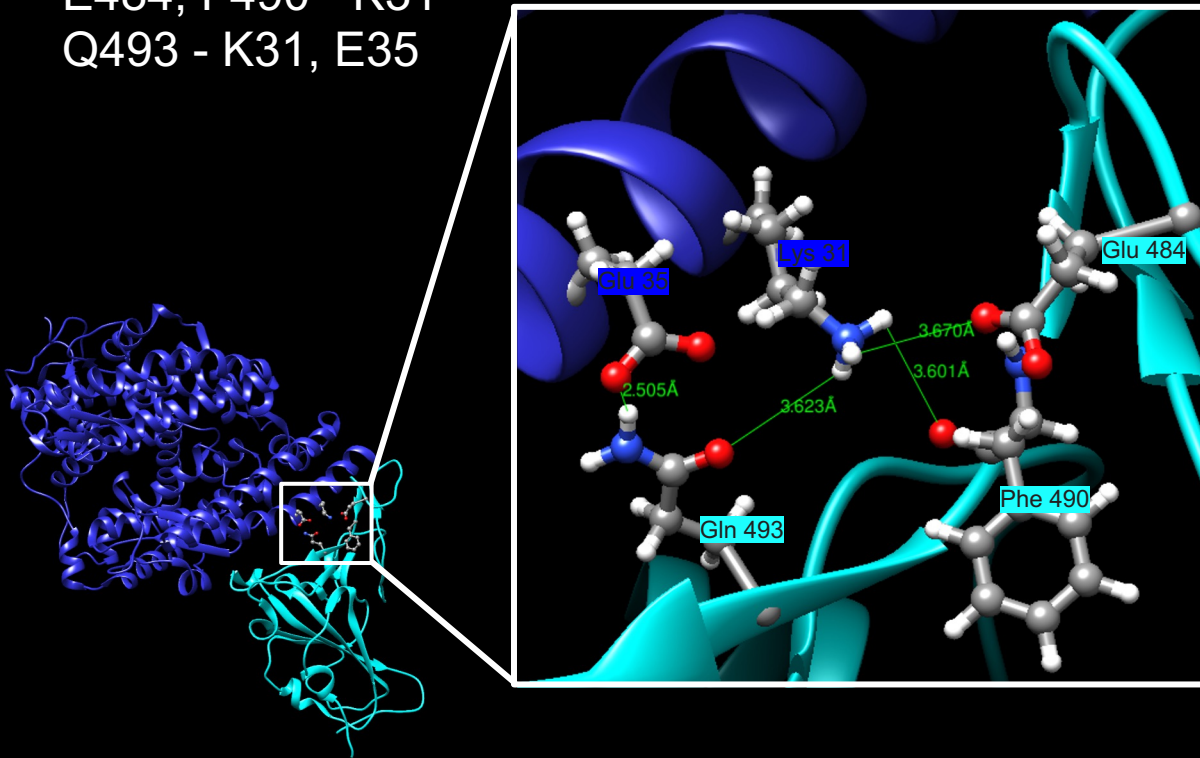
HYDROGEN BONDS

A475-S19



INTERACTIONS RBD-ACE2

E484, F490 - K31
Q493 - K31, E35



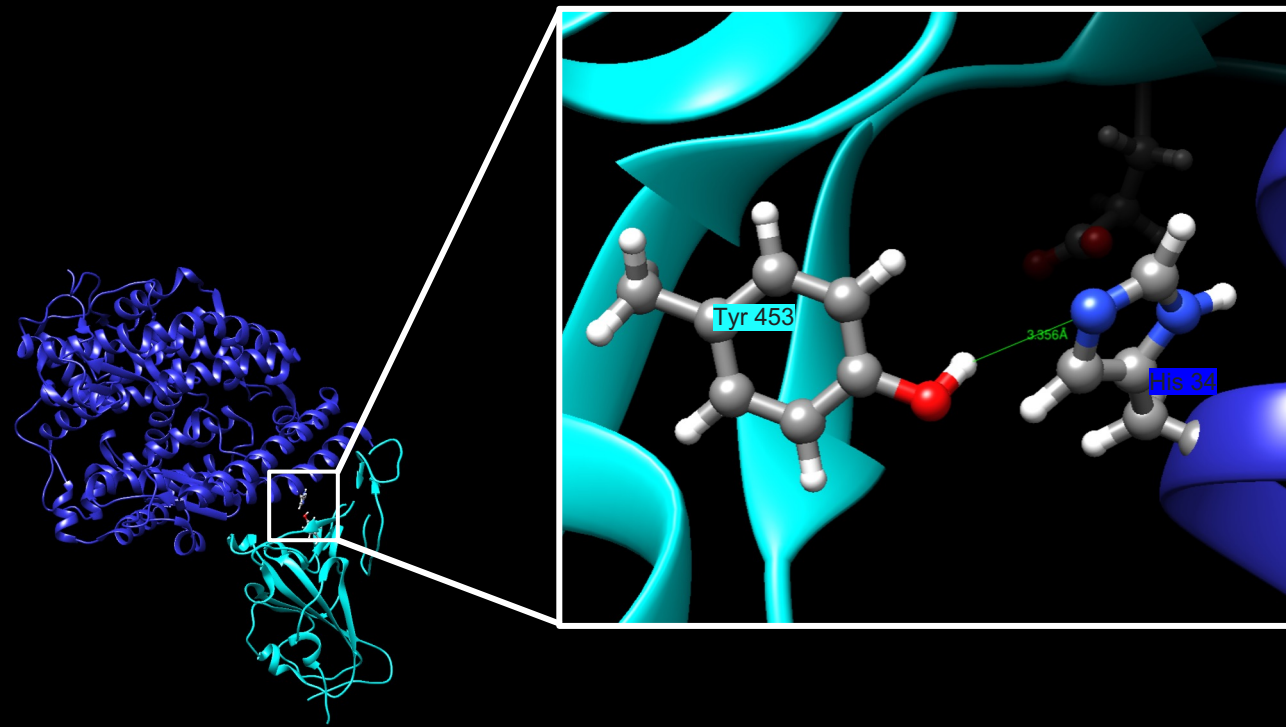
Protein residue	SARS-CoV-2 atom	ACE2 atom
GLU 484	O	N
PHE 490	O	N
GLN 493	O	N
GLN 493	N	O

475
a d s k **P** C t - p p
A G S K **P** C N G V E
A G S T P C N G V **E**
P D G K P C T - P P
P D G K P C T - P P
N Q Y S P C V S I V
V N N T F C P C A K
↑ ↑

490
- - - - - w **P** L q
- - - - - F P L Q
- - - - - **F** P L Q
- - - - - W P L N
- - - - - W P L N
Y R - K Q L S P L E
K P P S A S C P I G
↑ ↑

INTERACTIONS RBD-ACE2

Y453-H34

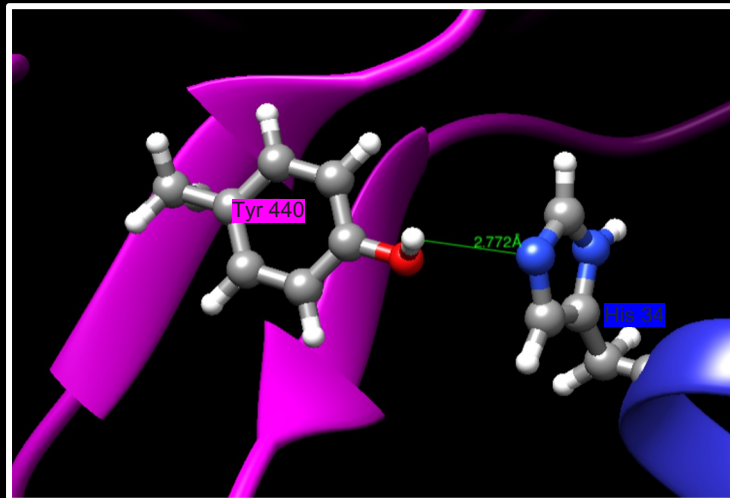


Protein residue	SARS-CoV-2 atom	ACE2 atom
TYR	OH	N

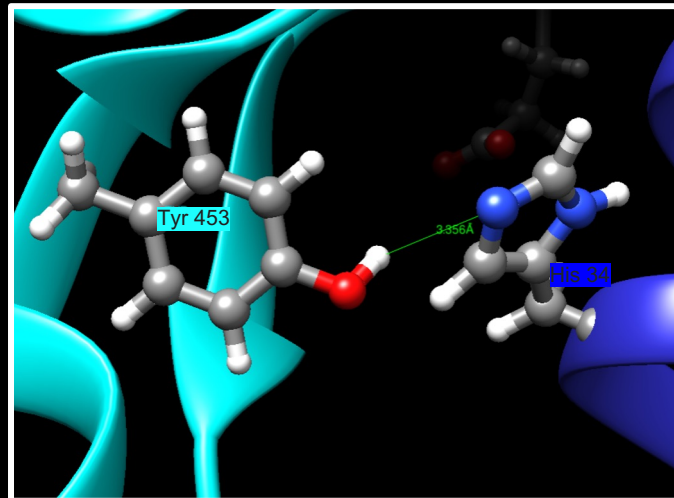
INTERACTIONS RBD-ACE2

Y453-H34

SARS-CoV



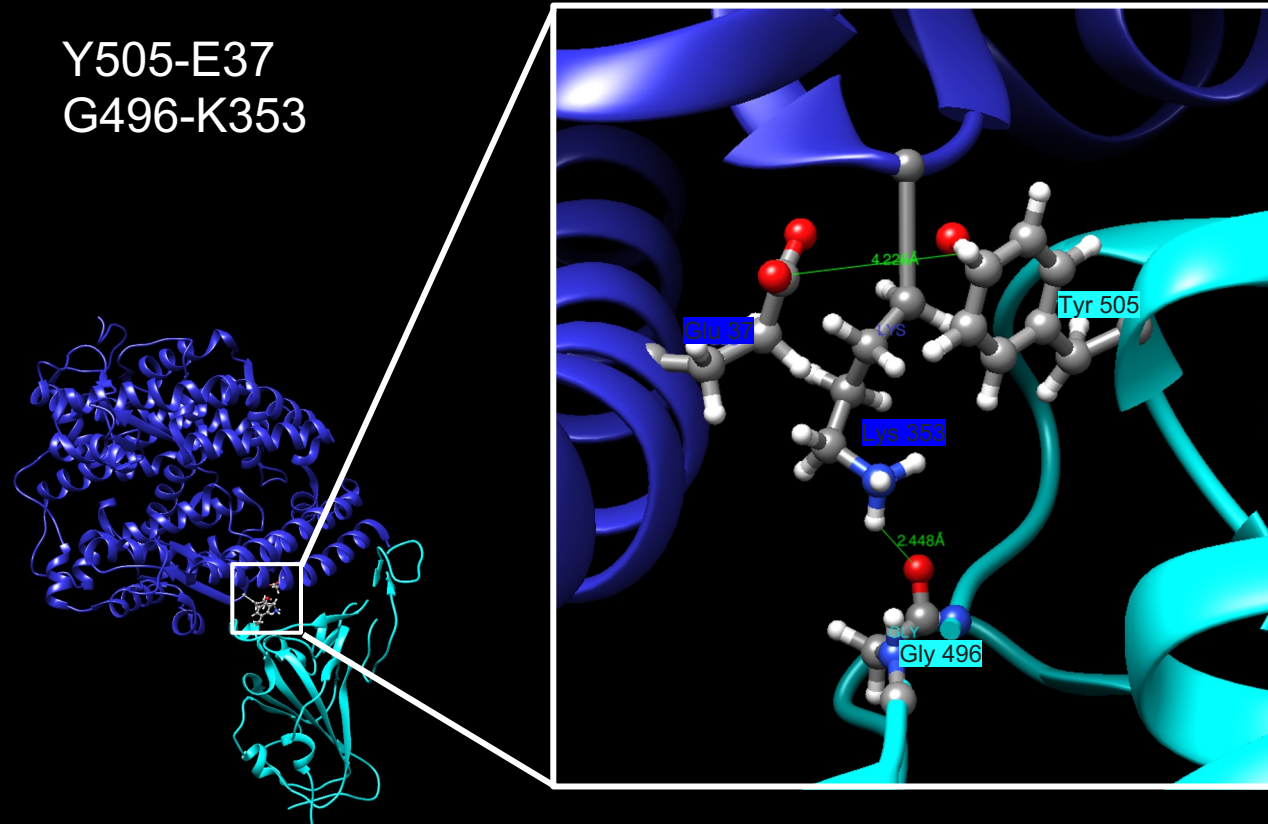
SARS-CoV-2



448
n y n Y s Y r l l r
N Y N Y R Y R L F R
N Y N Y L Y R L F R
N Y N Y K Y R Y L R
N Y N Y K Y R S L R
P L K Y S Y I N K C
Y N P S S W N R R Y

INTERACTIONS RBD-ACE2

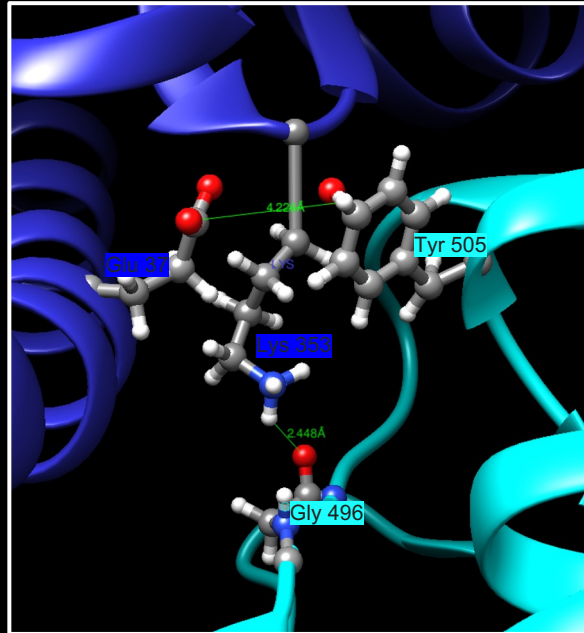
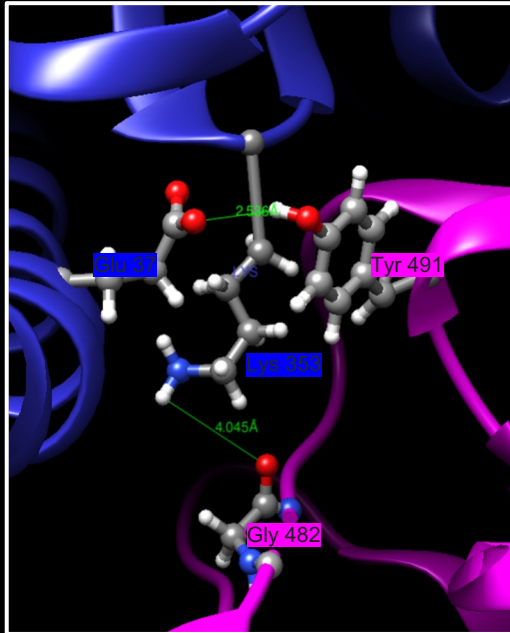
Y505-E37
G496-K353



Protein residue	SARS-CoV-2 atom	ACE2 atom
TYR 505	OH	O
GLY 496	O	N

INTERACTIONS RBD-ACE2

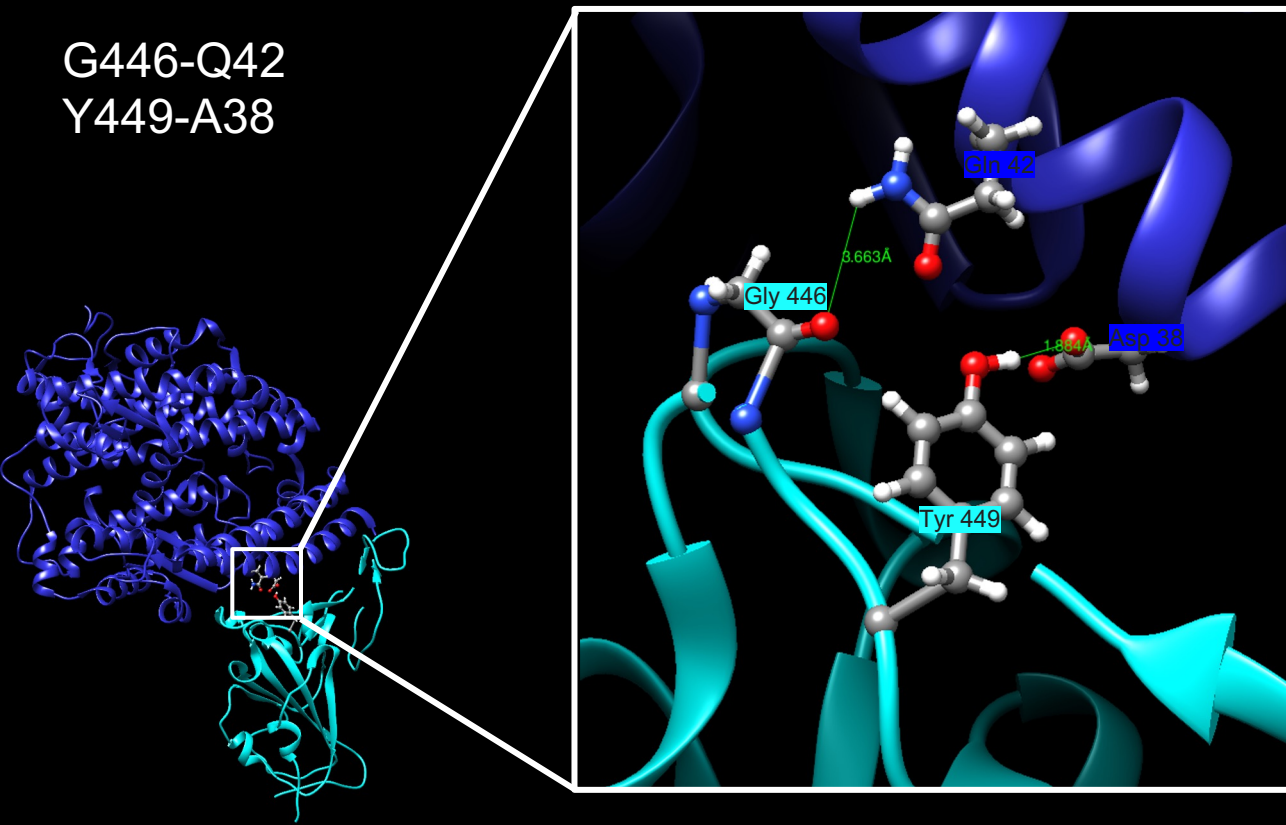
Y505-E37
G496-K353



494	s y G f q p t n G i	504	g y q p y r v v v l
	S Y G F Q P T N G V		G Y Q P Y R V V V L
	S Y G F Q P T N G V		G Y Q P Y R V V V L
	D Y G F Y T T T G I		G Y Q P Y R V V V L
	D Y G F Y I T N G I		G Y Q P Y R V V V L
	G G G W L V A S G S		T V A M T E Q L Q M
	T N Y R S C E S T T		V L D H T D W C R C
	↑ ↑ ↑ ↑ ↑		↑

INTERACTIONS RBD-ACE2

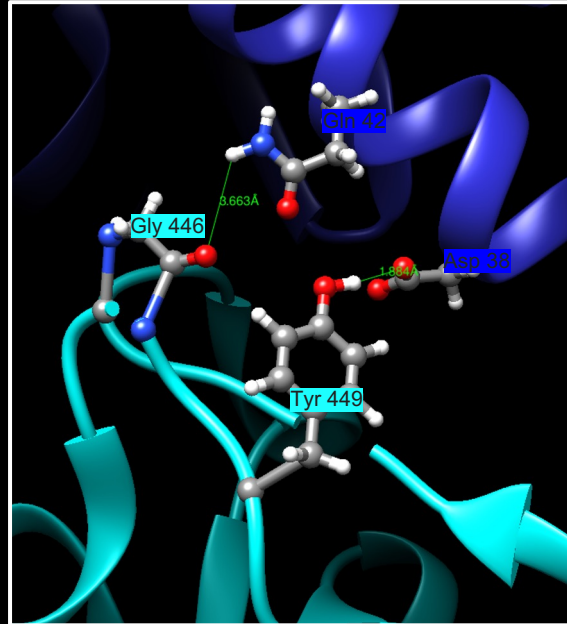
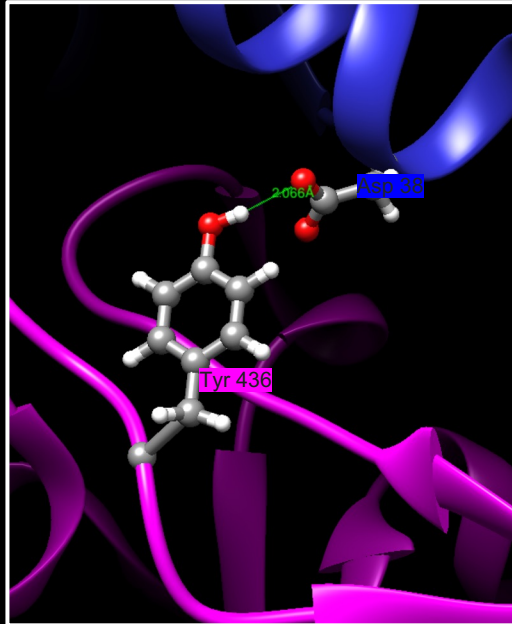
G446-Q42
Y449-A38



Protein residue	SARS-CoV-2 atom	ACE2 atom
GLY 446	O	NH2
TYR 449	OH	O

INTERACTIONS RBD-ACE2

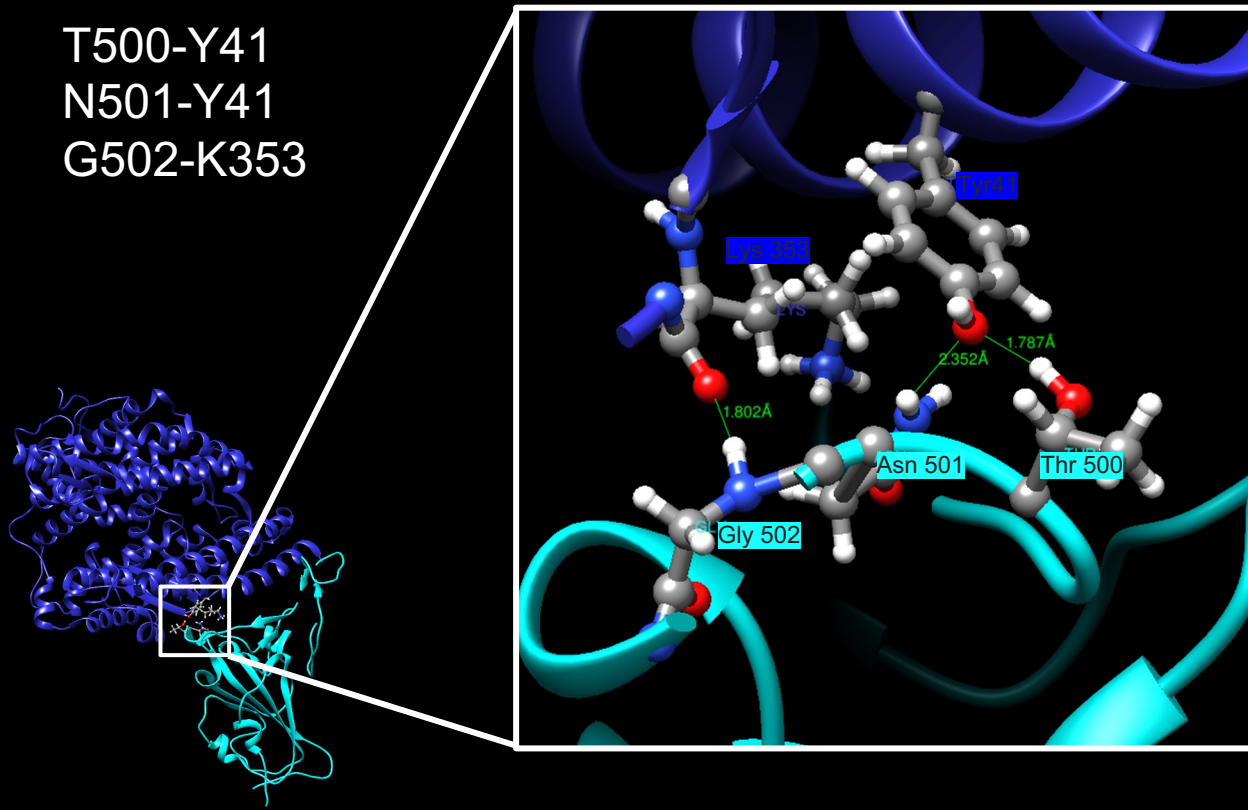
G446-Q42
Y449-A38



438	s p n i d a t i t g	448	n y n Y s Y r l l r
	S N N L D S K V G G	N Y N Y R Y R L F R	
	S N N L D S K V G G	N Y N Y L Y R L F R	
	T R N I D A T S T G	N Y N Y K Y R Y L R	
	T R N I D A T Q T G	N Y N Y K Y R S L R	
	V P H N L T T I T K	P L K Y S Y I N K C	
	L P A I N V T I N N	Y N P S S W N R R Y	
	↑	↑	

INTERACTIONS RBD-ACE2

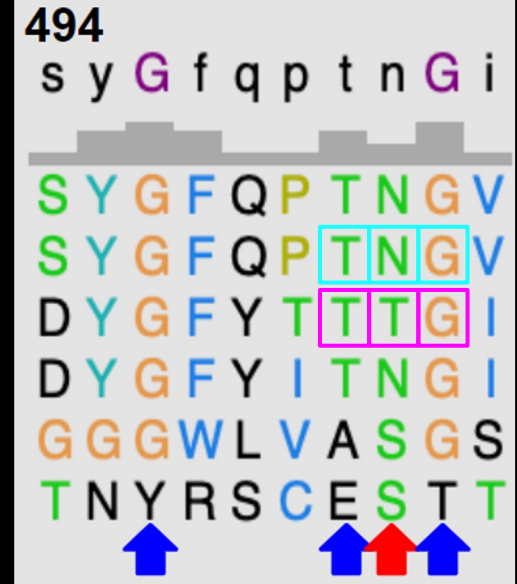
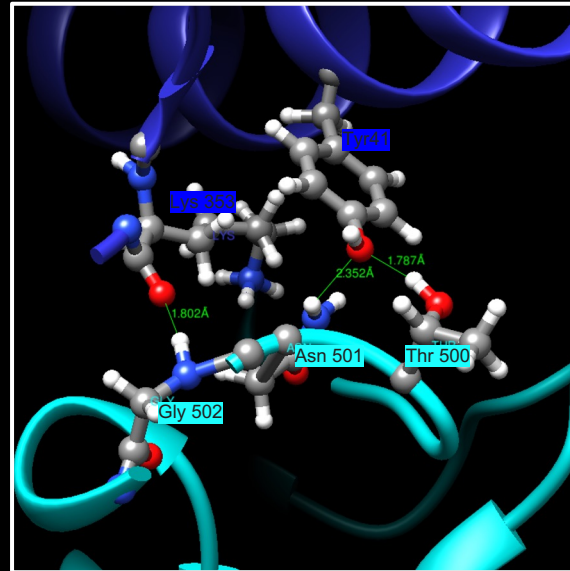
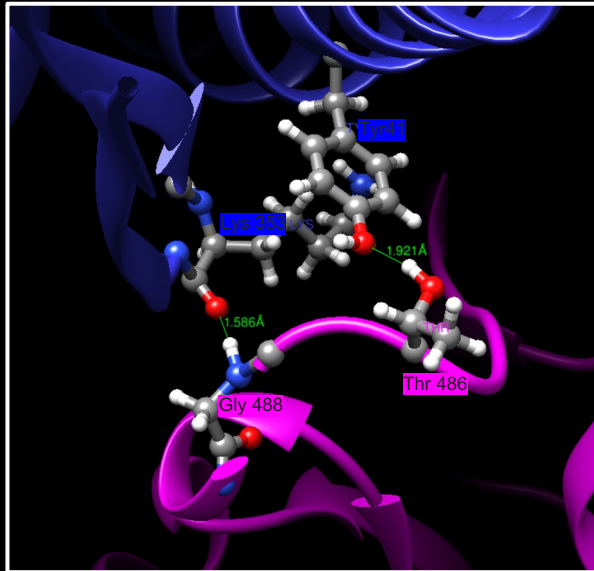
T500-Y41
N501-Y41
G502-K353



Protein residue	SARS-CoV-2atom	ACE2 atom
THR 500	O	OH
ASN 501	N	OH
GLY 502	N	O

INTERACTIONS RBD-ACE2

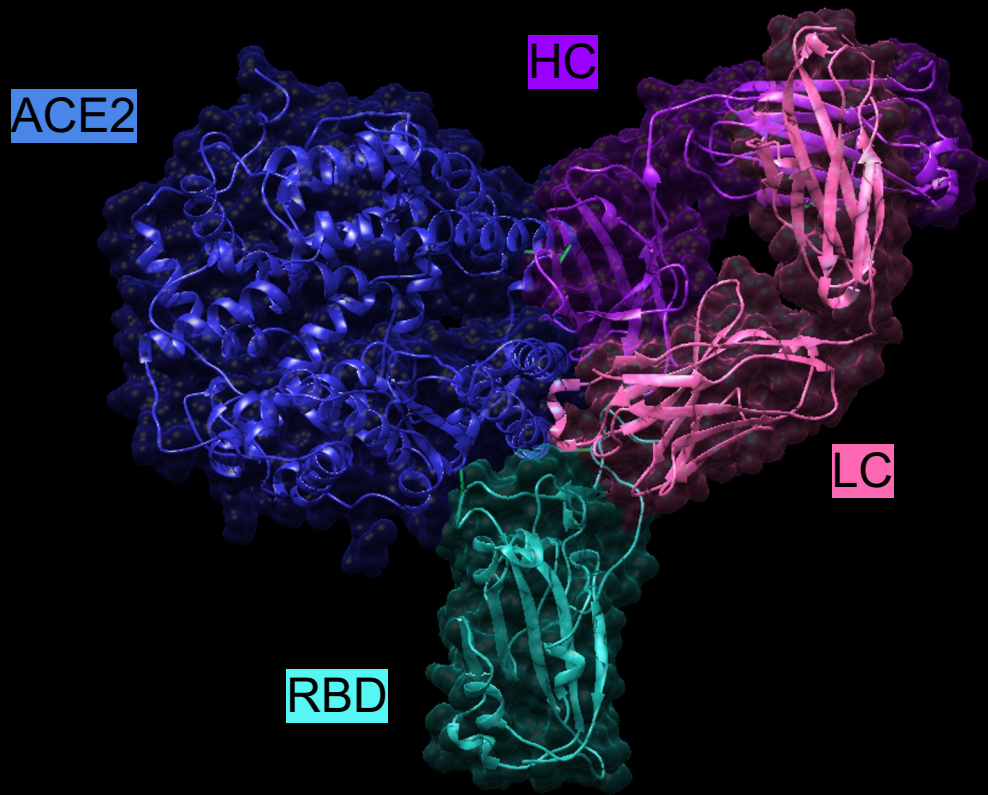
T500-Y41
N501-Y41
G502-K353



Neutralizing Ab

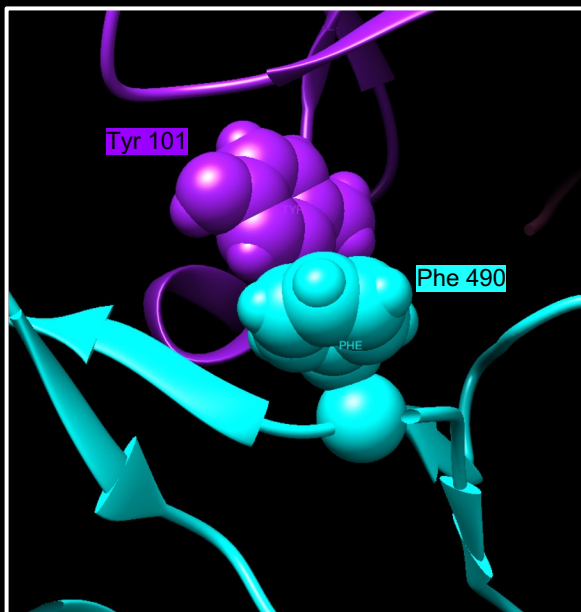
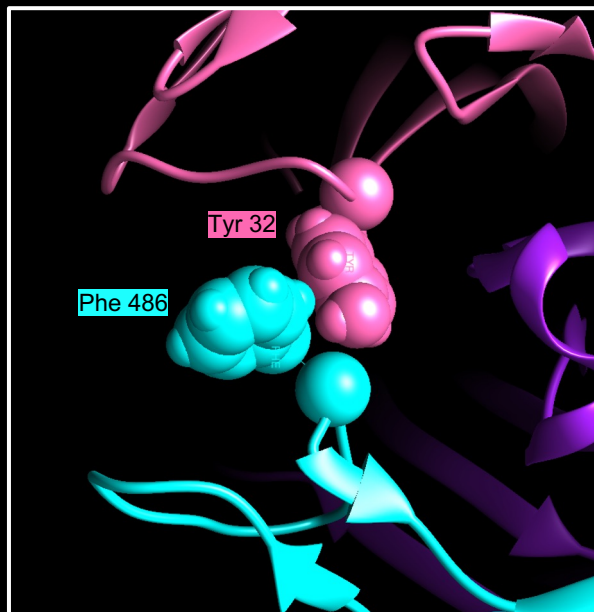
LY-CoV555:

- Binds to the RBD in the up or down conformation.
- Overlaps ACE2 binding site.
- Binds to shared residues with ACE2.



Neutralizing Ab: LY-CoV555

F486-Y32 and F490-Y101



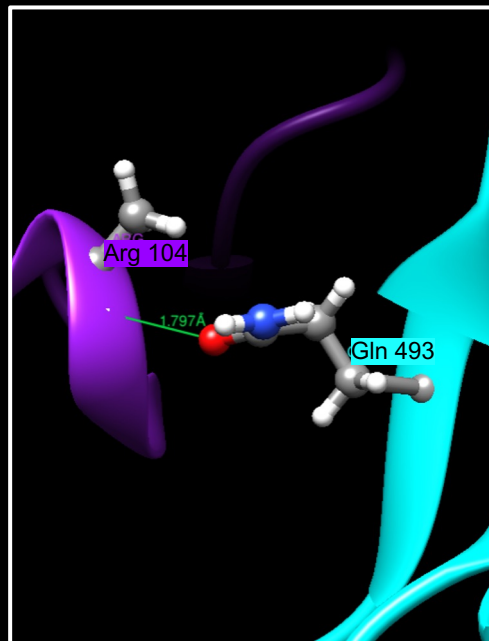
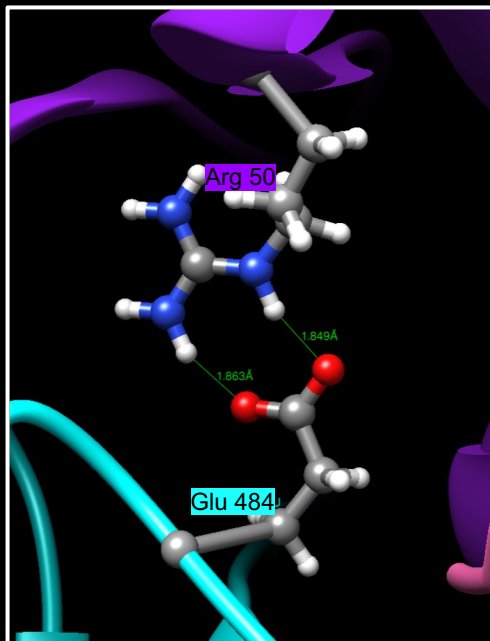
485																490			
a	f	n	c	y	-	-	-	-	-	-	-	-	-	-	w	P	L	q	
																			
G	F	N	C	Y	-	-	-	-	-	-	-	-	-	-	-	F	P	L	Q
G	F	N	C	Y	-	-	-	-	-	-	-	-	-	-	-	F	P	L	Q
A	L	N	C	Y	-	-	-	-	-	-	-	-	-	-	-	W	P	L	N
A	F	N	C	Y	-	-	-	-	-	-	-	-	-	-	-	W	P	L	N
P	S	T	V	W	E	D	G	D	Y	Y	R	-	K	Q	L	S	P	L	E
P	S	F	A	S	S	C	K	S	H	K	P	S	A	S	A	C	P	I	G
↑	↑	↑														↑	↑		

F486 → F28,
L79, M82, Y8

F490 → K31

Neutralizing Ab: LY-CoV555

E484-R50 and Q493-R104



475

a d s k P C t - p p

A	G	S	K	P	C	N	G	V	E
A	G	S	T	P	C	N	G	V	E
P	D	G	K	P	C	T	-	P	P
P	D	G	K	P	C	T	-	P	P
N	Q	Y	S	P	C	V	S	I	V
V	N	N	T	F	C	P	C	A	K

↑ ↑

490

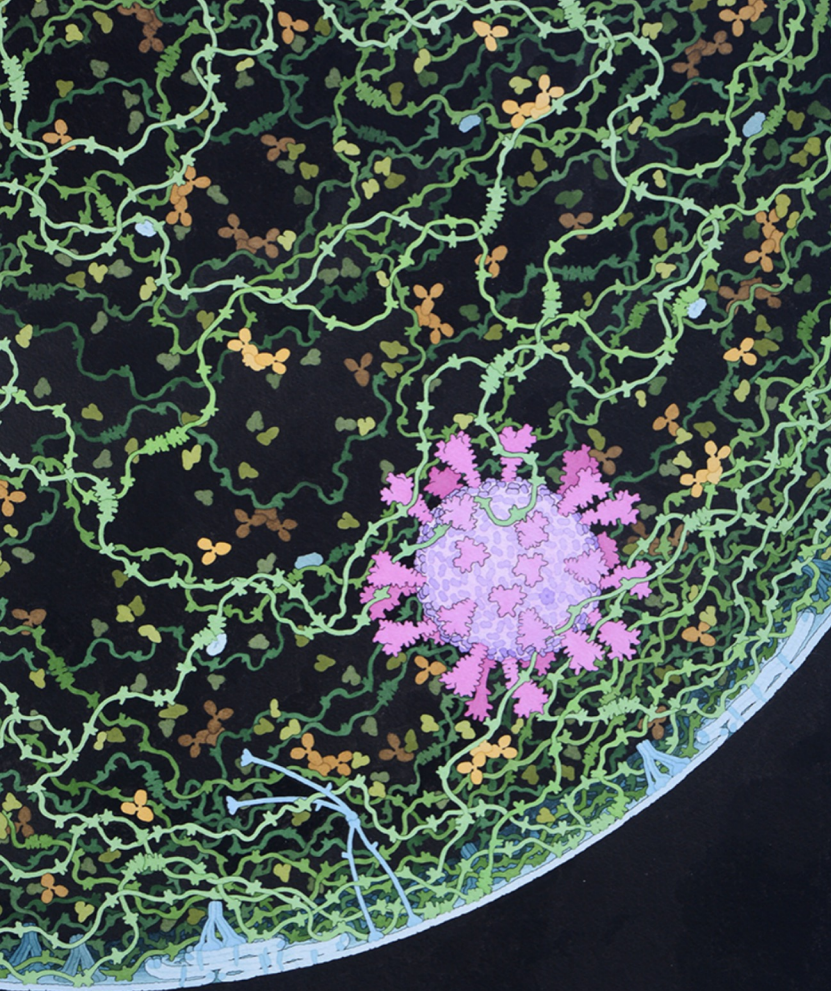
- - - - - w P L q

-	-	-	-	-	w	P	L	q
-	-	-	-	-	F	P	L	Q
-	-	-	-	-	F	P	L	Q
-	-	-	-	-	W	P	L	N
-	-	-	-	-	W	P	L	N
Y	R	-	K	Q	L	S	P	L
K	P	S	A	S	C	P	I	G

↑ ↑

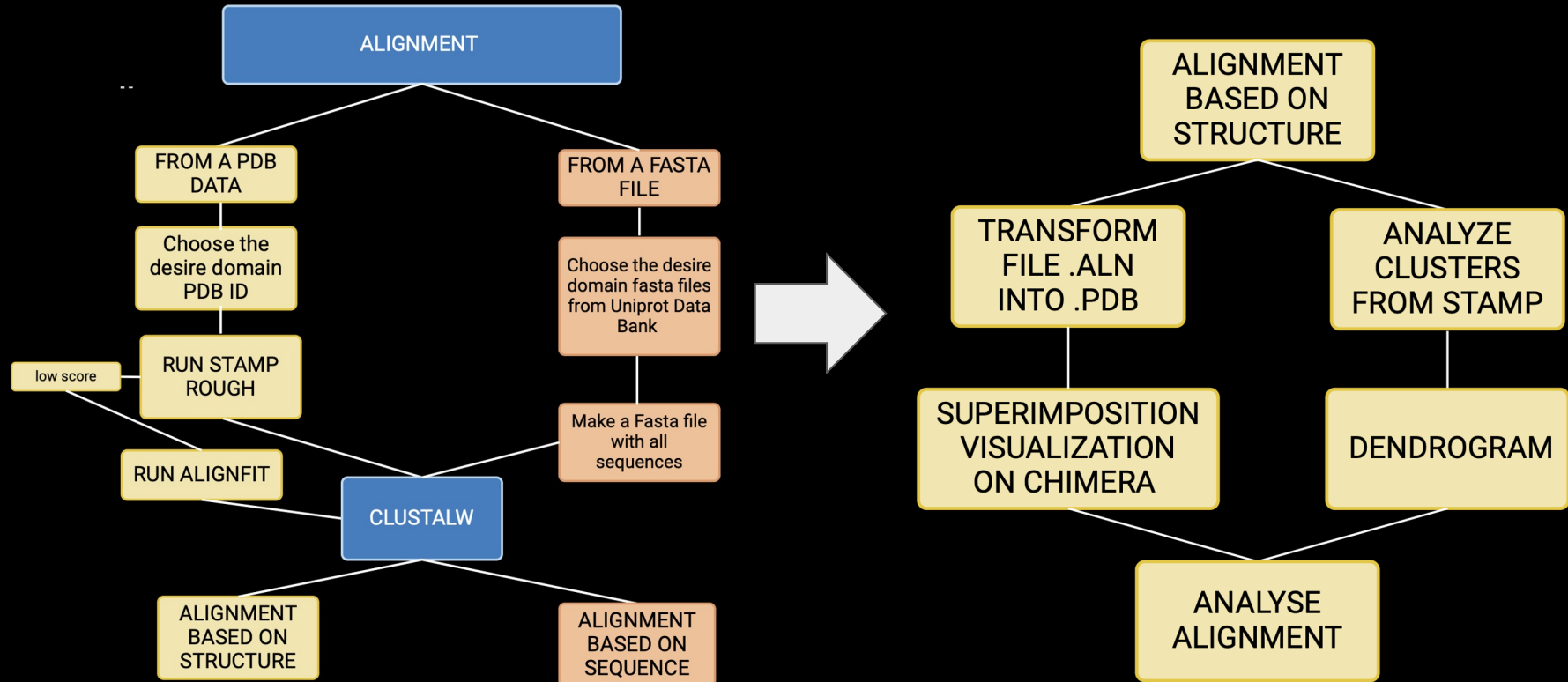
E484 ~~—~~ K31

Q493 ~~—~~ K31, E35



STRUCTURE DOMAIN ANALYSIS

METHODOLOGY



CTD SPIKE PROTEIN DENDROGRAM

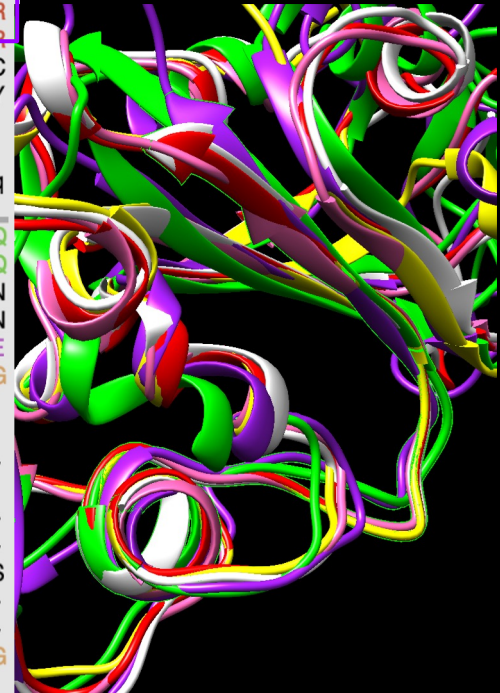


CTD SPIKE PROTEIN CONSERVATION

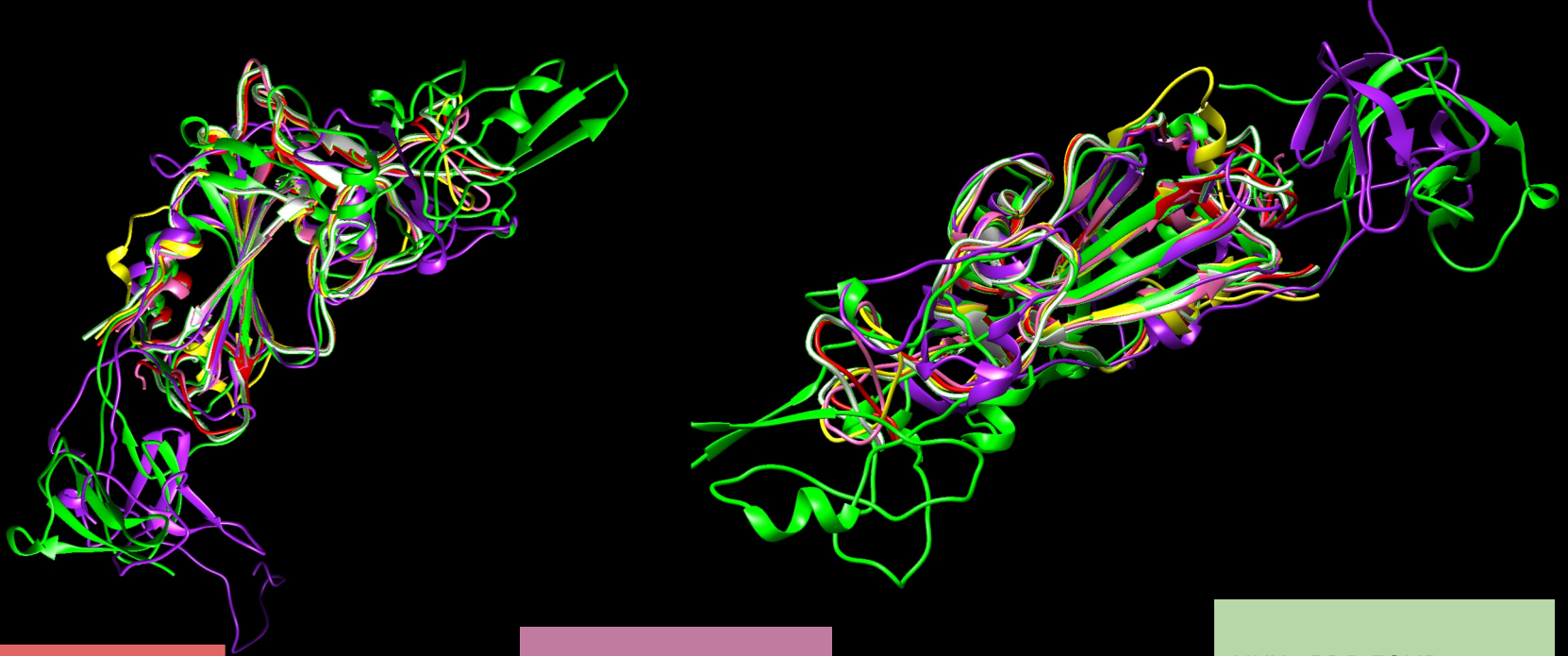
	408	418	428	438	448
Consensus	r q i a p G q t G k	l a d y N Y K l p d	d f t g C v i a w n	s p n i d a t i t g	n y n Y s Y r l l r
Conservation					
delta_SARS-CoV2	R Q I A P G Q T G K	I A D Y N Y K L P D	D F T G C V I A W N	S N N L D S K V G G	N Y N Y R Y R L F R
SARS-CoV2	R Q I A P G Q T G K	I A D Y N Y K L P D	D F T G C V I A W N	S N N L D S K V G G	N Y N Y L Y R L F R
SARS-CoV	R Q I A P G Q T G V	I A D Y N Y K L P D	D F M G C V L A W N	T R N I D A T S T G	N Y N Y K Y R Y L R
WIV1	R Q I A P G Q T G V	I A D Y N Y K L P D	D F T G C V L A W N	T R N I D A T Q T G	N Y N Y K Y R S L R
MERS-CoV	S D L S V S S A G P	I S Q F N Y K Q S F	S N P T C L I L A T	V P H N L T T I T K	P L K Y S Y I N K C
HKU1	S D L Q L G S S G F	L Q S S N Y K I D T	T S S S C Q L Y Y S	L P A I N V T I N N	Y N P S S W N R R Y
	458	465	475	485	490
Consensus	- - - h s n L k p f	e r d i s t e i f s	a d s k P C t - p p	a f n c y - - - -	- - - - - w P L q
Conservation					
delta_SARS-CoV2	- - - K S N L K P F F	E R D I S T E I Y Q	A G S K P C N G V E	G F N C Y - - - -	- - - - - F P L Q
SARS-CoV2	- - - K S N L K P F F	E R D I S T E I Y Q	A G S T P C N G V E	G F N C Y - - - -	- - - - - F P L Q
SARS-CoV	- - - H G K L R P F F	E R D I S N V P F S	P D G K P C T - P P	A L N C Y - - - -	- - - - - W P L N
WIV1	- - - H G K L R P F F	E R D I S N V P F S	P D G K P C T - P P	A F N C Y - - - -	- - - - - W P L N
MERS-CoV	- - - S R L L S D D	R T E V P Q L V N A	N Q Y S P C V S I V	P S T V W E D G D Y	Y R - K Q L S P L E
HKU1	G F N N F N L S S H	S V V Y S R Y C F S	V N N T F C P C A K	P S F A S S C K S H	K P P S A S C P I G
	494	504	514	424	
Consensus	s y G f q p t n G i	g y q p y r v v v l	S F e l l h a p a t	d c g - - - - -	- - - - -
Conservation					
delta_SARS-CoV2	S Y G F Q P T N G V	G Y Q P Y R V V V L	S F E L L H A P A T	V C G - - - - -	- - - - -
SARS-CoV2	S Y G F Q P T N G V	G Y Q P Y R V V V L	S F E L L H A P A T	V C G P - - - -	- - - - -
SARS-CoV	D Y G F Y T T T G I	G Y Q P Y R V V V L	S F E T N L C P F G	E V F N A T K F P S	V Y A W E R K K I S
WIV1	D Y G F Y I T N G I	G Y Q P Y R V V V L	S F E A T V C G P -	- - - - -	- - - - - K K -
MERS-CoV	G G G W L V A S G S	T V A M T E Q L Q M	G F G I T V Q Y G T	D T N S V C P K L E	F A N D T K I A -
HKU1	T N Y R S C E S T T	V L D H T D W C R C	S C L P D P I T A Y	D P R S C S Q K K S	L V G V G E H C A G

Sarbecovirus Conservation

Conservation



CTD SPIKE PROTEIN SUPERIMPOSITION



HKU1 PDB:5GNR

MERS-CoV PDB:7YMY

CTD N PROTEIN DENDROGRAM

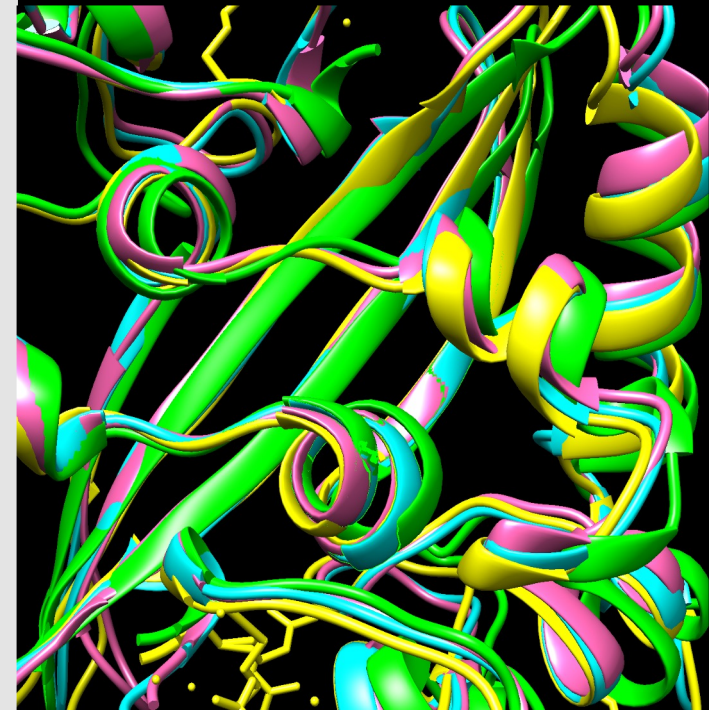


CTD N PROTEIN CONSERVATION

	151	161	171	181	191
Consensus	- - - - - p r	q K R T a t k a y n	v t Q a F G R R g p	e q t q G N F G D q	q l i r q G t d y k
Conservation					
SARS-CoV2	- - - - - K P R	Q K R T A I K A Y N	V T Q A F G R R S P	E Q T Q G N F G D Q	E L I R Q G T D Y K
SARS-CoV	S A A E A S K K P R	Q K R T A T K Q Y N	V T Q A F G R R S P	E Q T Q G N F G D Q	D L I R Q G T D Y K
MERS-CoV	- - - - - M R	H K R T S T K S F N	M V Q A F G L R S P	G D L Q G N F G D L	Q L N K L G T E D P
IBV	- - - - - R Y	C K R T I P P G Y K	V D Q V F G R R T K	G - K E G N F G D	K M N E E G I K D G
	201	211	221	231	241
Consensus	h w p q i a q l a P	s a s A f f g m S r	i g m e v q p s g -	- - - - t w L t y h	g a i k l d d k d P
Conservation					
SARS-CoV2	H W P Q I A Q F A P	S A S A F F G M S R	I G M E V T P S G	- - - - T W L T Y T	G A I K L D D K D P
SARS-CoV	H W P Q I A Q F A P	S A S A F F G M S R	I G M E V T P S G	- - - - T W L T Y H	G A I K L D D K D P
MERS-CoV	R W P Q I A E L A P	T A S A F M G M S Q	F K L T H Q N N D D	G N P V Y F L R Y S	G A I K L D P K N P
IBV	R V T A M L N L V P	S S H A C L F G S R	V T P K L Q P D G -	- - - - L H L K F E	F T I V V F R D D P
	251	261	271	281	291
Consensus	q f k d q v i l l n	q h i D a y k T f p	- - - - - K p r q K	R T a t k a y n v t	Q a F G R R g p e q
Conservation					
SARS-CoV2	N F K Q V I L L N	K H I D A Y K T - -	- - - - K P R Q K	R T A T K A Y N V T	Q A F G R R G P E Q
SARS-CoV	Q F K D N V I L L N	K H I D A Y K T F P	A E A S K K P R Q K	R T A T K Q Y N V T	C A F G R R G P E Q
MERS-CoV	N Y N K W L E L L E	Q N I D A Y K T F P	- - - - K M R H K	R T S T K S F N M V	C A F G L R G P G D
IBV	Q F D N Y V K T C D	Q C V D G V G T R P	- - - - K R Y C K	R T I P P G Y K V D	C V F G P R T K G -
	301	311	321	331	341
Consensus	t q G N F G D q q l	i r q G t d y k h w	p q i a q l a P s a	s A f f g m S r i g	m e v q p s g - - -
Conservation					
SARS-CoV2	T Q G N F G D Q E L	I R Q G T D Y K H W	P Q I A Q F A P S A	S A F F G M S R I G	M E V T P S G - - -
SARS-CoV	T Q G N F G D Q D L	I R Q G T D Y K H W	P Q I A Q F A P S A	S A F F G M S R I G	M E V T P S G - - -
MERS-CoV	L Q G N F G D L Q L	N K L G T E D P F W	P Q I A E L A P T A	S A F I G M S Q F K	L T H Q N N D D G N
IBV	K E G N F G D D K M	N E E G I K D G R Y	T A M L N L V P S S	H A C L F G S R V T	P K L Q P D G - - -
	351	361	371	381	
Consensus	- - t w L t y h g a	i k l d d k d P q f	k d q v i l l n q h	i D a y k T f p - -	
Conservation					
SARS-CoV2	- - T W L T Y T G A	I K L D D K I P N F	K D Q V L L N K H	I D A Y K T - - - -	
SARS-CoV	- - T W L T Y H G A	I K L D D K I P Q F	K D N V L L N K H	I D A Y K T F P - -	
MERS-CoV	P V Y F L R Y S G A	I K L D P K I P N Y	N K W L E L L E Q N	I D A Y K T F P - -	
IBV	- - L H L K F E F T	T V V P R D L Q F	D N Y V K I C D Q C	V D G V G T R P K D	

Beta Coronavirus Conservation

Conservation



NUCLEOCAPSID PROTEIN SUPERIMPOSITION



SARS-CoV2 PDB:7F2E

SARS-CoV PDB:2CJR



MERS-CoV PDB:6G13

IBV PDB:2GE7

CONCLUSIONS

- Structure and function of CTD domains of Spike and Nucleocapsid proteins are conserved
- SARS-Cov 2 has a high variance on CTD Spike domain that interact with residues of ACE2 residues → high mutational rate
- Regarding the N-NTD, almost all the interactions between this domain and the ssRNA are conserved, it could be a good drug target
- Regarding the N-CTD, if some amino acid change and the octamer is not build, the virus cannot have helical symmetry

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PEM QUESTIONS

1. SARS-CoV2 genome codify for ...

- a) Non-structural proteins such as RNA dependent RNA polymerase and Structural proteins such as Spike, nucleocapsid, envelope and Membrane proteins.
- b) Non-structural proteins such as Spike, nucleocapsid, envelope and Membrane proteins and Structural proteins such as RNA dependent RNA polymerase.
- c) Proteins for the membrane and cell attachment
- d) Spike protein and regulates the efficacy of infection
- e) Non-structural proteins such as RNA dependent RNA polymerase and structural proteins related only to membrane formation

2. As we have seen in the clusters results of stamp, some CoV have structural similarities. Which of this sentences is more accurate?

- a) SARS-CoV2 CTD Spike protein Domain has more similarities with SARS-CoV than with WIV1
- b) MERS-CoV has the most similar CTD Spike protein domain sequence with SARS-CoV2 in comparison to the other Coronaviruses analyzed.
- c) IBV CTD N protein domain present some more differences in their structure and function than MERS-CoV in comparative to the other CoV analyzed.
- d) SARS-CoV2, Delta and HKU1 shares the same subgenera.
- e) All of the above are true

3. The conclusion of the SARS-Cov2 CTD Spike protein conservation is...

- a) SARS-Cov2 CTD S protein domain has a high variance in all the sequence
- b) CTD S protein domain preserve their function and structure between the coronaviruses analyzed, however they have variance on residues with interaction with ACE2.
- c) A and B are true
- d) CTD spike protein is not important for infectious function
- e) All of above are true

PEM QUESTIONS

4. SARS-CoV2 belongs to the Subgenera of....

- a) Embecovirus
- b) Merbecovirus
- c) Sarbecovirus
- d) Beta Coronaviruses
- e) Gamma Coronaviruses

5. The Spike protein domain that participates in the binding with its receptor ACE2 is:

- a) HR1
- b) HR2
- c) a and b are correct
- d) NTD
- e) RBD/CTD

6. Select the correct statement:

- a) Most of the interactions between SARS-CoV-2 and ACE2 are salt bridges.
- b) None of the SARS-CoV-2 residues that interact with ACE2 are conserved in SARS-CoV.
- c) a and b are correct.
- d) Hydrophobic interactions also participate in the binding of SARS-CoV-2 and ACE2.
- e) All of the above are correct.

PEM QUESTIONS

7. The neutralizing Ab LY-CoV555, select the correct answer:

- a) Binds to the RBD of the SPIKE protein just in the up conformation.
- b) Overlaps the ACE2 binding domain, so ACE2 and the SPIKE protein are unable to interact.
- c) A and B are correct.
- d) Binds to both the RBD and NTD domains of the SPIKE protein.
- e) None of the above is correct.

8. Which domain is the responsible for de octamer formation and the helical shape of the ribonucleoprotein?

- a) The Nucleoprotein CTD
- b) The Nucleoprotein NTD
- c) A and B are correct.
- d) The Spike CTD
- e) The ribonucleoprotein doesn't have an helical shape

9. The dimerization interface of the Nucleoprotein CTD consists of:

- a) Helixes alfa
- b) Helixes beta
- c) A and B are correct
- d) Helixes 3^10
- e) All are correct

10. Which interactions are more important to conserve to form de octamer of the N-CTD?

- a) Intra-monomer
- b) Intra-dimer
- c) A and B are correct
- d) Inter-dimer
- e) All of them are correct