vaxine

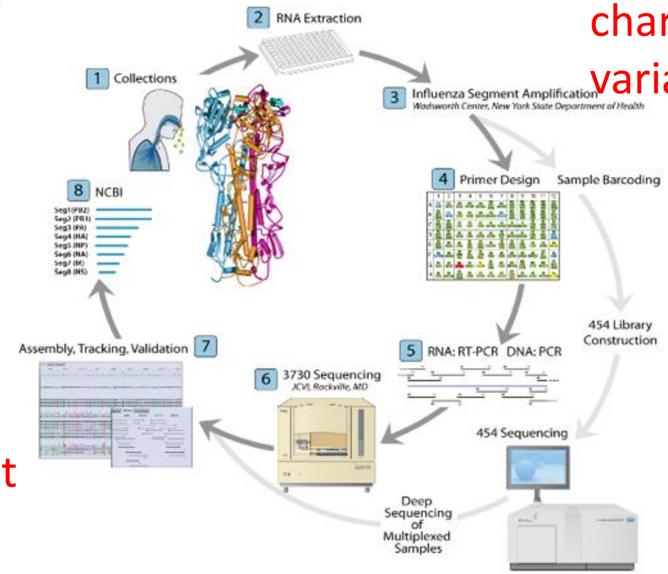
Prof. Nikolai Petrovsky

Chairman and Research Director

Potential for AI to accelerate pandemic vaccine development

AI to model initial virus structure

Jan 2019 – COVID19 virus isolated and sequenced

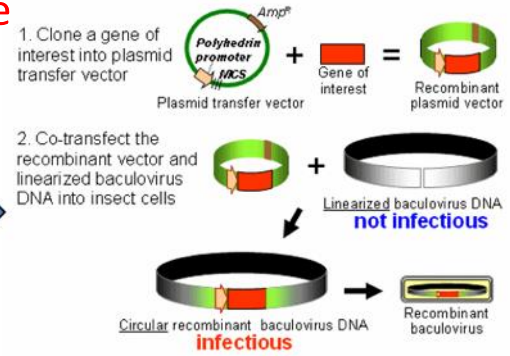


AI to characterise variants

AI to identify virus receptor

AI to predict potential variants

Spike protein gene cloned into baculovirus



Insect cell expression

AI for yield optimisation

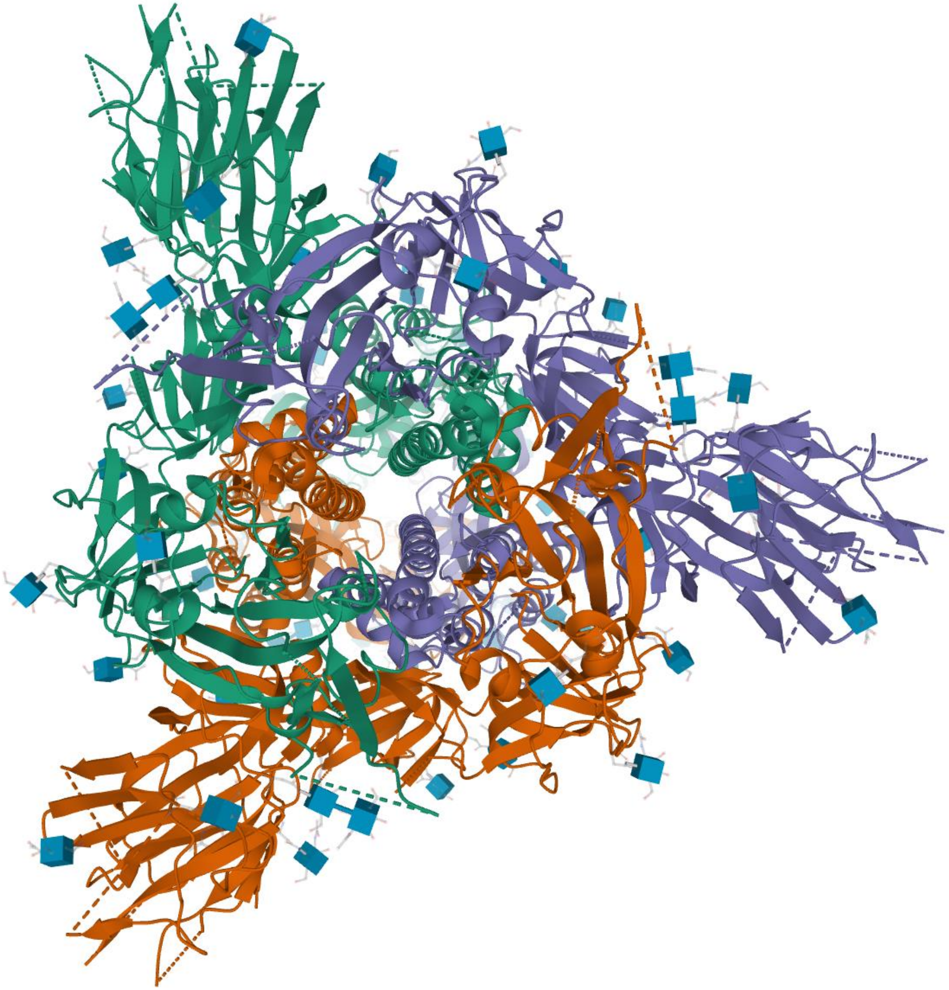
Preparation for large scale cell culture and protein purification through manufacturing partners

Animal studies confirm high immunogenicity with Advax for adjuvant

Formulation with Advax adjuvant

AI for adjuvant design

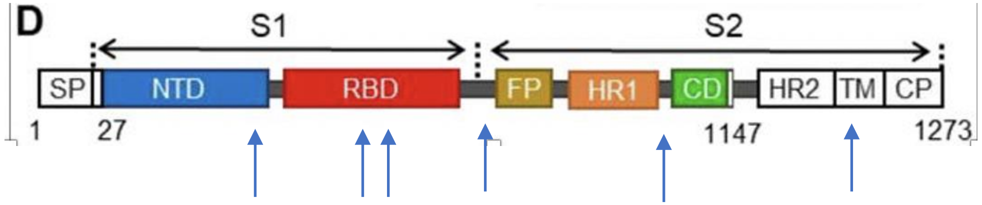
From genome sequence to *in silico* modelling of the COVID-19 spike protein



1. Covid-19 genome sequence
2. Alignment to SARS CoV spike
3. SARS CoV spike PDB structure
4. Homology model Covid-19 spike
5. MDS Covid-19 spike
6. Docking with putative receptors (DPP4, ACE2) to identify ACE2 as the receptor
7. Engineering spike protein then MDS to assess structural stability
8. Target species ACE2 homology models then spike docking to identify susceptible species

Spikogen/COVAX-19™ vaccine design

Protein engineering



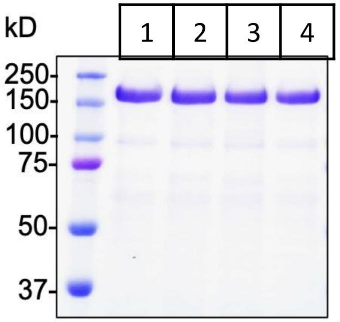
Mellitin leader sequence

Incorporate variant mutations

Delete furin cleavage site

Stabilising mutations

Modify TM and CP domains



Spike ECD

S1

S2

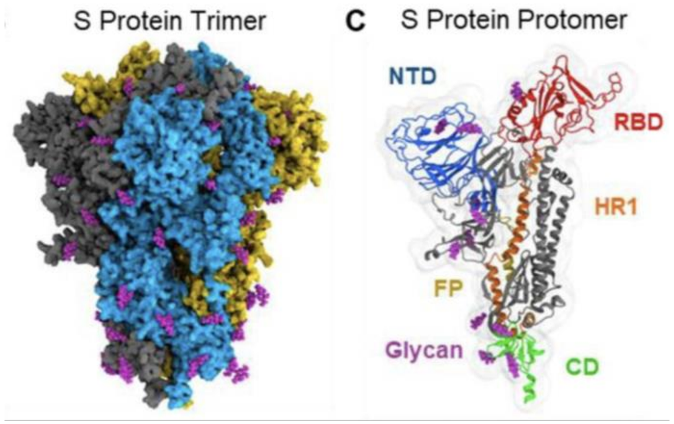
1: 4°C for 5 days

2: 22°C for 5 days

3: 37°C for 5 days

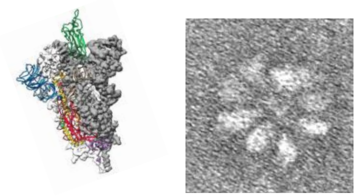
4: -80°C for 5 days/thawed

ANTIGEN STRUCTURE



ADJUVANT STRUCTURE

Spike ECD Trimers



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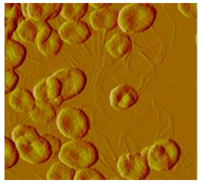
Advax-SM55.2 adjuvant



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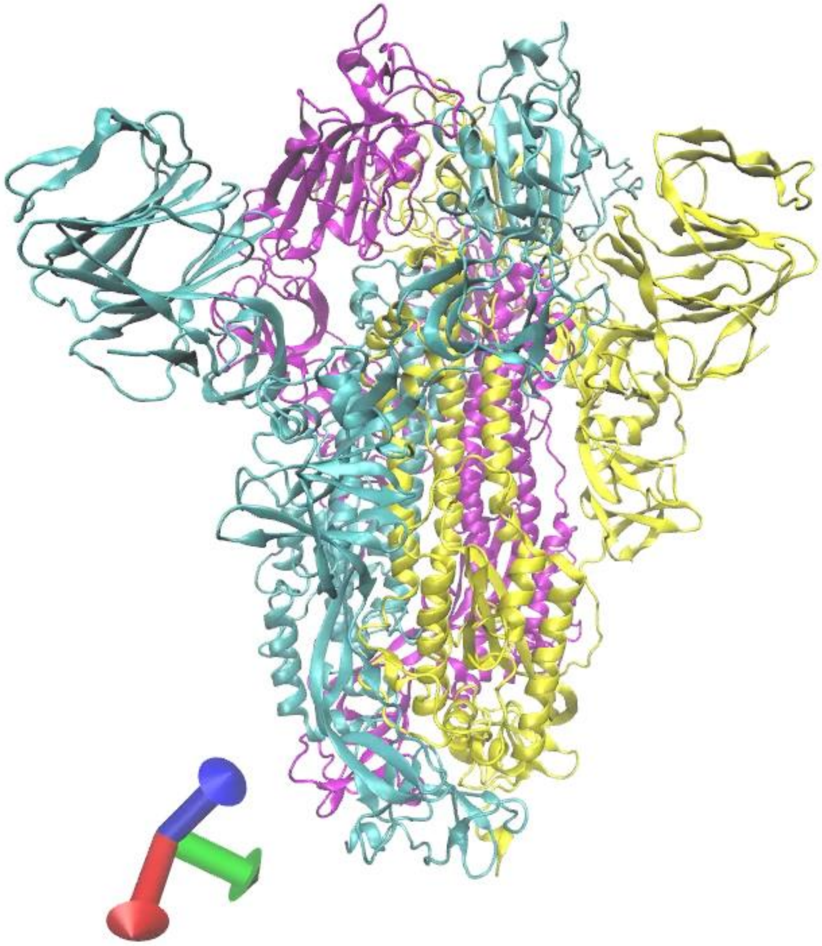
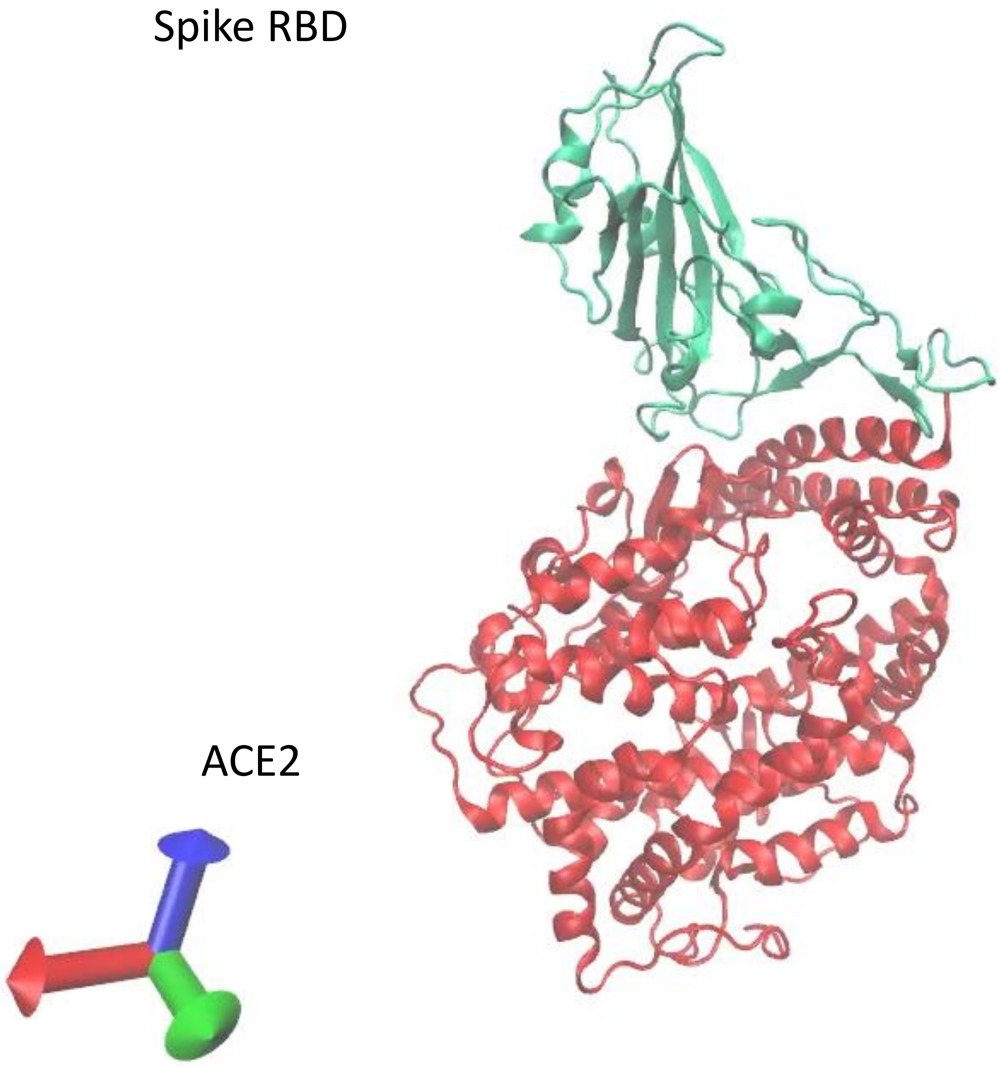
MDS to ensure stability of engineered spike trimer ECD (Wuhan)



Li et al, Vaccine. 2021 Aug 3 doi: 10.1016/j.vaccine.2021.07.087.

Docking and MDS to identify human receptor for Covid-19



Piplani et al, Sci Rep. 2021 Jun 24;11(1):13063.

Docking and MDS to predict susceptible animal species

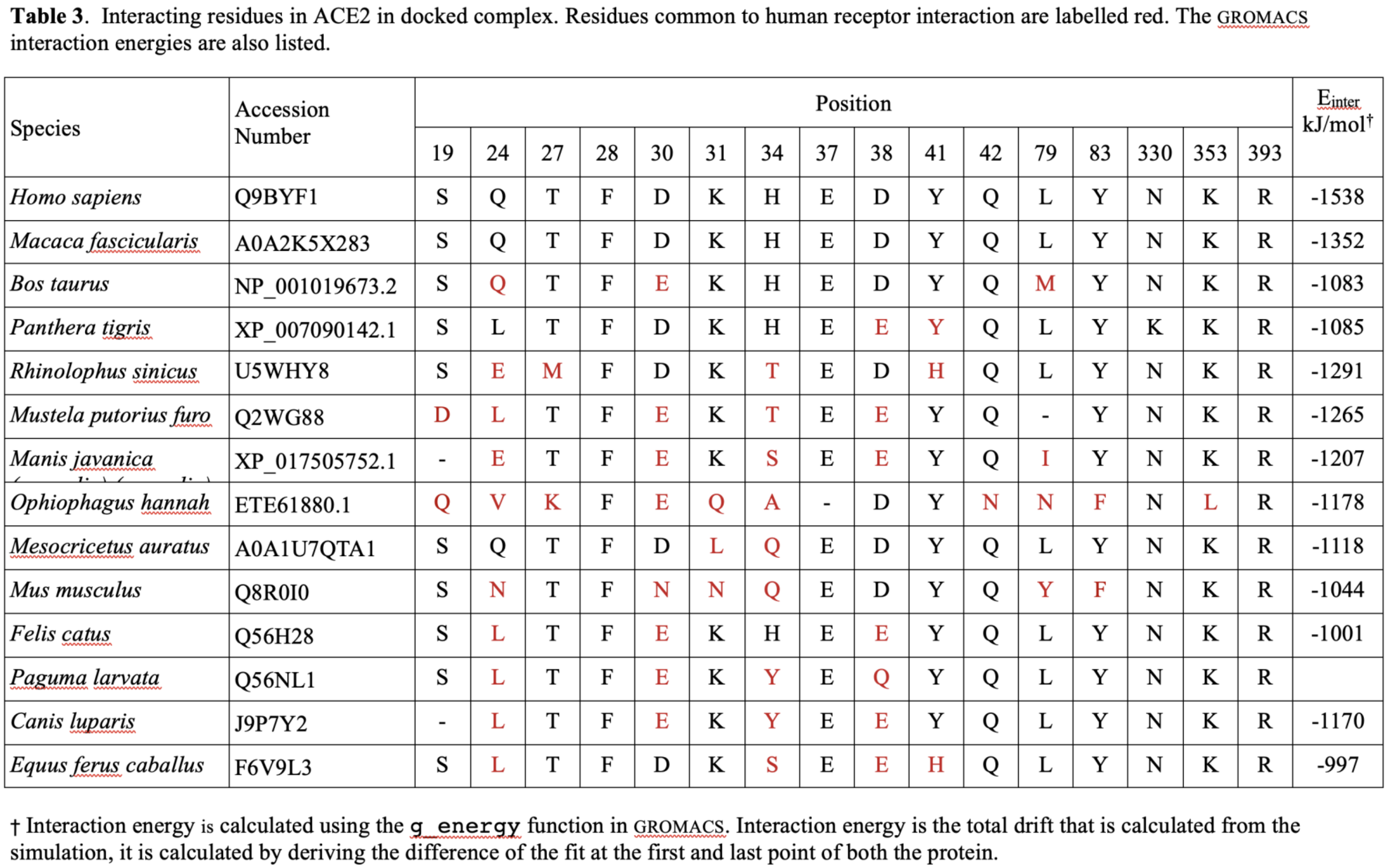


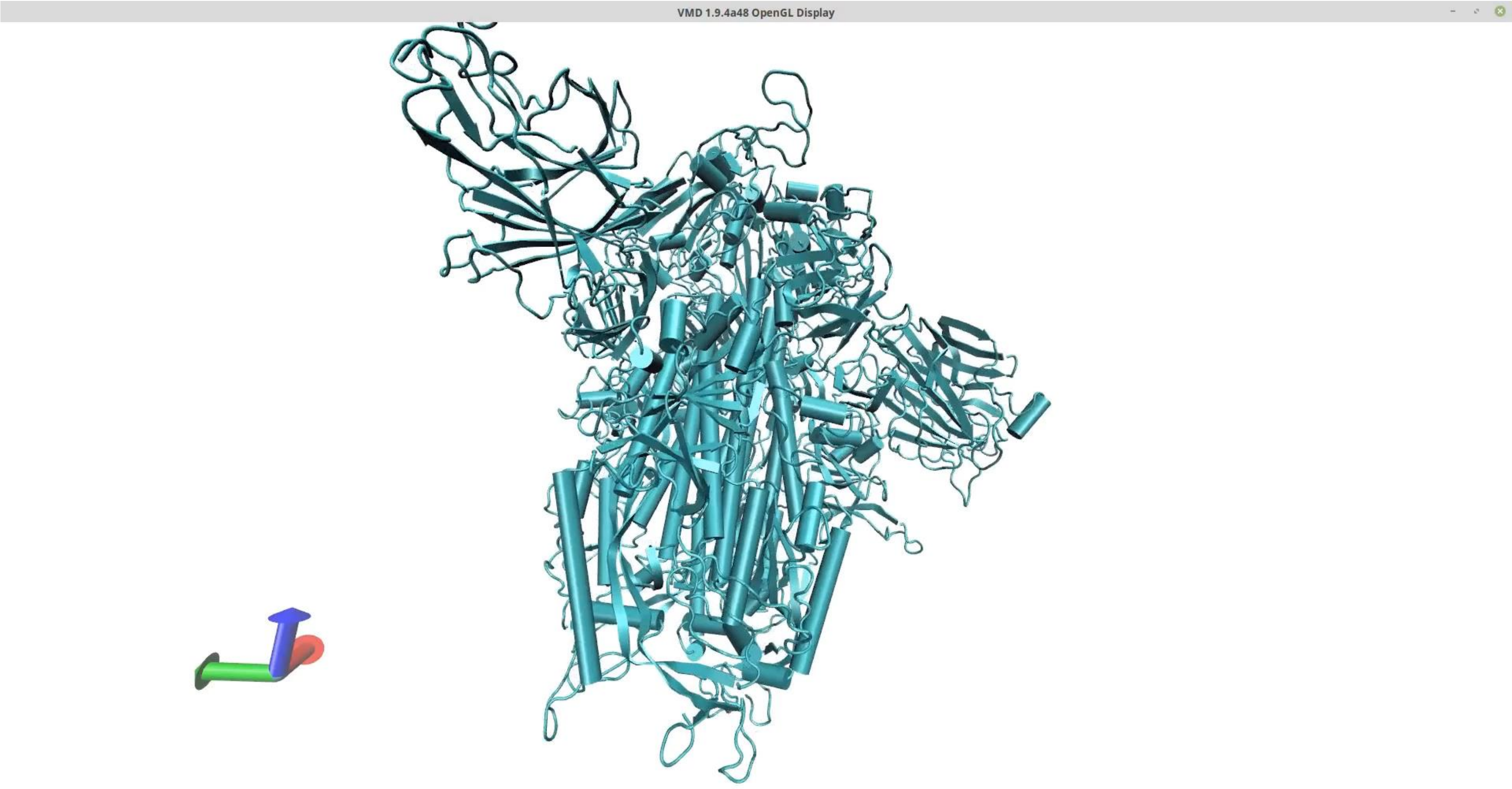
Table 3. Interacting residues in ACE2 in docked complex. Residues common to human receptor interaction are labelled red. The GROMACS interaction energies are also listed.

Species	Accession Number	Position																E_{inter} kJ/mol†
		19	24	27	28	30	31	34	37	38	41	42	79	83	330	353	393	
Homo sapiens	Q9BYF1	S	Q	T	F	D	K	H	E	D	Y	Q	L	Y	N	K	R	-1538
Macaca fascicularis	A0A2K5X283	S	Q	T	F	D	K	H	E	D	Y	Q	L	Y	N	K	R	-1352
Bos taurus	NP_001019673.2	S	Q	T	F	E	K	H	E	D	Y	Q	M	Y	N	K	R	-1083
Panthera tigris	XP_007090142.1	S	L	T	F	D	K	H	E	E	Y	Q	L	Y	K	K	R	-1085
Rhinolophus sinicus	U5WHY8	S	E	M	F	D	K	T	E	D	H	Q	L	Y	N	K	R	-1291
Mustela putorius furo	Q2WG88	D	L	T	F	E	K	T	E	E	Y	Q	-	Y	N	K	R	-1265
Manis javanica	XP_017505752.1	-	E	T	F	E	K	S	E	E	Y	Q	I	Y	N	K	R	-1207
Ophiophagus hannah	ETE61880.1	Q	V	K	F	E	Q	A	-	D	Y	N	N	F	N	L	R	-1178
Mesocricetus auratus	A0A1U7QTA1	S	Q	T	F	D	L	Q	E	D	Y	Q	L	Y	N	K	R	-1118
Mus musculus	Q8R0I0	S	N	T	F	N	N	Q	E	D	Y	Q	Y	F	N	K	R	-1044
Felis catus	Q56H28	S	L	T	F	E	K	H	E	E	Y	Q	L	Y	N	K	R	-1001
Paguma larvata	Q56NL1	S	L	T	F	E	K	Y	E	Q	Y	Q	L	Y	N	K	R	
Canis luparis	J9P7Y2	-	L	T	F	E	K	Y	E	E	Y	Q	L	Y	N	K	R	-1170
Equus ferus caballus	F6V9L3	S	L	T	F	D	K	S	E	E	H	Q	L	Y	N	K	R	-997

† Interaction energy is calculated using the `g_energy` function in GROMACS. Interaction energy is the total drift that is calculated from the simulation, it is calculated by deriving the difference of the fit at the first and last point of both the protein.

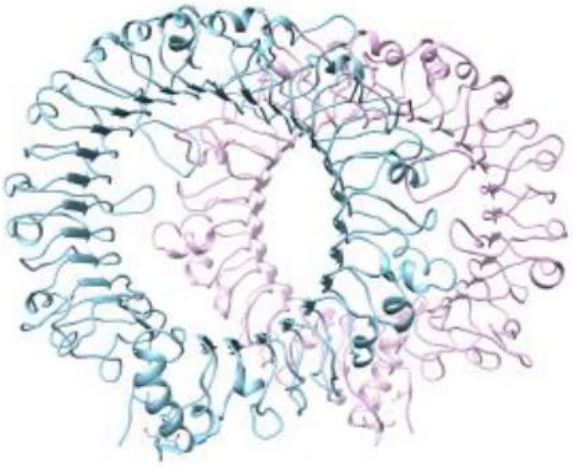
Piplani et al, Sci Rep. 2021 Jun 24;11(1):13063.

MDS to predict stability of engineered Omicron spike protein

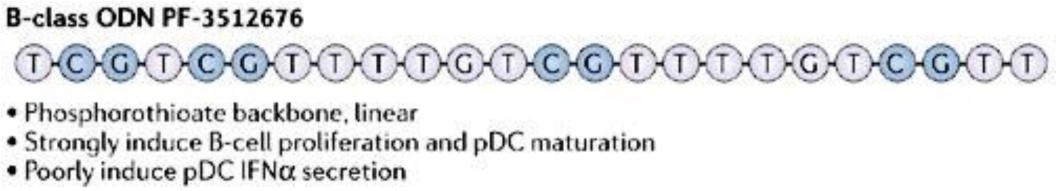


Machine learning approach to identify CpG55.2 adjuvant

TLR9 Receptor



DNA-based ligands

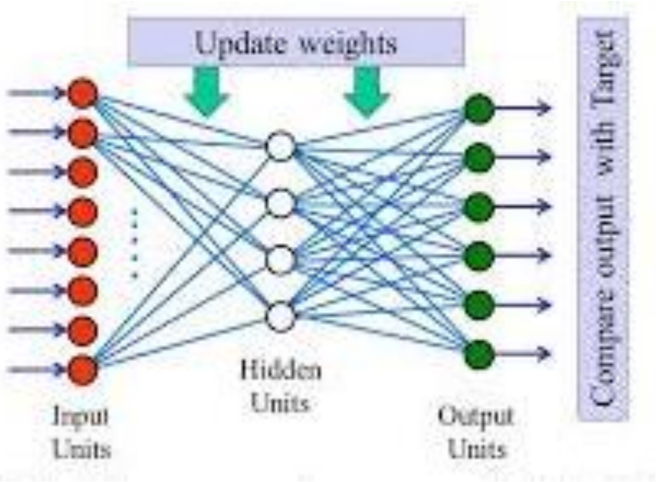


B-class ODN PF-3512676

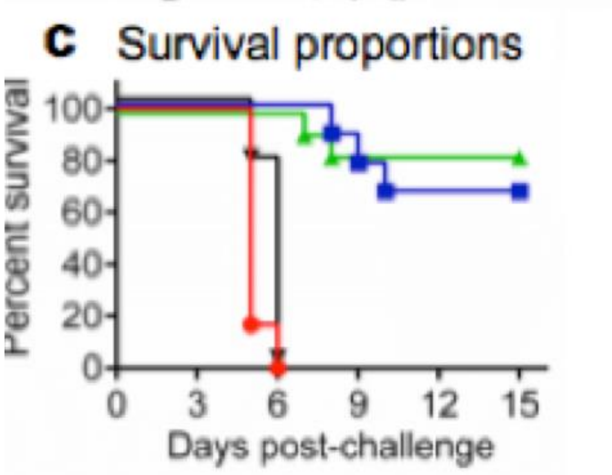
T-C-G-T-C-G-T-T-T-T-G-T-C-G-T-T-T-T-G-T-C-G-T-T

- Phosphorothioate backbone, linear
- Strongly induce B-cell proliferation and pDC maturation
- Poorly induce pDC IFNα secretion

Artificial Intelligence



Enhanced Vaccine Protection



BMC Mol Cell Biol. 2019 Dec 20;20(Suppl 2):56.

Potential in silico approaches to accelerate pandemic preparedness

- Initial virus characterisation
- Receptor identification
- Potential host species
- Vaccine antigen design
- Vaccine adjuvant design
- Monoclonal antibody design
- Prediction of variants
- Optimisation of antigen expression