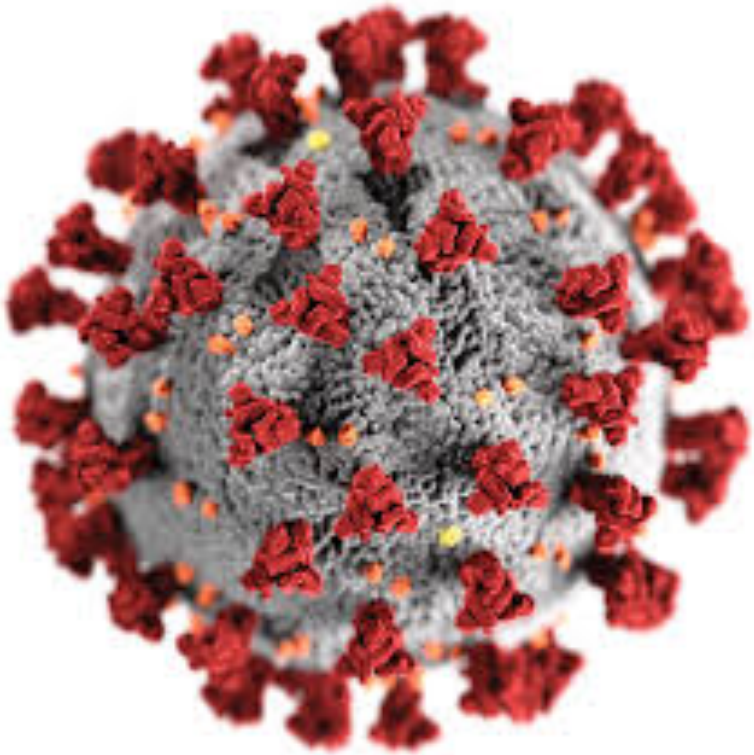
Brief excursus on Virus, COVID-19 and Vaccines



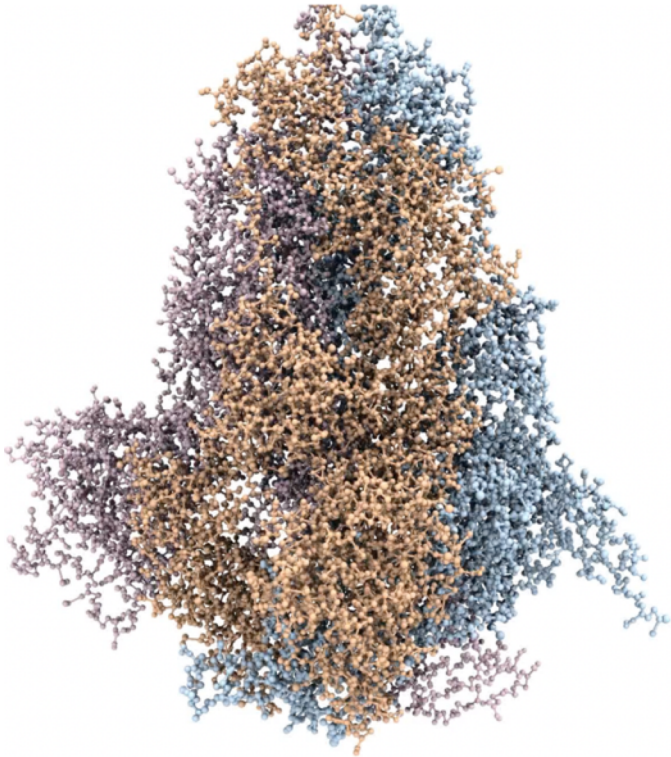
SARS-CoV-2/host cell interaction: viral side

The viral S protein is a **transmembrane glycoprotein** (2-acetamido-2-deoxy-beta-D-glucopyranose, NAG)

It forms **homotrimers** which protrudes from the viral the viral surface

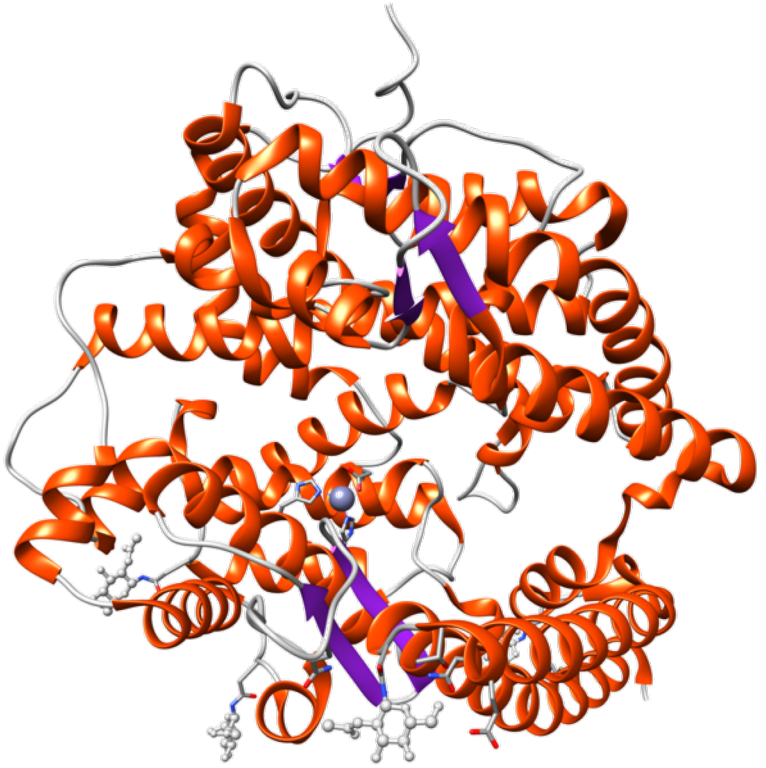
A specific protein domain (the so-called **receptor binding domain or RBD**) specifically recognize its binding region on ACE2

Host susceptibility to SARS-CoV-2 is determined by **the strong affinity between the S-RBD and ACE2** during viral attachment and adsorption



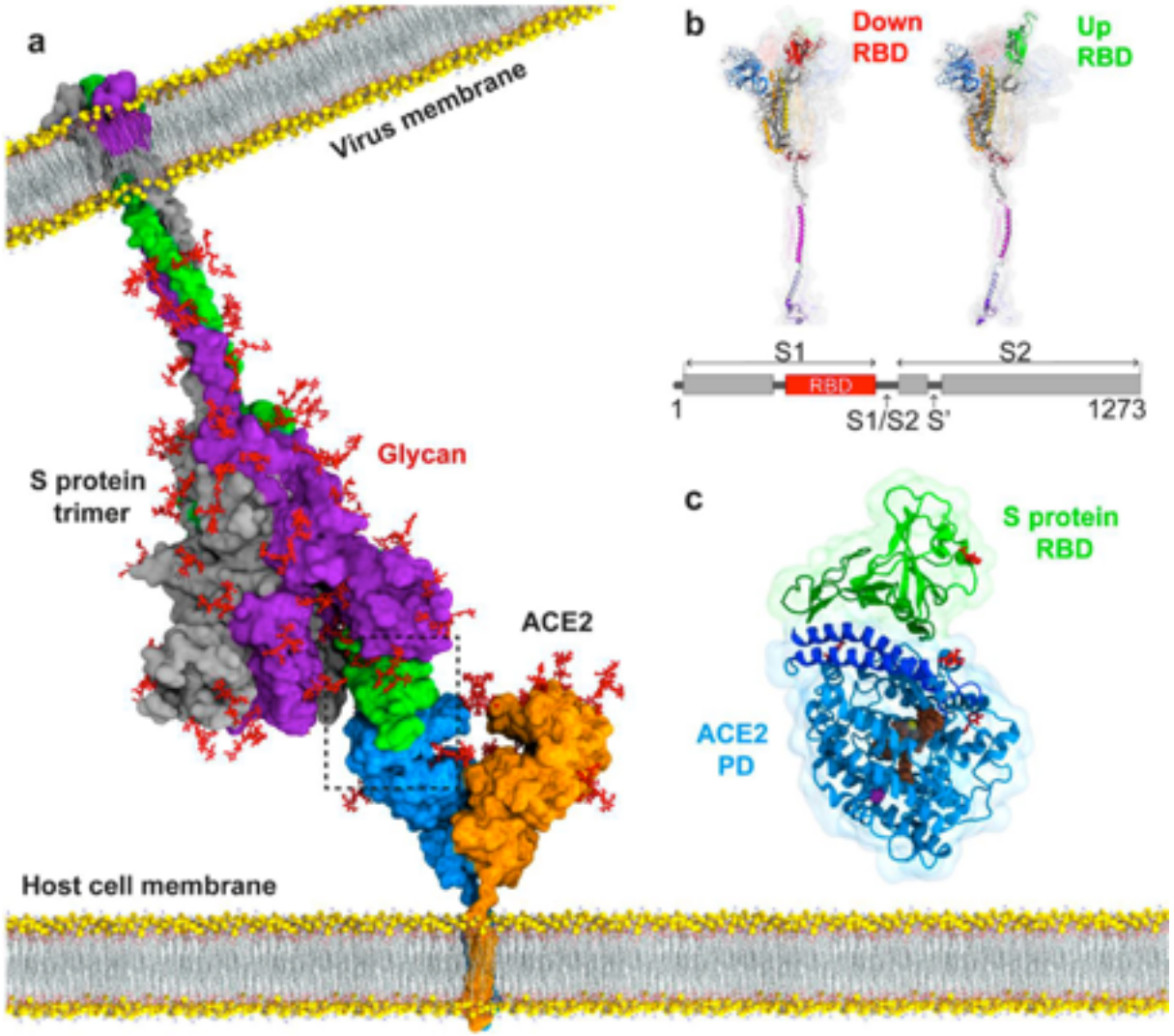
SARS-CoV-2/host cell interaction: human side

- The angiotensin-converting enzyme 2 is also a glycosylated (NAG) transmembrane receptor
  - part of the Renin-Angiotensin-Aldosterone (RAAS) system which controls the extracellular fluid volume
    - specifically blood volume – master of body pressure



- ACE2 is expressed almost ubiquitously
  - Epithelial cells of lungs, kidneys, intestine, heart, etc.
- ACE2 is a metalloprotein
  - The presence of a Zn^{2+} ion is essential for the catalytic activity of the enzyme

SARS-CoV-2/host cell interaction: the complex



S-protein:
Two conformations for the RBD (**Up and Down**)
binds ACE2 in the **down conformation**

SARS-CoV-2/host cell interaction: the S-protein variants

One of the most concerning features of the spike protein of SARS-CoV-2 is how it changes over time during the evolution of the virus.

Encoded within the viral genome, the protein can mutate and changes its biochemical properties as the virus evolves.

Most mutations will not be beneficial and either stop the spike protein from working or have no effect on its function.

But some may cause changes that give the new version of the virus a selective advantage by making it more transmissible or infectious.

One way this could occur is through a mutation on a part of the spike protein that prevents protective antibodies from binding to it.

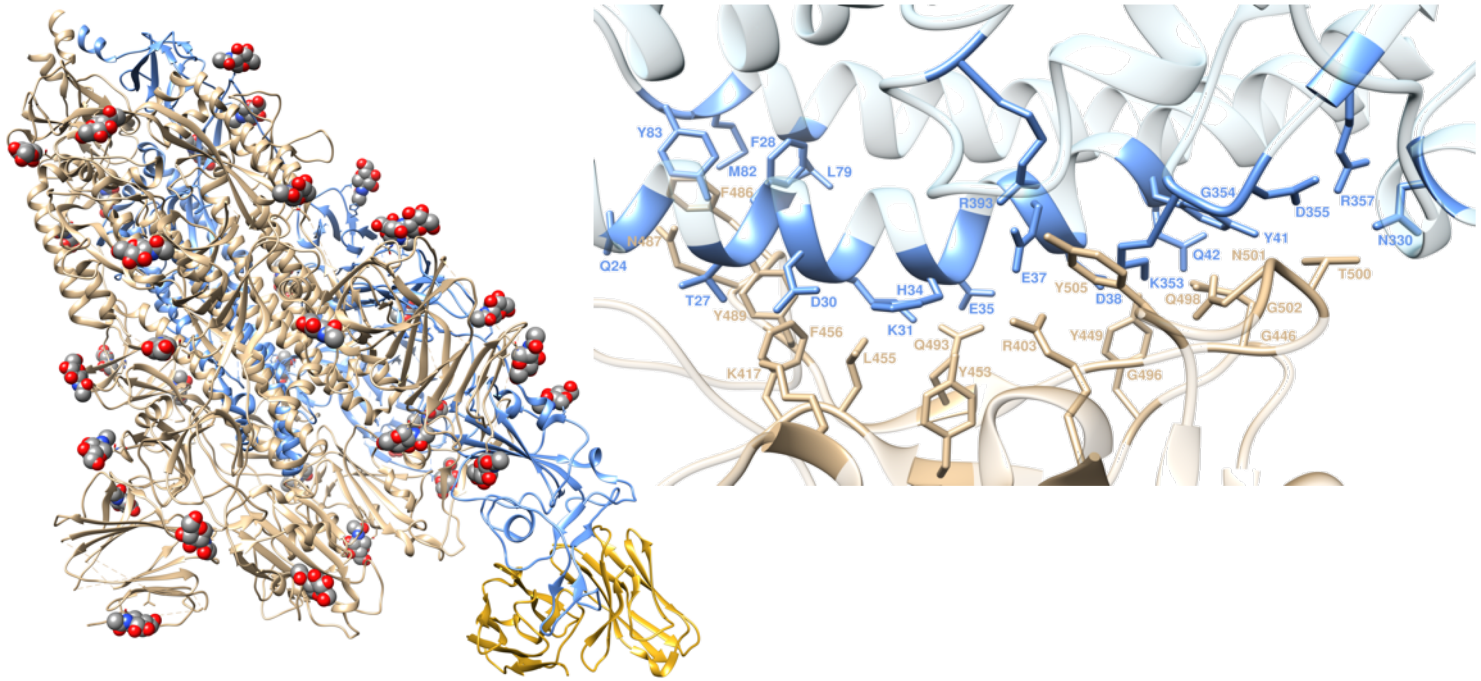
Another way would be to make the spikes "stickier" to our ACE2 receptor.

This is why new mutations that alter how the spike functions are of particular concern – they may impact how we control the spread of SARS-CoV-2.

SARS-CoV-2/host cell interaction: the S-protein UK variants

The new variants found in the UK and elsewhere have mutations across spike and **in parts of the protein involved in binding ACE2**.

Experiments will have to be conducted in the lab to ascertain if – and how – these mutations significantly change the spike, and whether our current control measures remain effective (**including vaccines**)



gene	nucleotide	amino acid
ORF1ab	C3267T	T1001I
	C5388A	A1708D
	T6954C	I2230T
	11288-11296 deletion	SGF 3675-3677 deletion
spike	21765-21770 deletion	HV 69-70 deletion
	21991-21993 deletion	Y144 deletion
→	A23063T	N501Y
	C23271A	A570D
	C23604A	P681H
	C23709T	T716I
	T24506G	S982A
	G24914C	D1118H
Orf8	C27972T	Q27stop
	G28048T	R52I
	A28111G	Y73C
N	28280 GAT->CTA	D3L
	C28977T	S235F