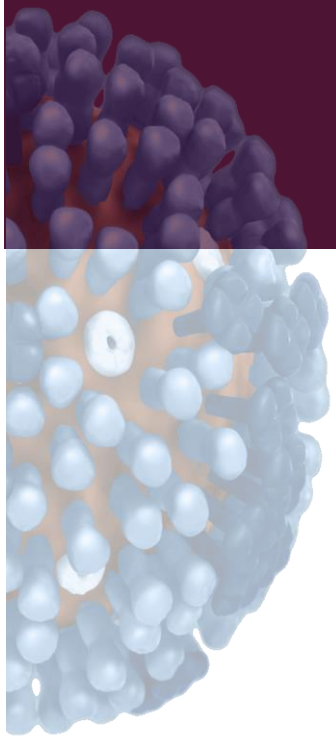
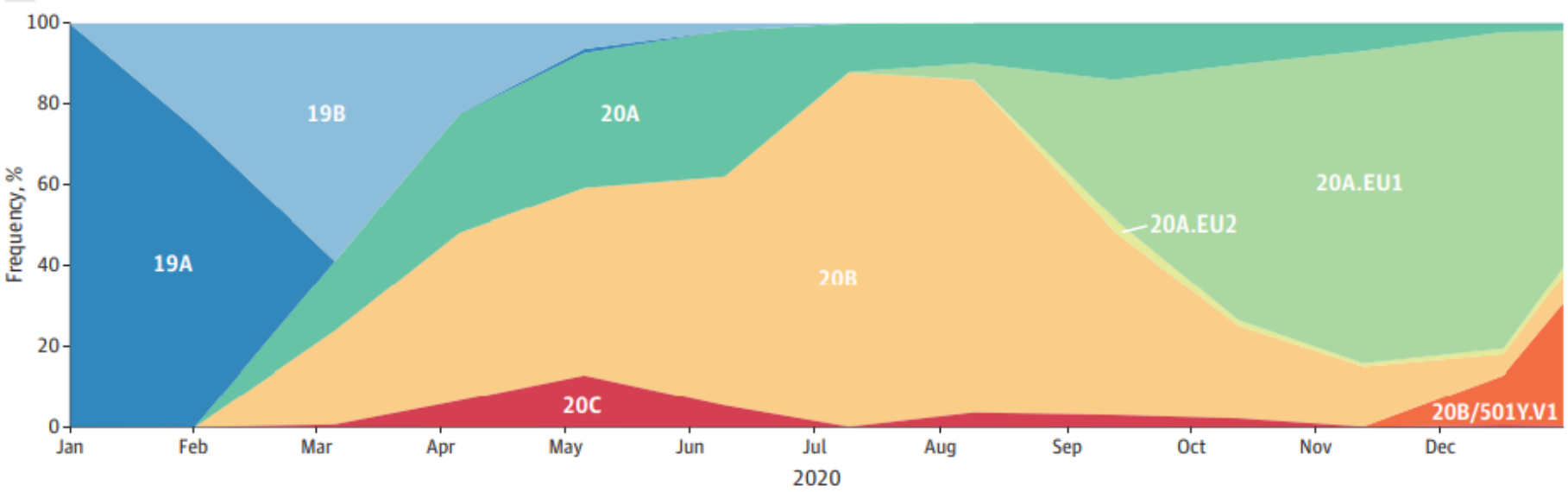


It is Time to Make Pan-Sarbecovirus Vaccines

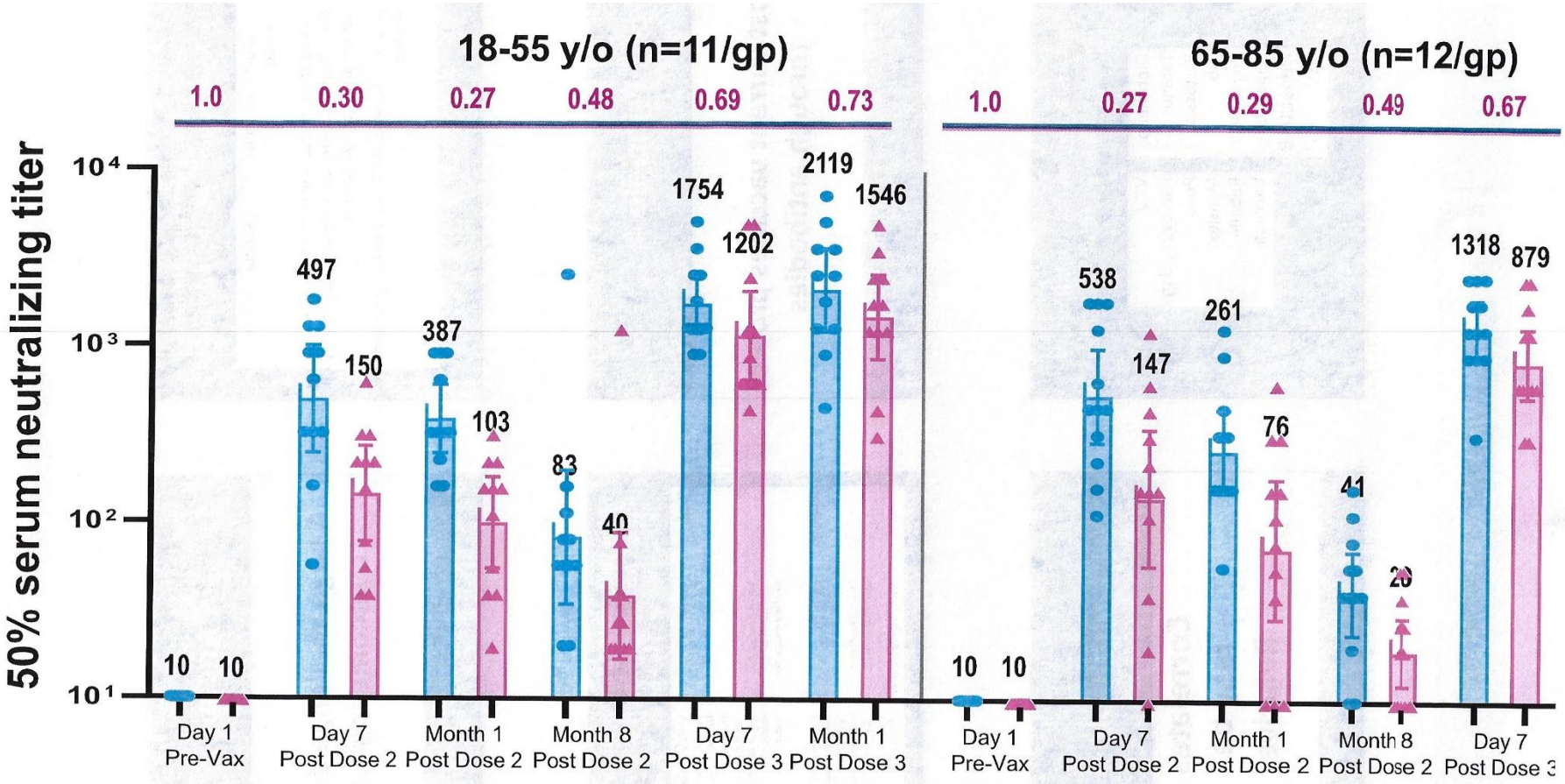
By Stanley A. Plotkin

Frequencies of circulating lineages of SARS-CoV-2 over time



Lauring, A., Hodcroft, E., *JAMA* 2021;325;6

Covid-19 Vaccine: Neutralization Titers Much Higher Post 3rd Than Post 2nd for Wild Type and Beta Variants[1,2]



1. Initial data, Phase 1 sentinel subjects received dose 1 & 2 of 30mcg BNT162b2 21 days apart, subjects then came back and received BNT162b2 30 mcg as a 3rd
2. Samples were tested against each variant separately; PRNT: Plaque Reduction Neutralizing Test; GMR: Geometric Mean Ratio; WT: Wild Type; LOD: Limit of

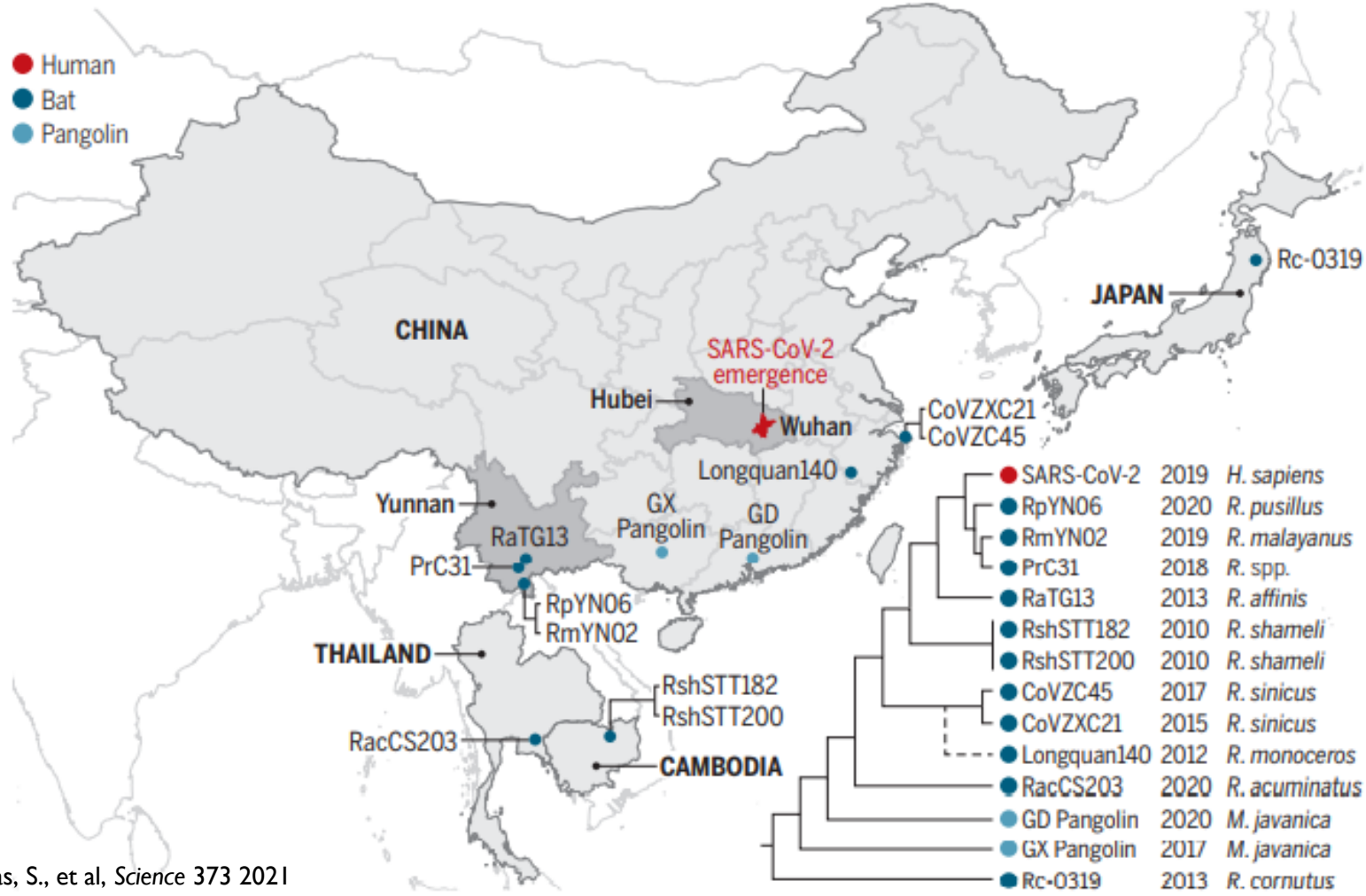
Pfizer

Second Quarter 2021 Earnings

Data submitted for publication

Sarbecoviruses closely related to SARS-CoV-2

Coronaviruses that are evolutionarily closest to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been sampled in China, Cambodia, Japan, and Thailand (*5*). The phylogenetic tree, inferred from a genomic region minimized for recombination (*5*), shows sarbecoviruses closely related to SARS-CoV-2. Host species for each virus, horseshoe bat (*Rhinolophus*), human (*Homo sapiens*), and pangolin (*Manis javanica*) and the year of sample collection are shown in the key. Longquan140 is inferred from another genomic region (*5*) (dashed line). See supplementary table S1 for more details.



Lytras, S., et al, *Science* 373 2021

Impact of SARS-CoV-2 Variants on Vaccine Efficacy and Effectiveness

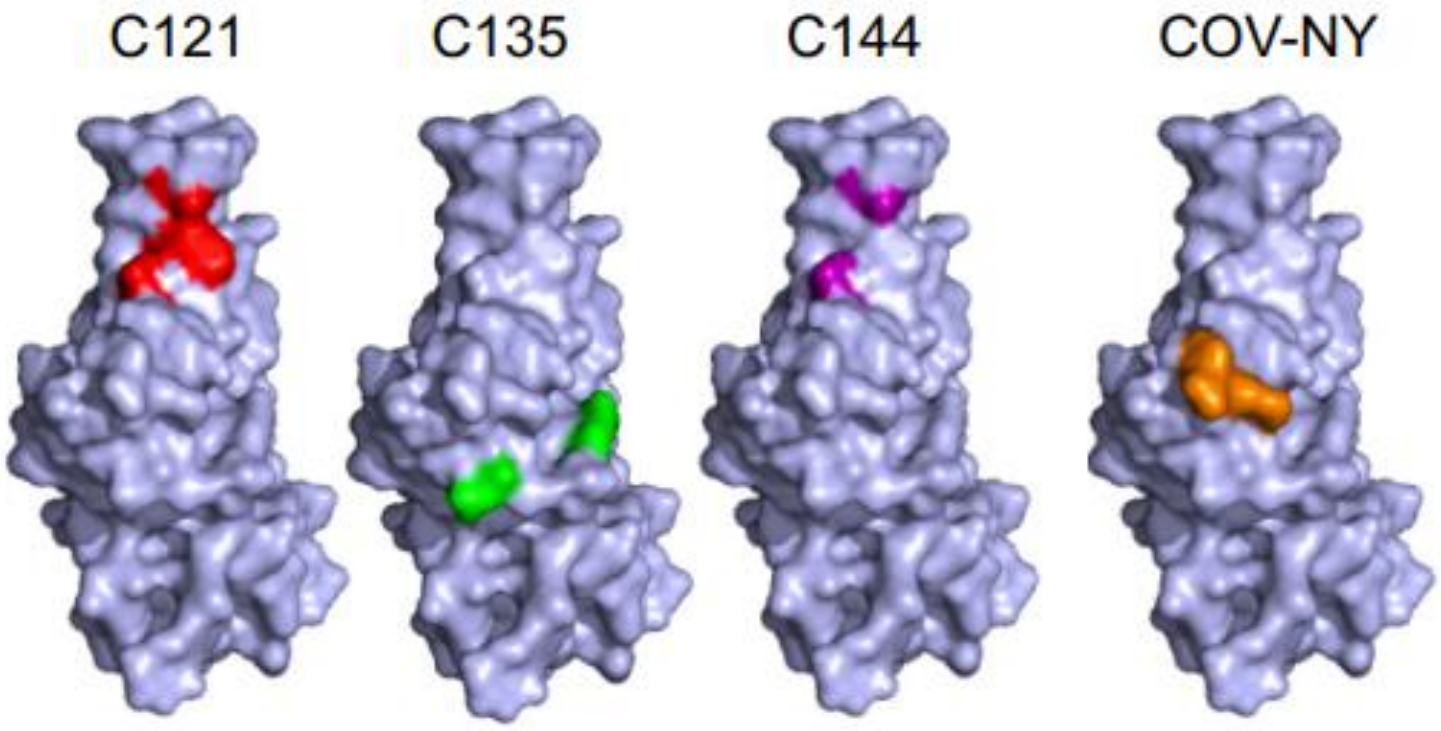
SARS-CoV-2 Variant (also known as)	Vaccine-mediated Protection: AZD1222 (AstraZeneca University of Oxford)	Vaccine-mediated Protection: BnT162b2 (Pfizer – BionTech)
Wuhan reference strain	55–81%	95%
Alpha, B.1.1.7 (British/ Kent;VOC 202012/01; 20B/501Y.V1	75%	90%
Beta, B.1.351 (South African; 20H/501Y.V2)	10%	75%
Gamma, P.1 (B.1.1.28.1)	Unknown	No evidence of reduced protection
Delta, B.1.617.2	92% effective against hospitalization; one-dose effectiveness estimated at 60–71%	Lower mean plaque reduction neutralization titres but sera can neutralize titres of at least 40; one dose of vaccine is 88% effective

Tregoning, J., et al, *Nat Rev Immunol.*; 2021 Oct;21(10):626-636

The degree to which SARS-CoV-2 will adapt to evade neutralizing antibodies is unclear. Using a recombinant chimeric VSV/SARS-CoV-2 reporter virus, we show that functional SARS-CoV-2 S protein variants with mutations in the receptor-binding domain (RBD) and N-terminal domain that confer resistance to monoclonal antibodies or convalescent plasma can be readily selected.

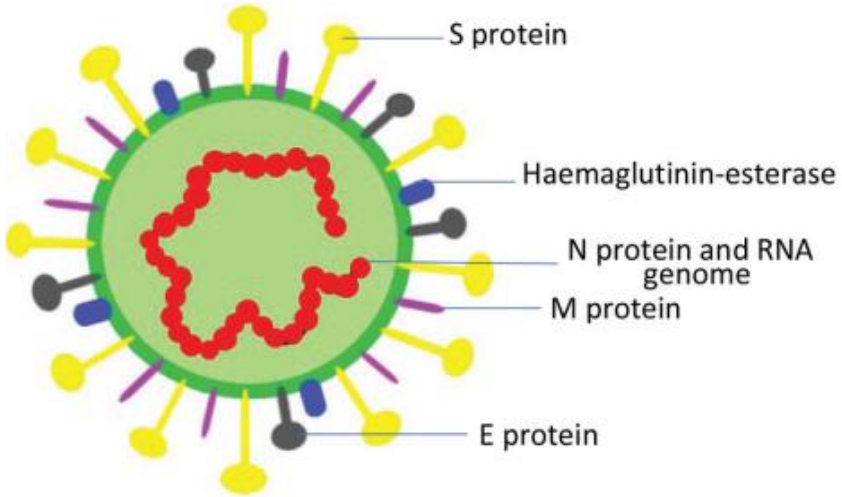
Weisblum, Schmidt, et al, *eLife* 2020;9

Neutralization of rVSV/SARS-CoV-2/GFP RBD mutants by monoclonal antibodies

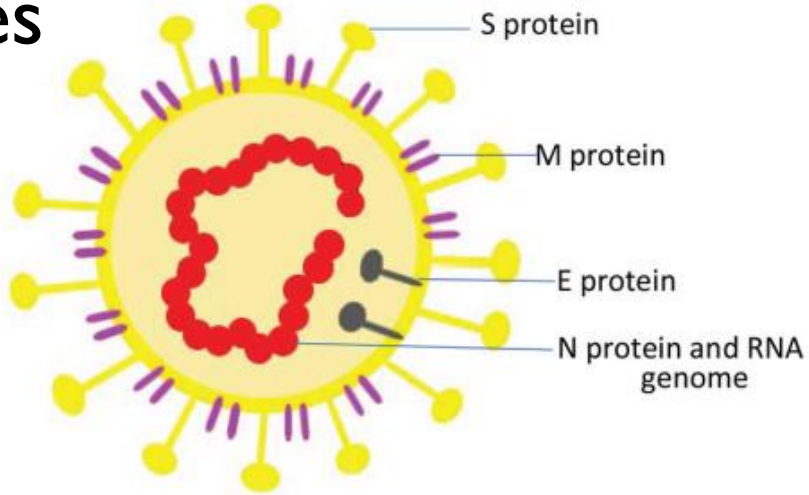


Weisblum, Schmidt, et al, *eLife* 2020;9

Structures of Coronaviruses



SARS-2



SARS-1

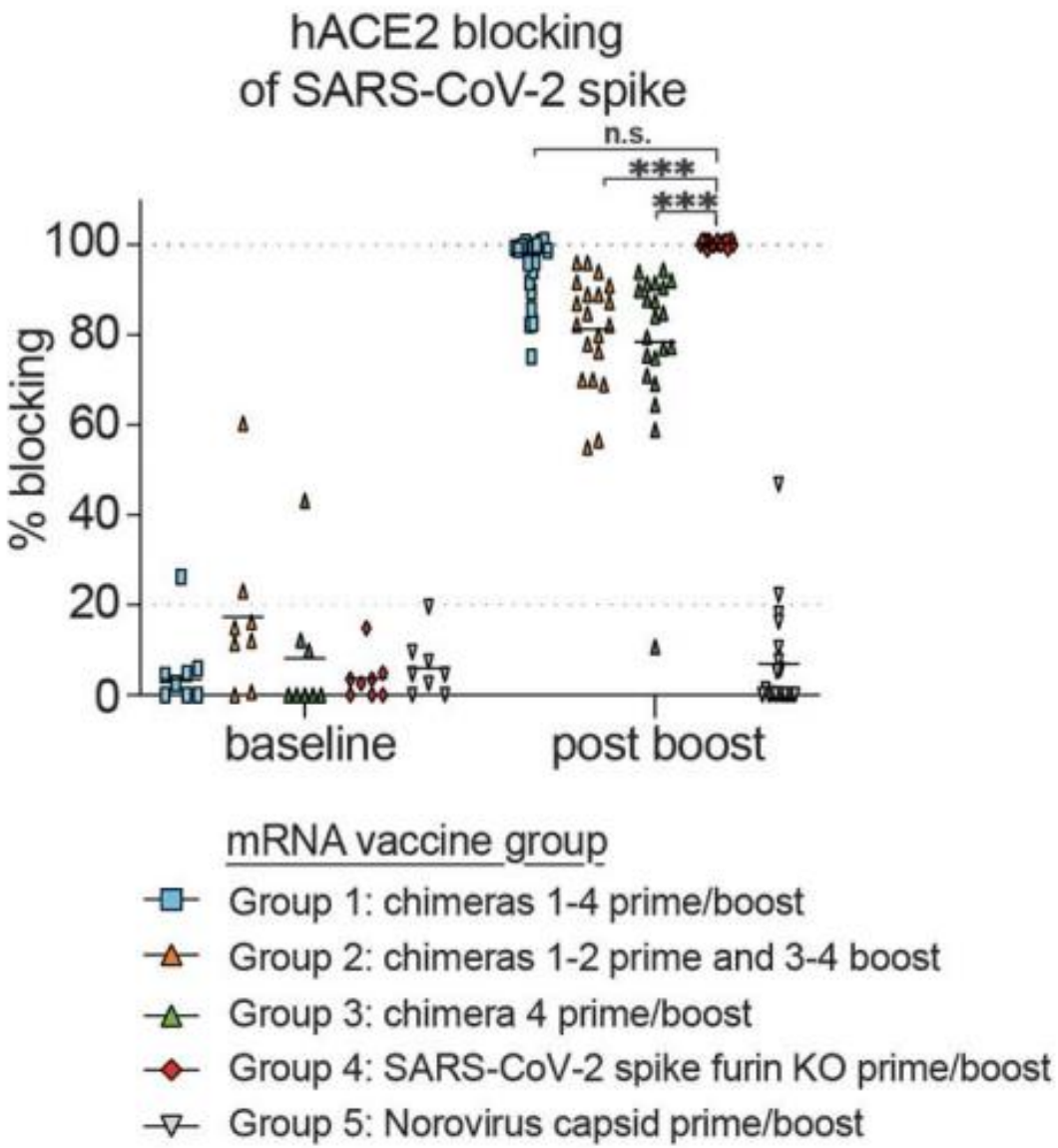
Salvamani, S., et al, *British Journal of Biomedical Medical Science* 2020, Vol 77

Genetic design of chimeric Sarbecovirus spike vaccines

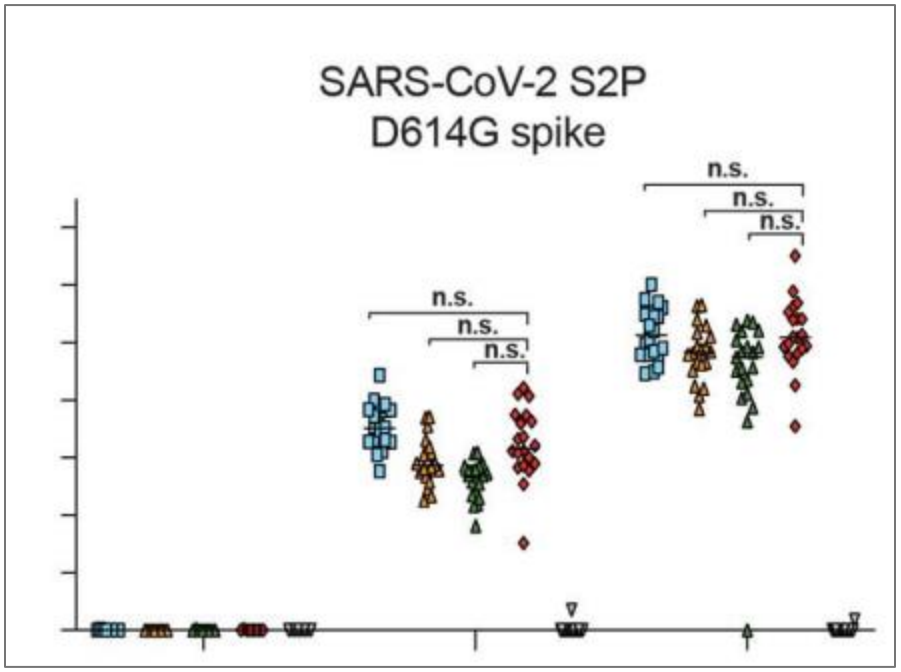
Chimeric spike mRNA-LNP immunogens

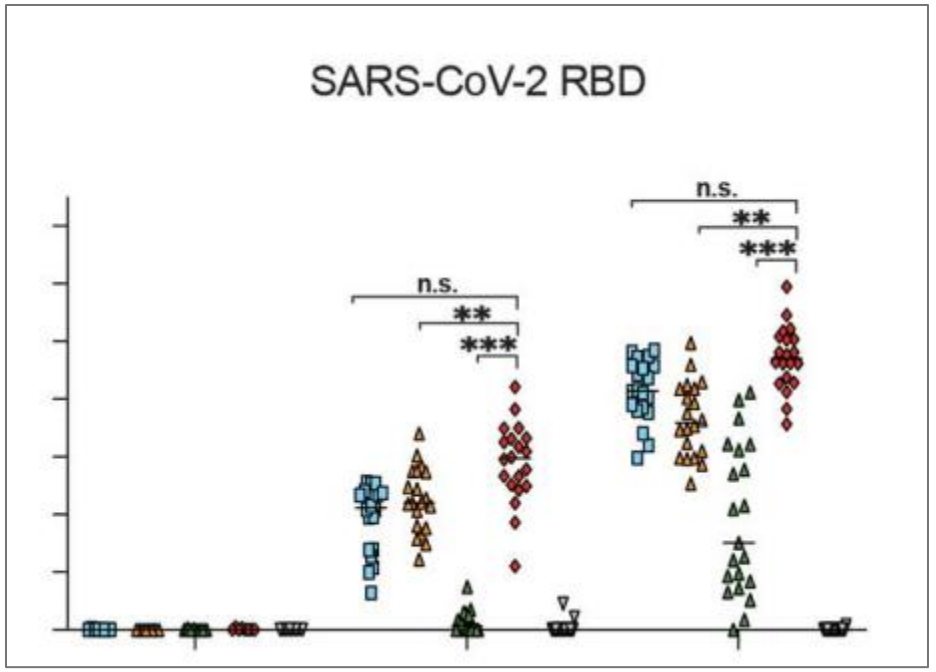
Chimera	RBD	NTD	S2
1	SARS-CoV	HKU3-1	SARS-CoV-2
2	SARS-CoV-2	SARS-CoV	SARS-CoV
3	SARS-CoV	SARS-CoV-2	SARS-CoV-2
4	RsSHC014	SARS-CoV-2	SARS-CoV-2

Martinez, DR, et al, *Science* 373 2021

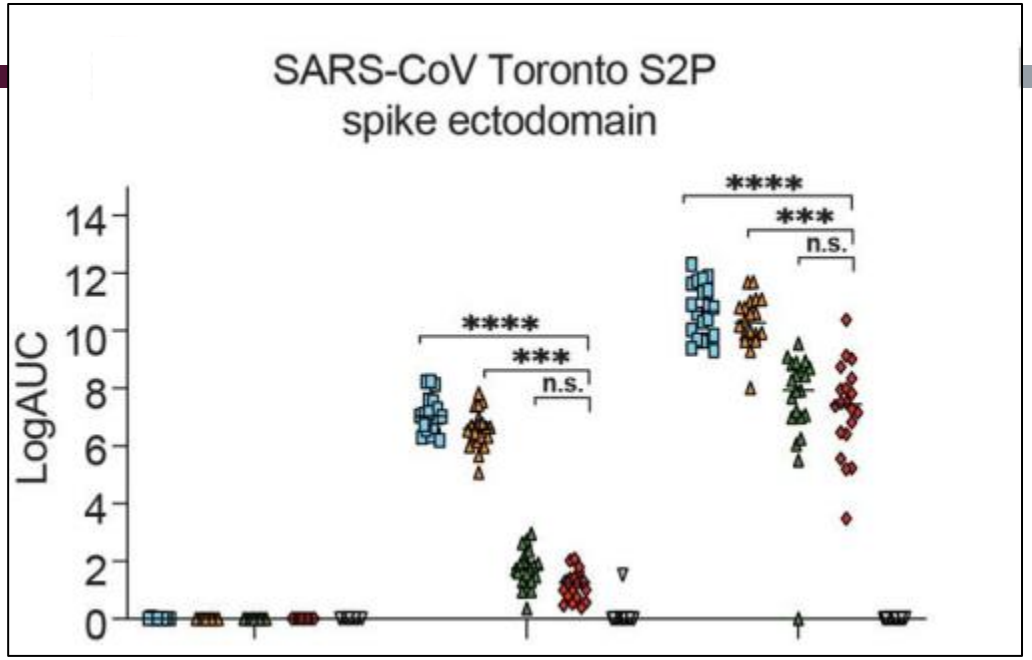


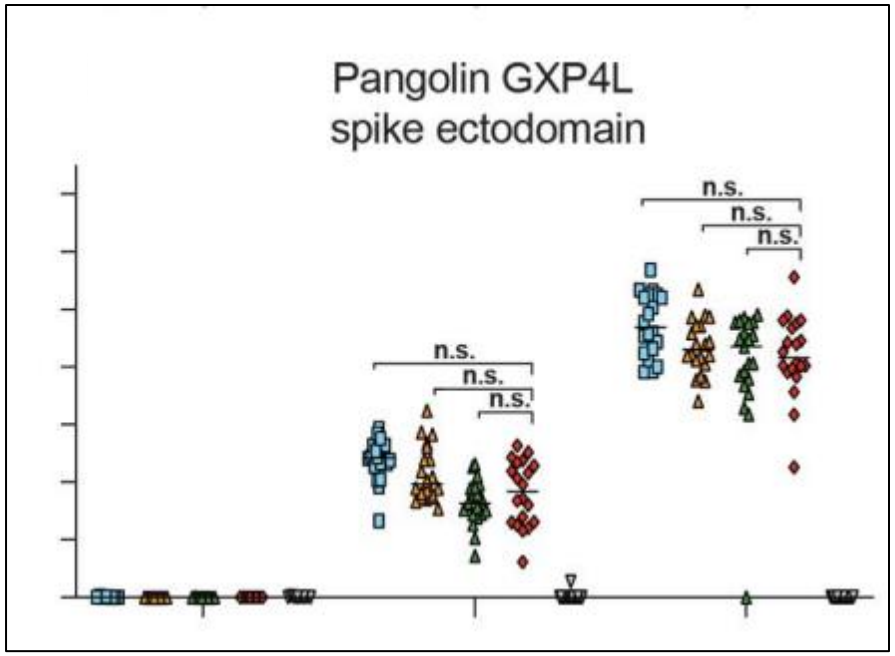
Martinez *et al.*, *Science* 373, 991-998 2021

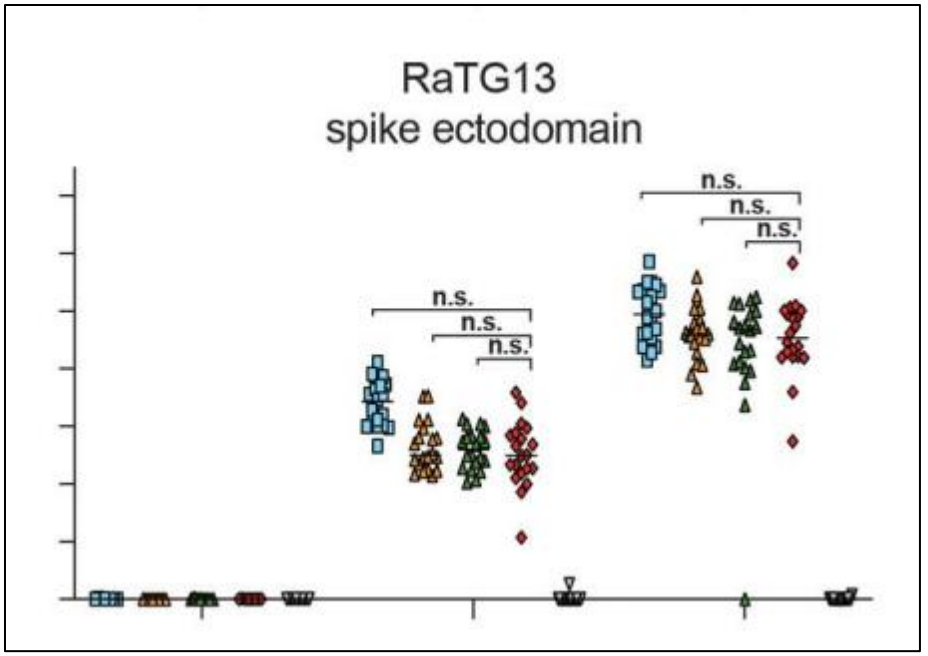




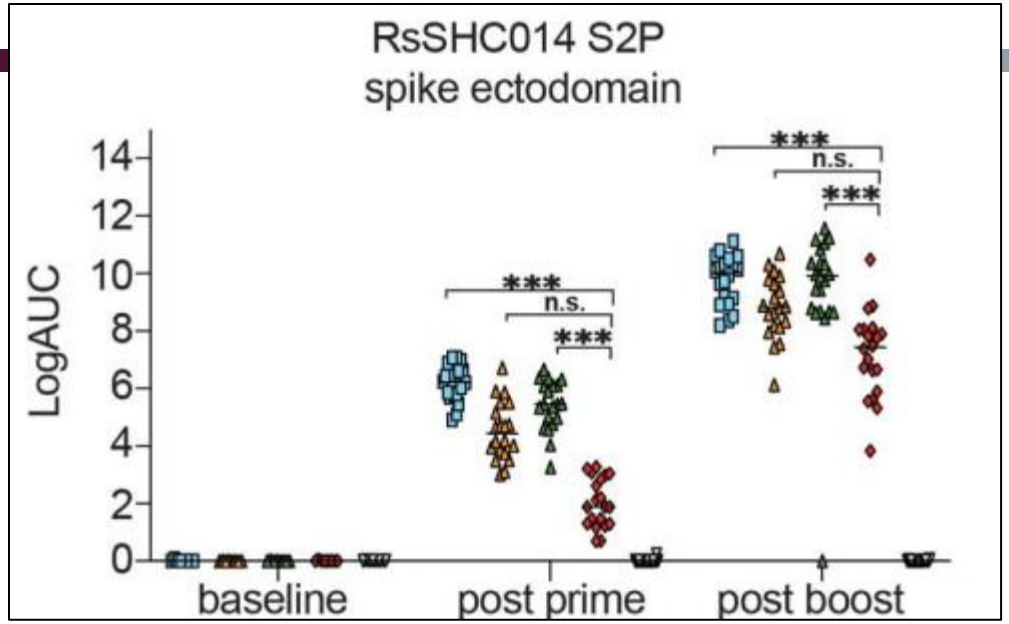
Martinez *et al.*, *Science* 373, 991-998 2021







Martinez *et al.*, *Science* 373, 991-998 2021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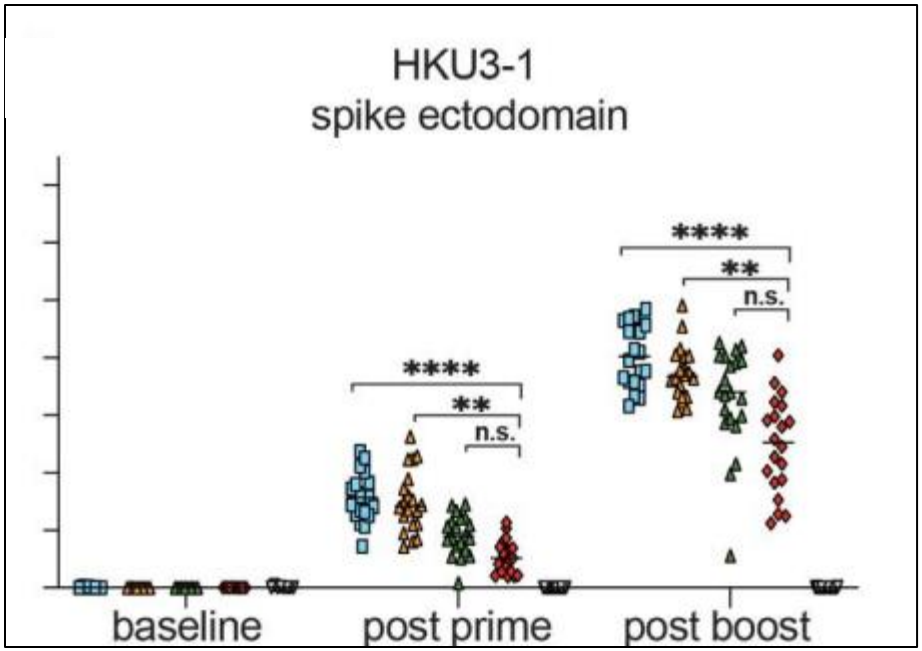
post boost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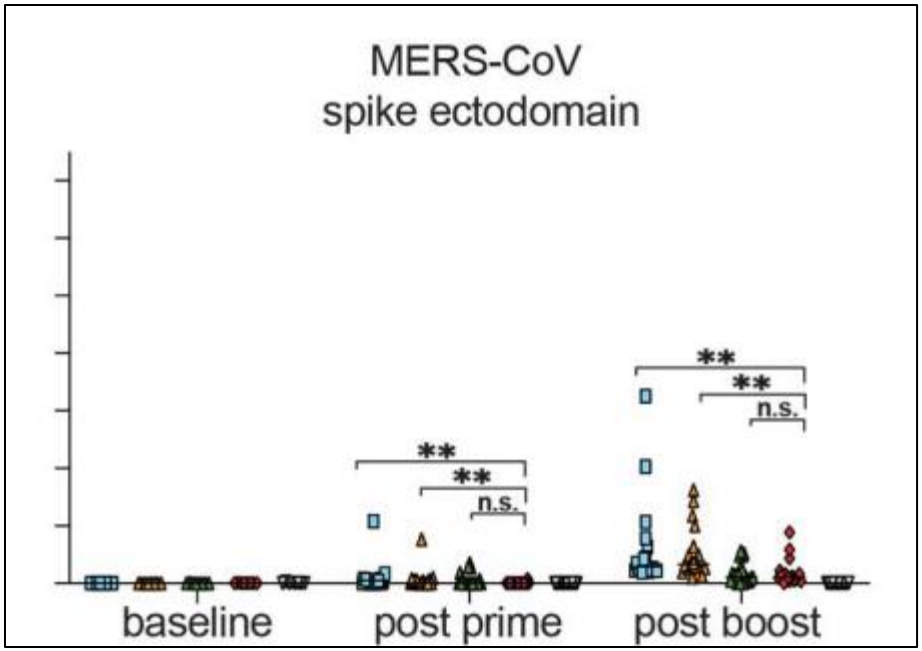
post prime
post boost


MERS-CoV
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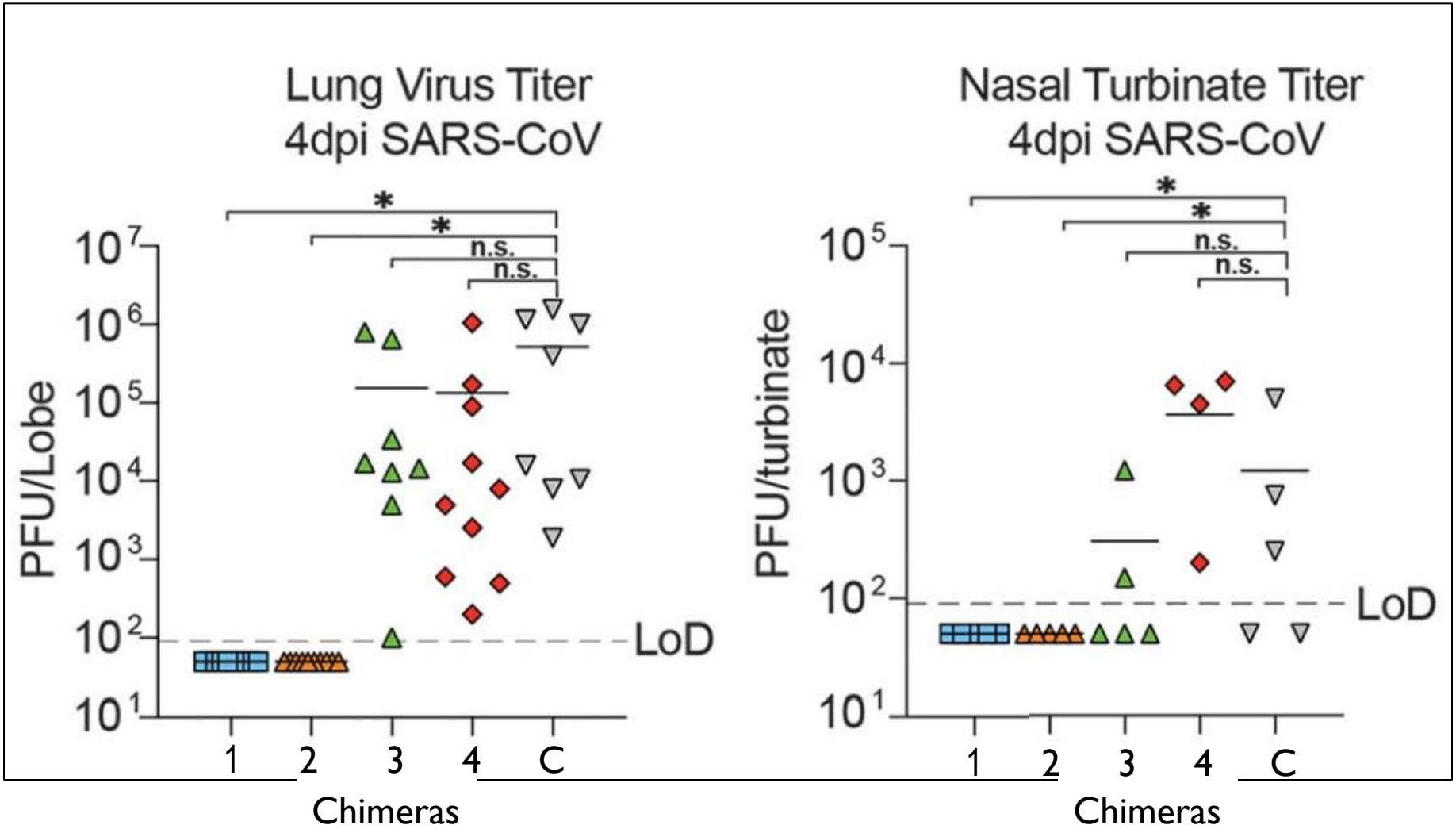
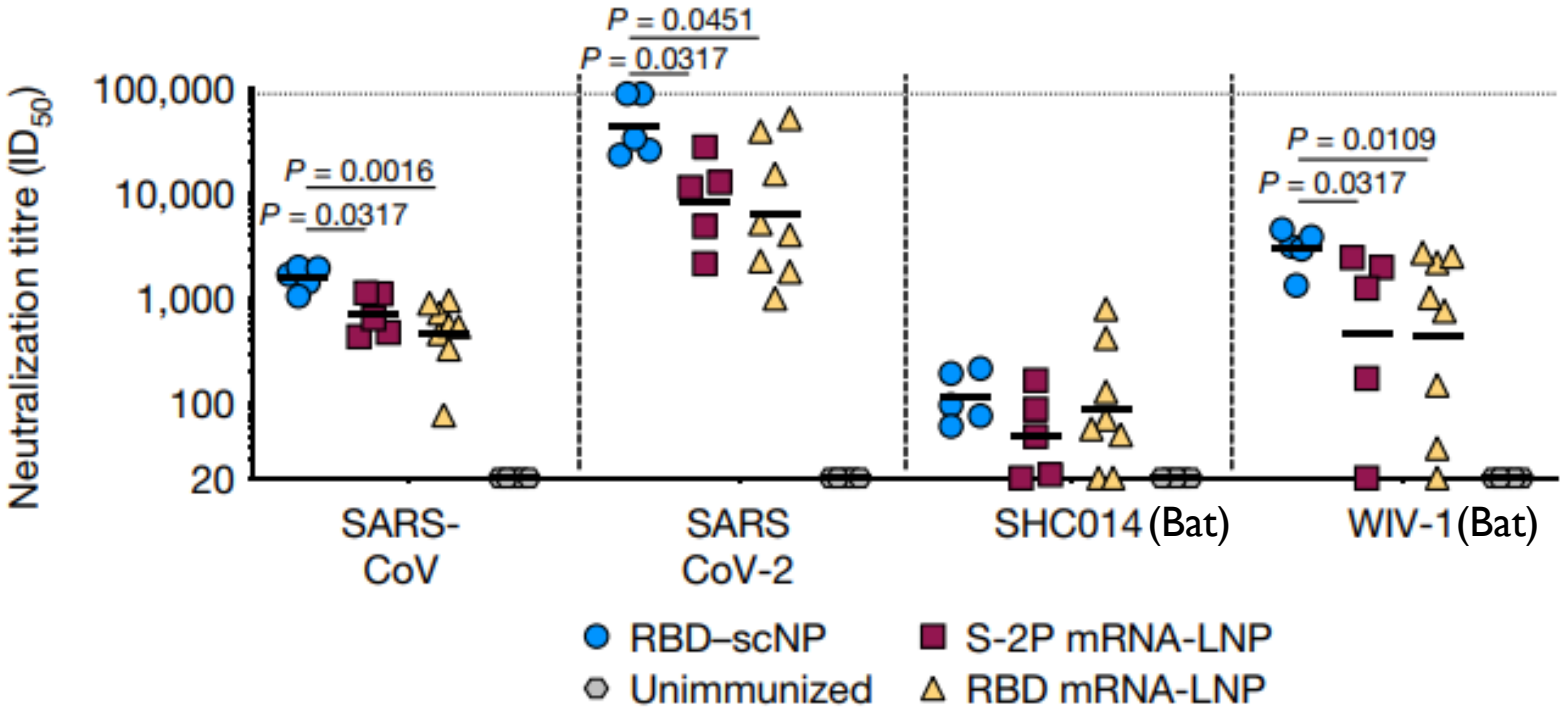
In vivo protection against Sarbecovirus challenge after mRNA-LNP vaccination



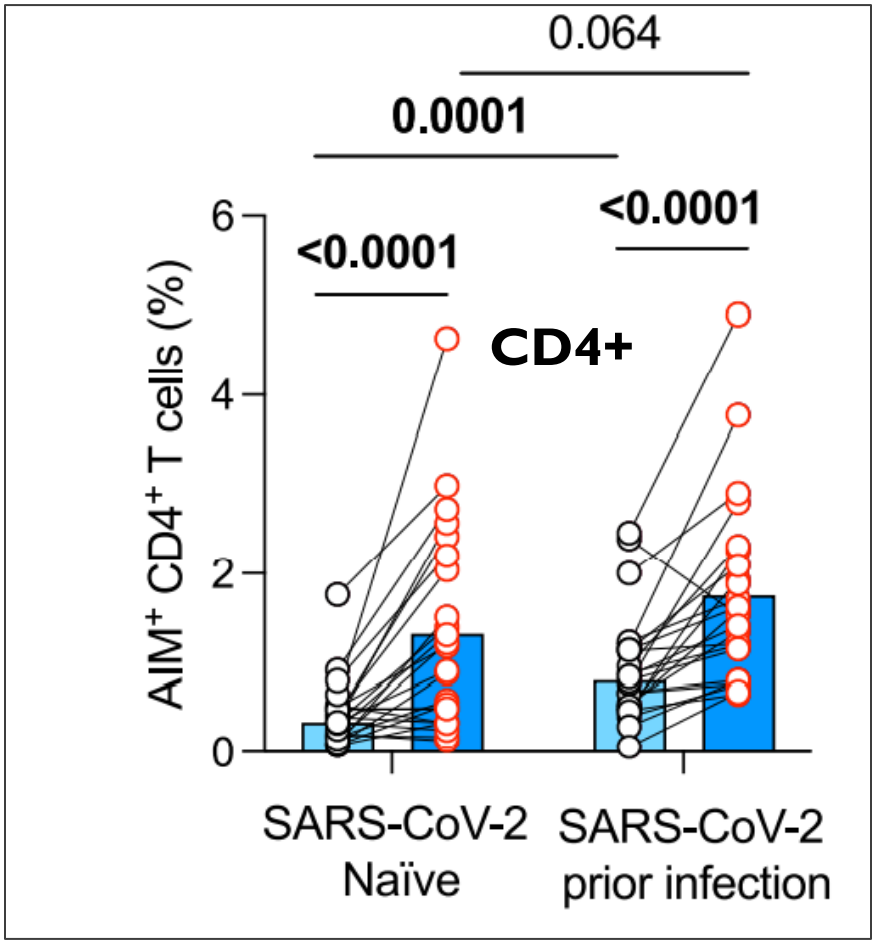
Martinez, DR, et al, *Science* 373 2021

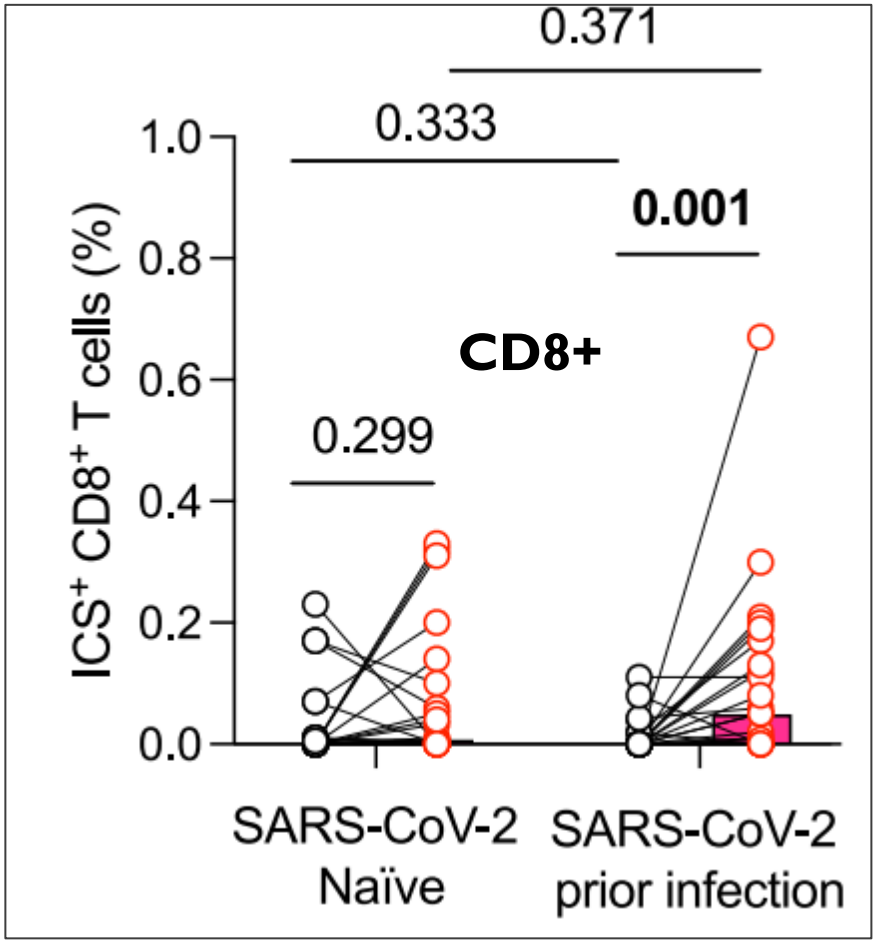
Serum cross-neutralization of infections with SARS-related betacoronaviruses induced by RBD–sortase-A nanoparticle in monkeys



Saunders, K., et al, *Nature* 594 2021

Spike-specific CD4+ and CD8+ T cell vaccine responses quantitatively and qualitatively differ in SARS-CoV-2 naive versus previously infected individuals





Tauzin, A., et al, Cell Host & Microbe 29, 2021