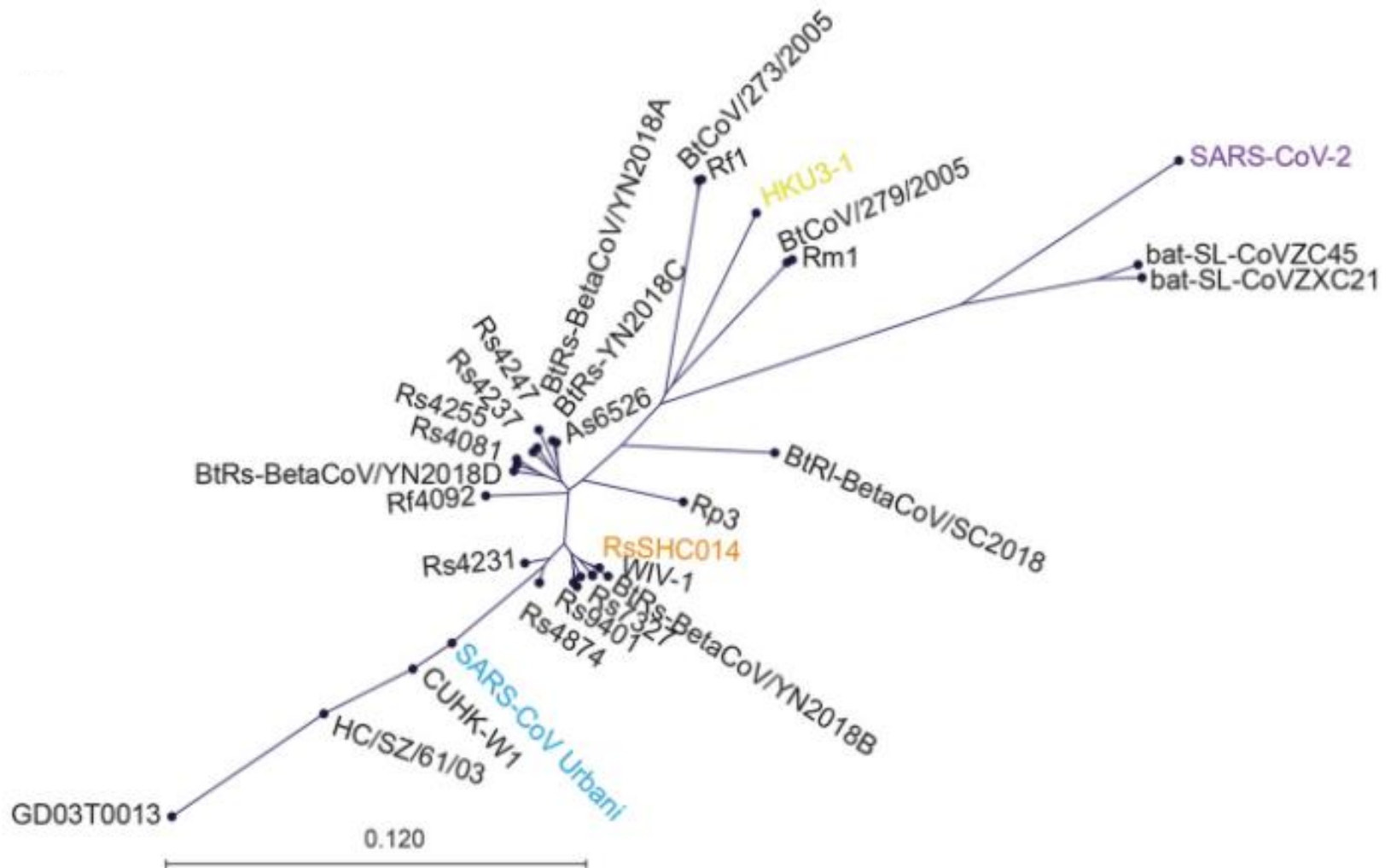


We Need a **PANSARBECOVIRUS** Vaccine

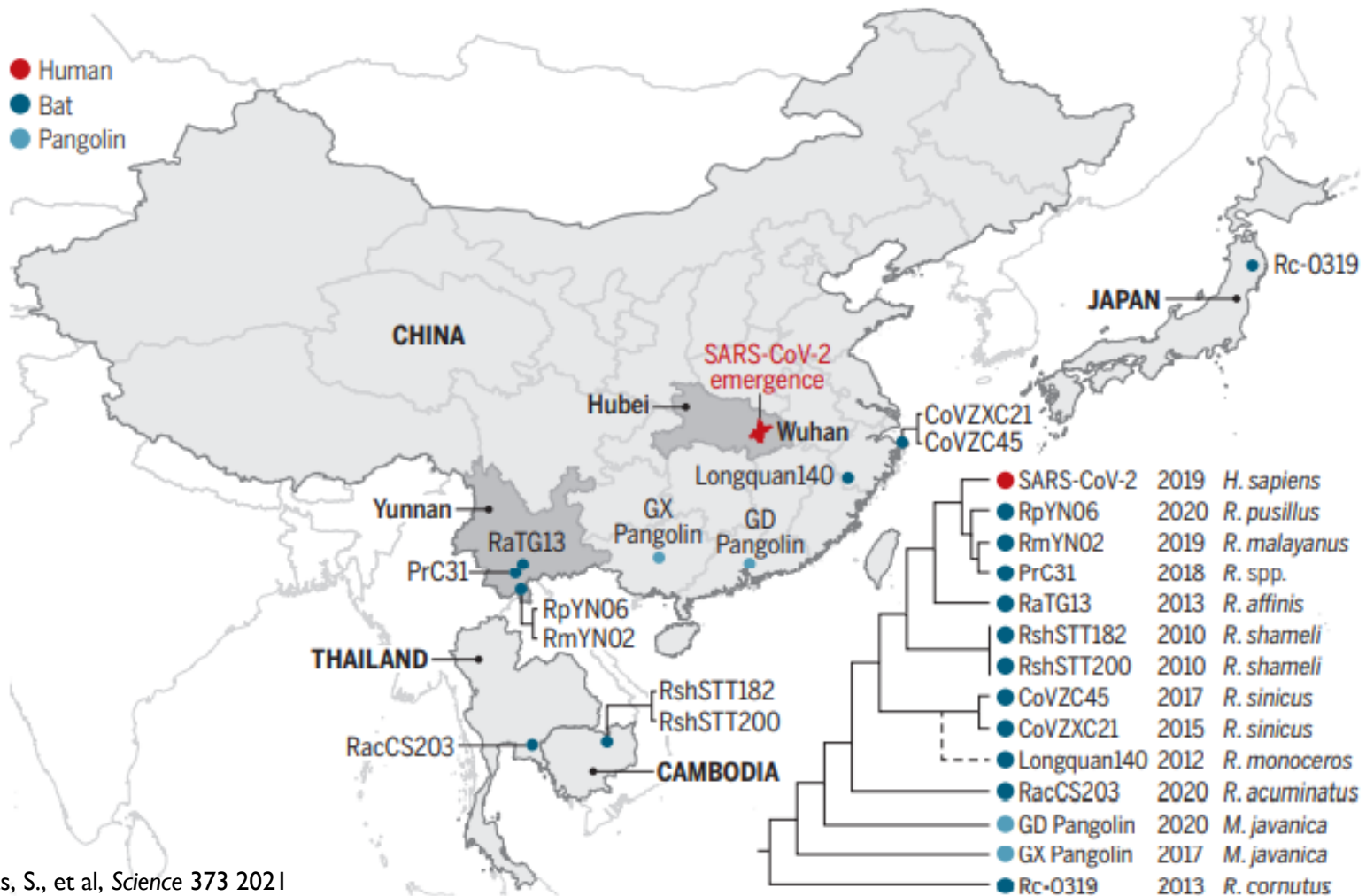
by Stanley A. Plotkin
University of Pennsylvania

Sarbecoviruses



Sarbecoviruses closely related to SARS-CoV-2

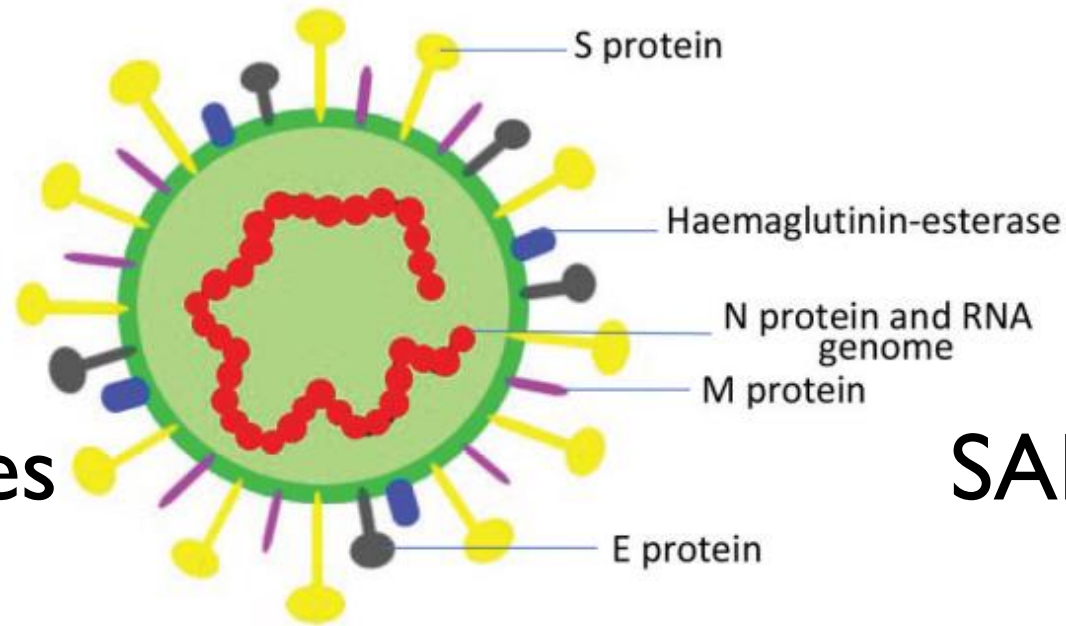
Coronaviruses that are evolutionarily closest to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been sampled in China, Cambodia, Japan, and Thailand (5). The phylogenetic tree, inferred from a genomic region minimized for recombination (5), shows sarbecoviruses closely related to SARS-CoV-2. 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.



Temmam, S., Eloit, M., *Nature*; In Press

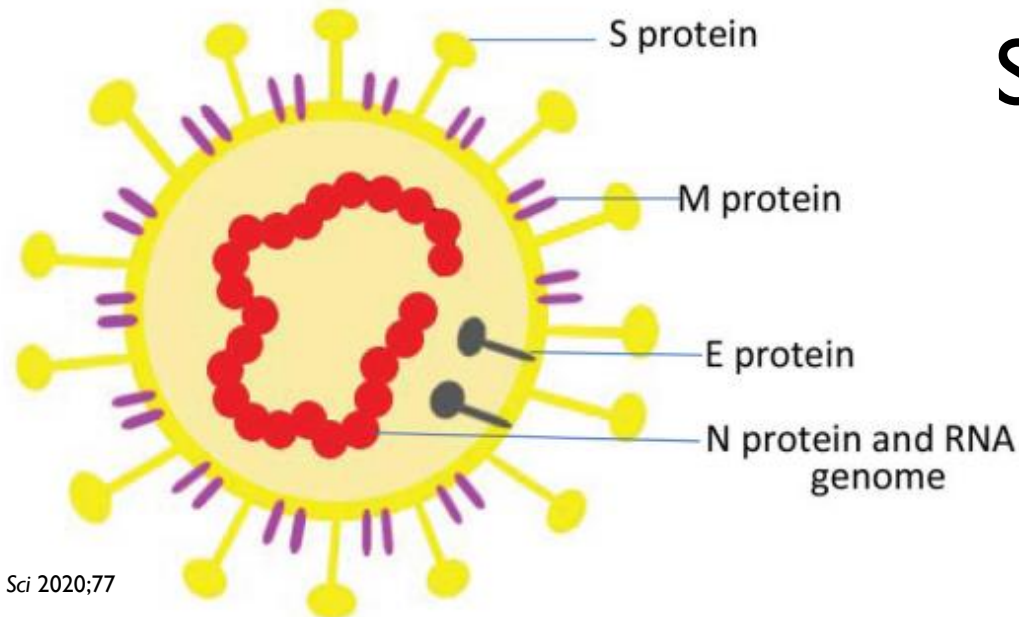
SARS-CoV-2 progenitor bat viruses genetically close to SARS-CoV-2 and able to enter human cells through a human ACE2 pathway have not yet been identified. Here we show that such viruses indeed circulate in cave bats living in the limestone karstic terrain in North Laos, within the Indochinese peninsula. We found that the RBDs of these viruses differ from that of SARS-CoV-2 by only one or two residues at the interface with ACE2, bind more efficiently to the hACE2 protein than the SARS-CoV-2 Wuhan strain.

Structures of Coronaviruses



(A)

SARS-2



SARS-1

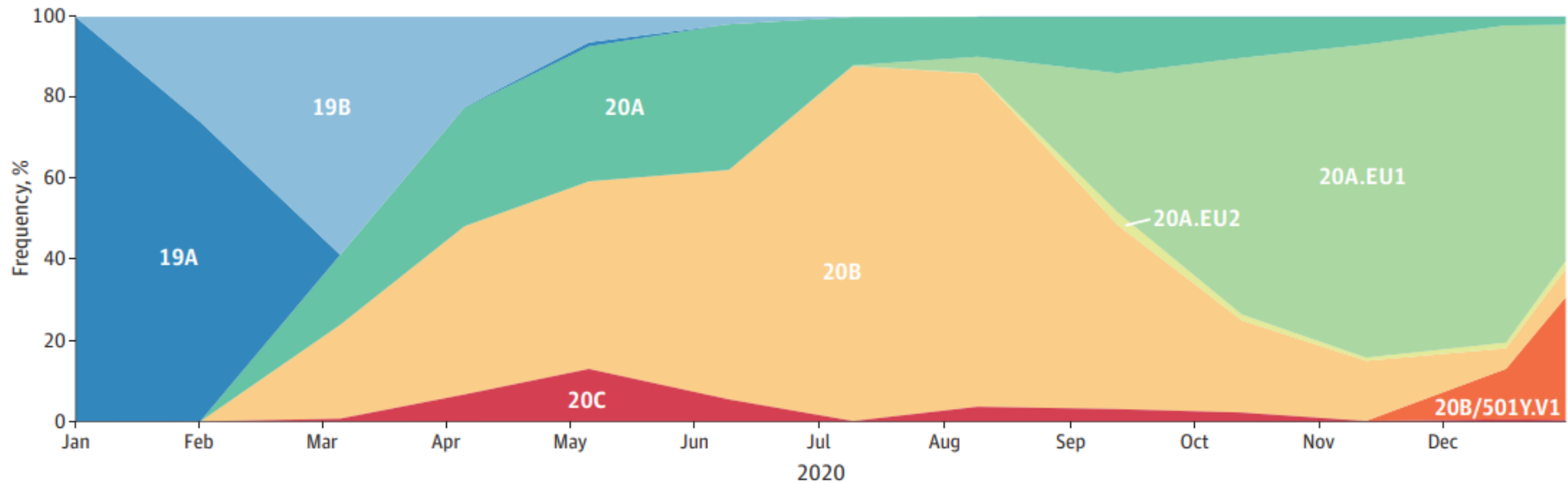
Classification of circulating genetic variants of SARS-CoV-2

| Lineage | Label | First detected in | Earliest samples |
|------------------|---------|-------------------|------------------|
| B.1.1.7 | Alpha | United Kingdom | September 2020 |
| B.1.1.7 + E484K | Alpha | United Kingdom | February 2021 |
| B.1.351 | Beta | South Africa | May 2020 |
| B.1.1.28.1 (P.1) | Gamma | Brazil | November 2020 |
| B.1.1.28.2 (P.2) | Zeta | Brazil | April 2020 |
| B.1.1.28.3 (P.3) | Theta | Philippines | January 2021 |
| B.1.617.1 | Kappa | India | October 2020 |
| B.1.617.2 | Delta | India | October 2020 |
| B.1.617.3 | | India | October 2020 |
| B.1.427/B.1.429 | Epsilon | USA | March 2020 |
| B.1.525 | Eta | Nigeria | December 2020 |
| B.1.526 | Iota | USA | November 2020 |
| B.1.620 | | Lithuania | February 2021 |
| B.1.621 | | Colombia | January 2021 |
| B.1.1.318 | | United Kingdom | February 2021 |
| A.23.1 + E484K | | United Kingdom | February 2021 |
| AV.1 | | United Kingdom | May 2021 |
| C.36.3 | | Thailand/Egypt | May 2021 |
| C.37 | Lambda | Peru | December 2020 |

Currently designated variants of concern (VOCs)

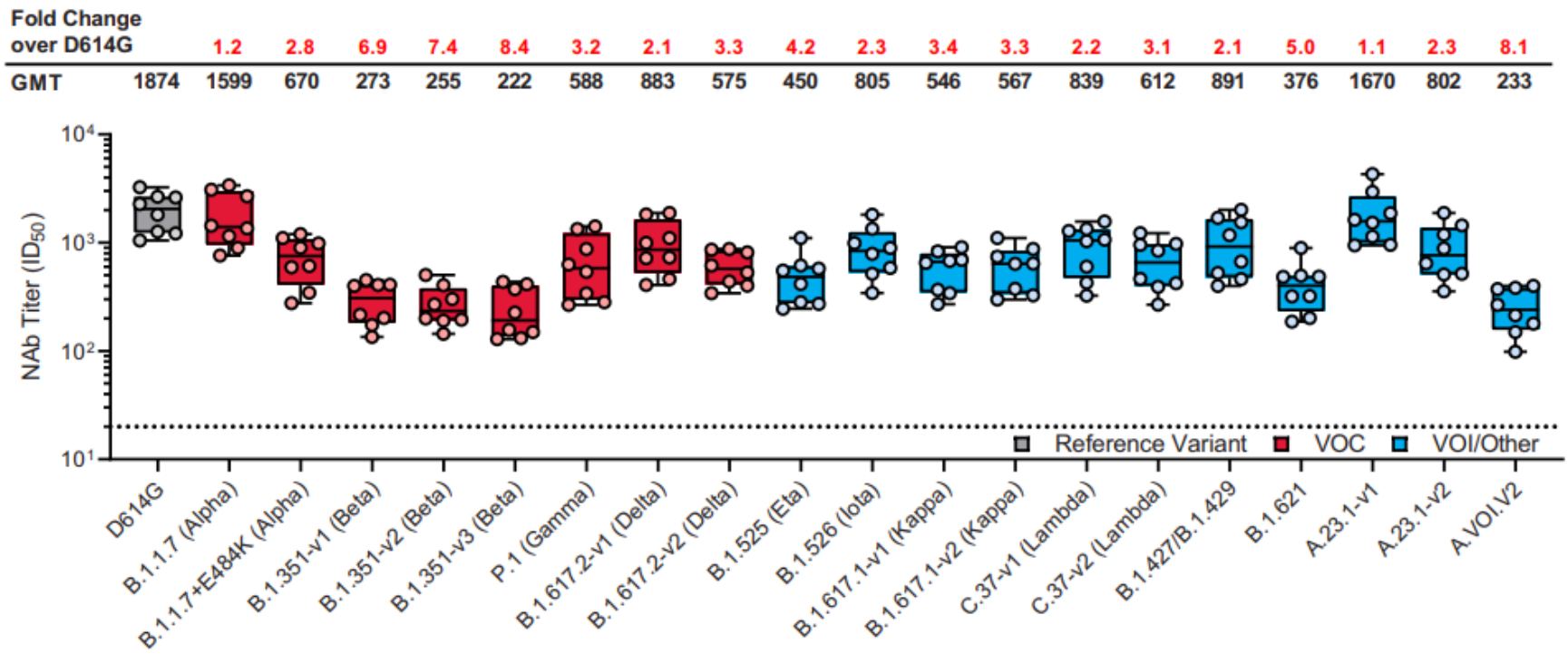
| WHO Label | Pango Lineage | Earliest Documented Samples |
|---|----------------------|------------------------------------|
| Alpha | B.1.1.7 | United Kingdom Sept. 2020 |
| Beta | B.1.351 | South Africa May 2020 |
| Gamma | P.1 | Brazil Nov. 2020 |
| Delta | B.1.617.2 | India Oct. 2020 |
| Omicron | B.1.1.529 | Multiple Countries Nov. 2021 |
| https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ | | |

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

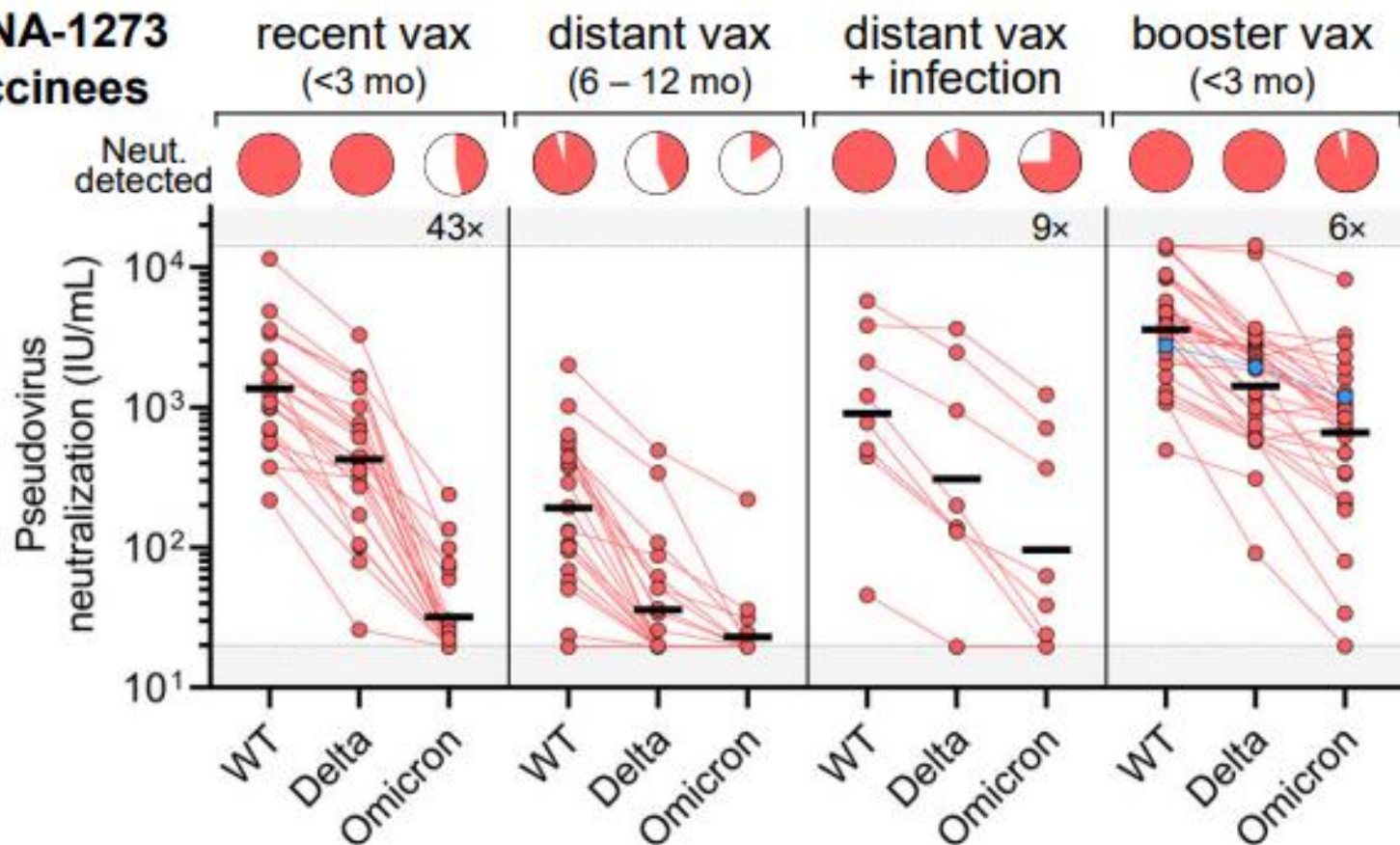


Lauring, A., Hodcroft, E., JAMA 2021;325:6

Neutralization of SARS-CoV-2 pseudoviruses in serum samples.



mRNA-1273 vaccinees



T cell responses to spike only may be insufficient



Cell Reports

Isolation and characterization of cross-neutralizing coronavirus antibodies from COVID-19+ subjects

Authors

Madeleine F. Jennewein,
Anna J. MacCamy, Nicholas R. Akins, ...,
Mehul S. Suthar, Andrew T. McGuire,
Leonidas Stamatatos

Highlights

- Fourteen anti-SARS-CoV-2 neutralizing mAbs isolated from four patients
- Three anti-RBD and one anti-S2 mAb neutralized SARS-CoV-1 and the B.1.351 variant
- Mouse studies show potential protective effect of anti-NTD mAbs

Elicitation of broadly protective sarbecovirus immunity by receptor-binding domain nanoparticle vaccines

In brief

Multivalent sarbecovirus RBD-Nanoparticle vaccines elicit heterotypic protection against sarbecoviruses.

Walls et al., 2021, Cell 184, 5432–5447
October 14, 2021 © 2021 Elsevier Inc.
<https://doi.org/10.1016/j.cell.2021.09.015>

Article

Neutralizing antibody vaccine for pandemic and pre-emergent coronaviruses

Kevin O. Saunders,.... Barton F. Haynes
Nature. 2021 June ; 594(7864): 553–559

“ ... macaque immunization with a multimeric SARS-CoV-2 receptor binding domain (RBD) nanoparticle adjuvanted with 3M-052/ Alum elicited cross-neutralizing antibody (cross-nAb) responses against batCoVs, SARS-CoV-1, SARS-CoV-2, and SARS-CoV-2 variants B.1.1.7, P.1, and B.1.351.”

We Need a Pan Sarbecovirus Vaccine Because:

Variants of SARS-2 beta coronavirus may continue to escape neutralizing antibodies induced by vaccines against prior variants

The reservoir of beta coronaviruses in bats is large and new crossovers to humans is likely

If we prepare now, the time required for large scale vaccine manufacture will be reduced and lives will be saved