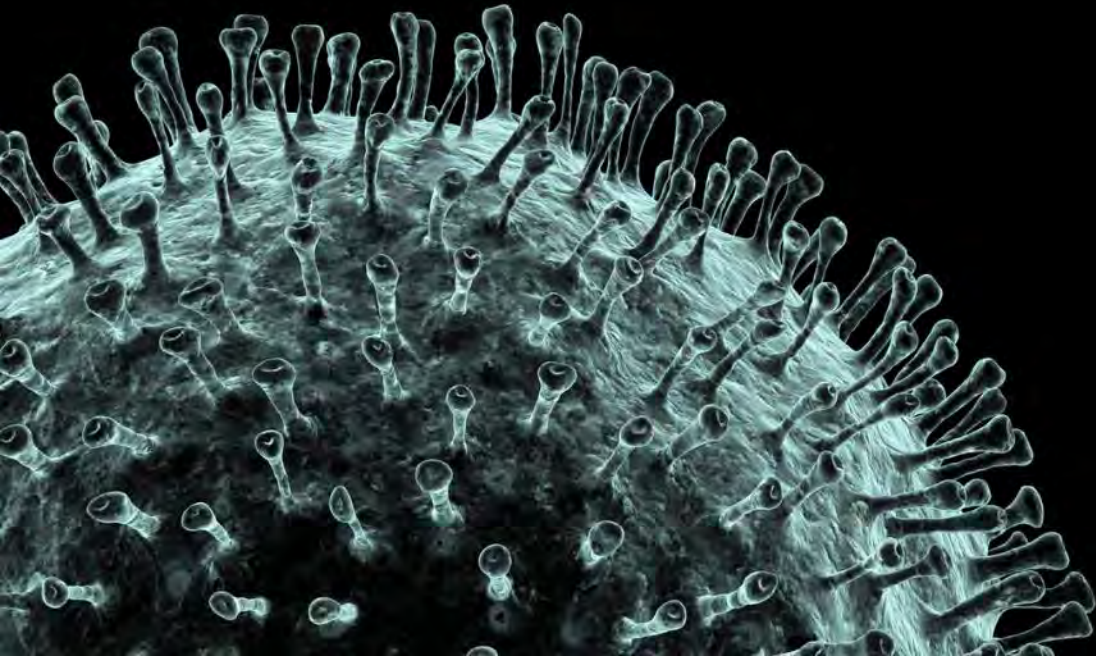


COVID-19 Conversations



Angela Rasmussen

**VIDO-InterVac, University of Saskatchewan
Center for Global Health Science and Security,
Georgetown University**



COVID19Conversations.org

[#COVID19Conversations](https://twitter.com/COVID19Conversations)



Viruses, Variants, and Vaccines: Making Sense of Mutation



Angela L. Rasmussen, Ph.D.

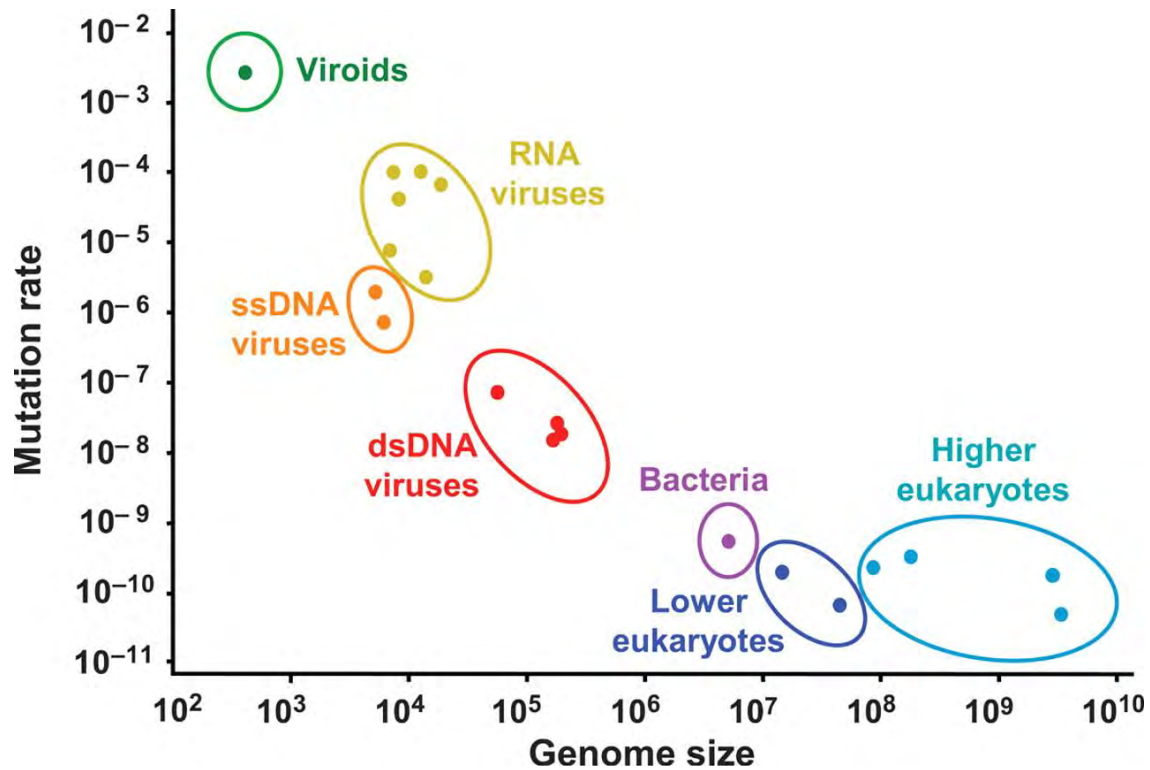
Georgetown Center for Global Health Science and Security
(soon: VIDO-InterVac, University of Saskatchewan)

Territorial Acknowledgement and Equity Statement

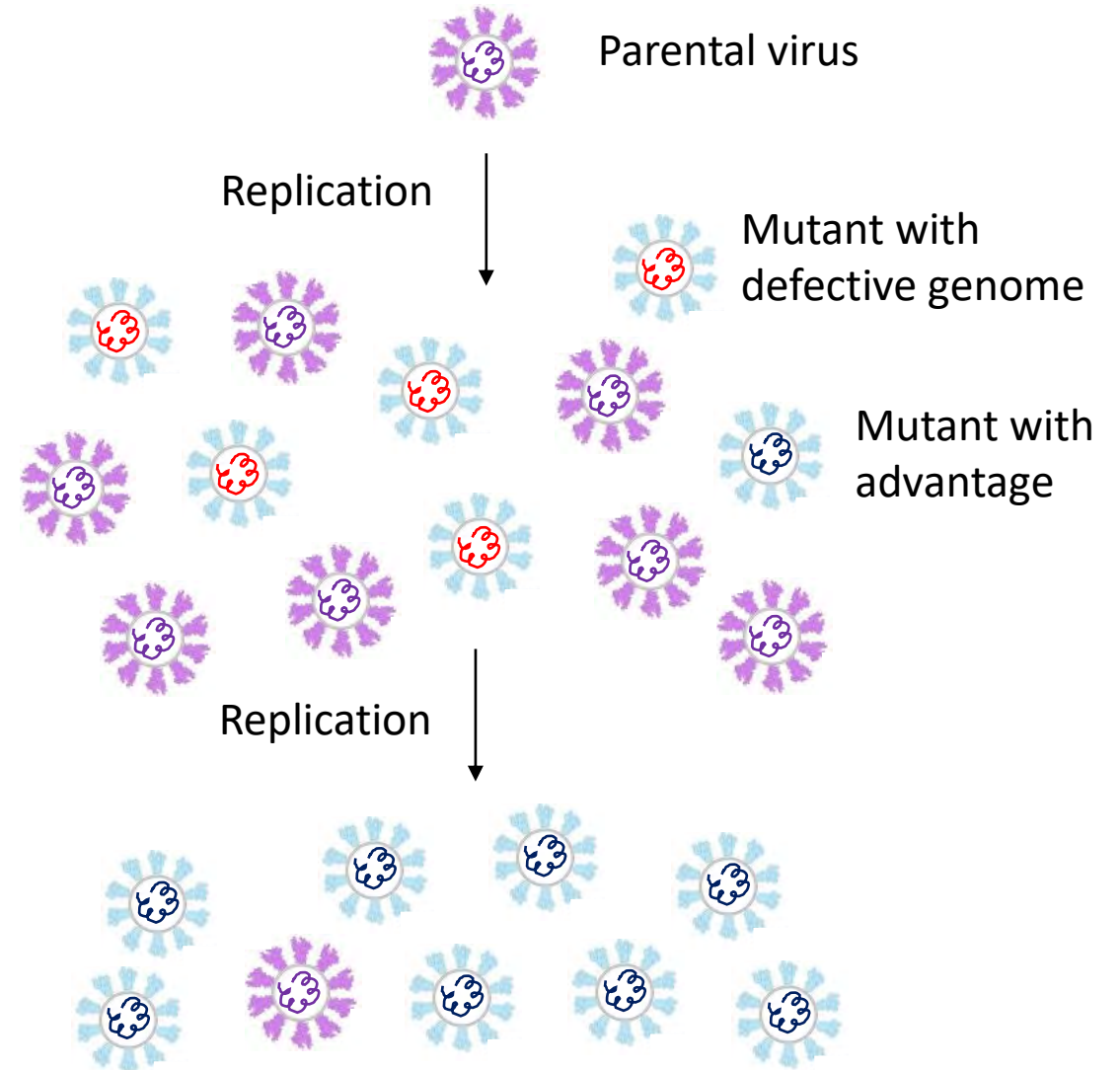
I am presenting today from the unceded ancestral homelands of the Duwamish people. I acknowledge and honor the First people of these territories and their Tribal governments, their histories and ancestry, and their roles today in caring for these lands.

I also would like to acknowledge that there is a history of systemic inequity in academic science that spans centuries. My prior institution, Columbia University, and my current institution, Georgetown University, were founded using profits from the trans-Atlantic slave trade and the sale of enslaved people. In addition, they excluded women and people of color from the academic community for more than 200 years, leaving a long and painful legacy of racial and gender-based inequality that continues to this day. I encourage all to consider how they can contribute to making public health research a more equitable enterprise.

Mutation and virus evolution



Gago et al, Science, 2009

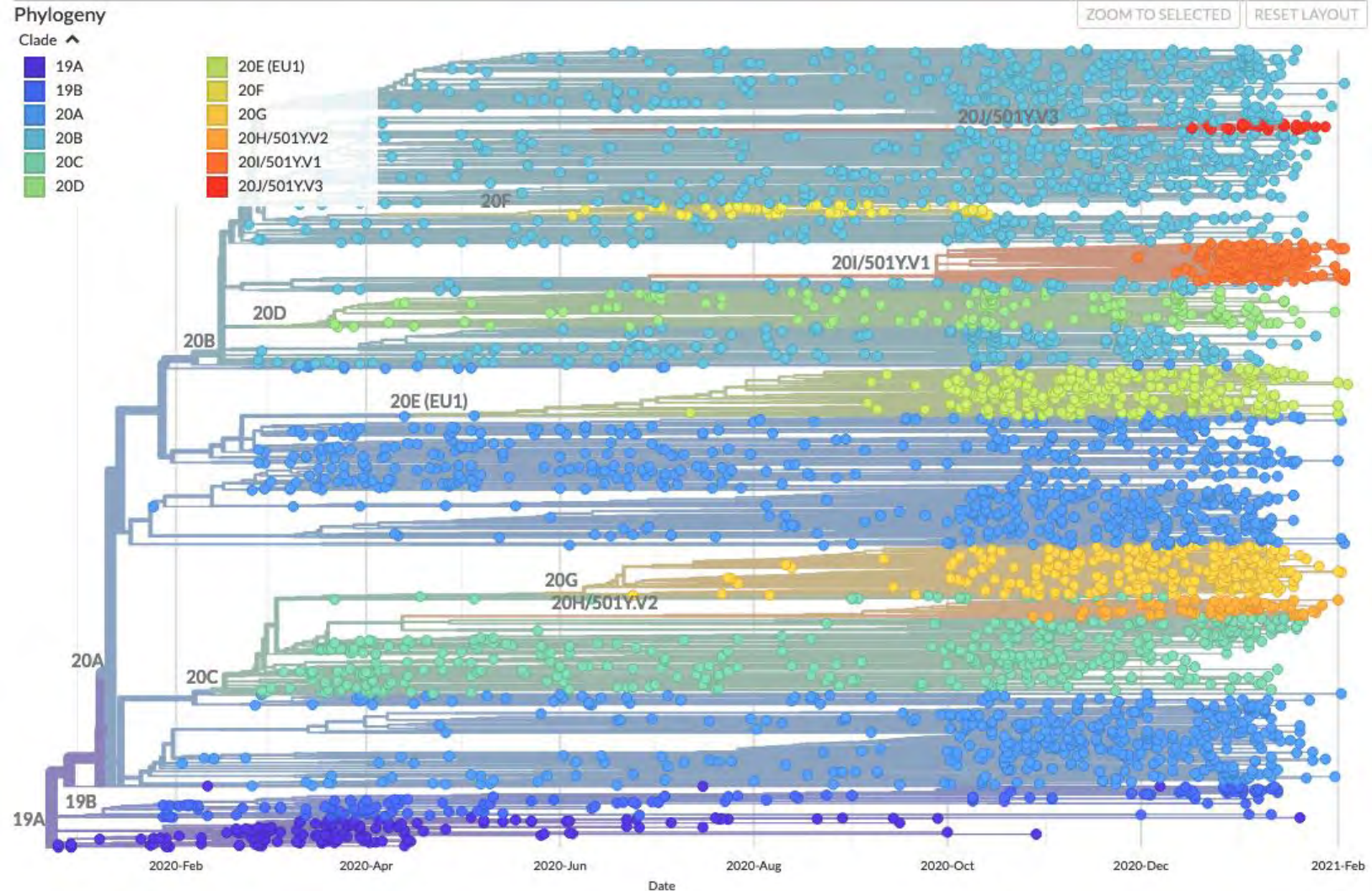


There are many variants

Genomic epidemiology of novel coronavirus - Global subsampling

Maintained by the [Nextstrain team](#). Enabled by data from [GISAID](#)

Showing 4014 of 4014 genomes sampled between Dec 2019 and Feb 2021.

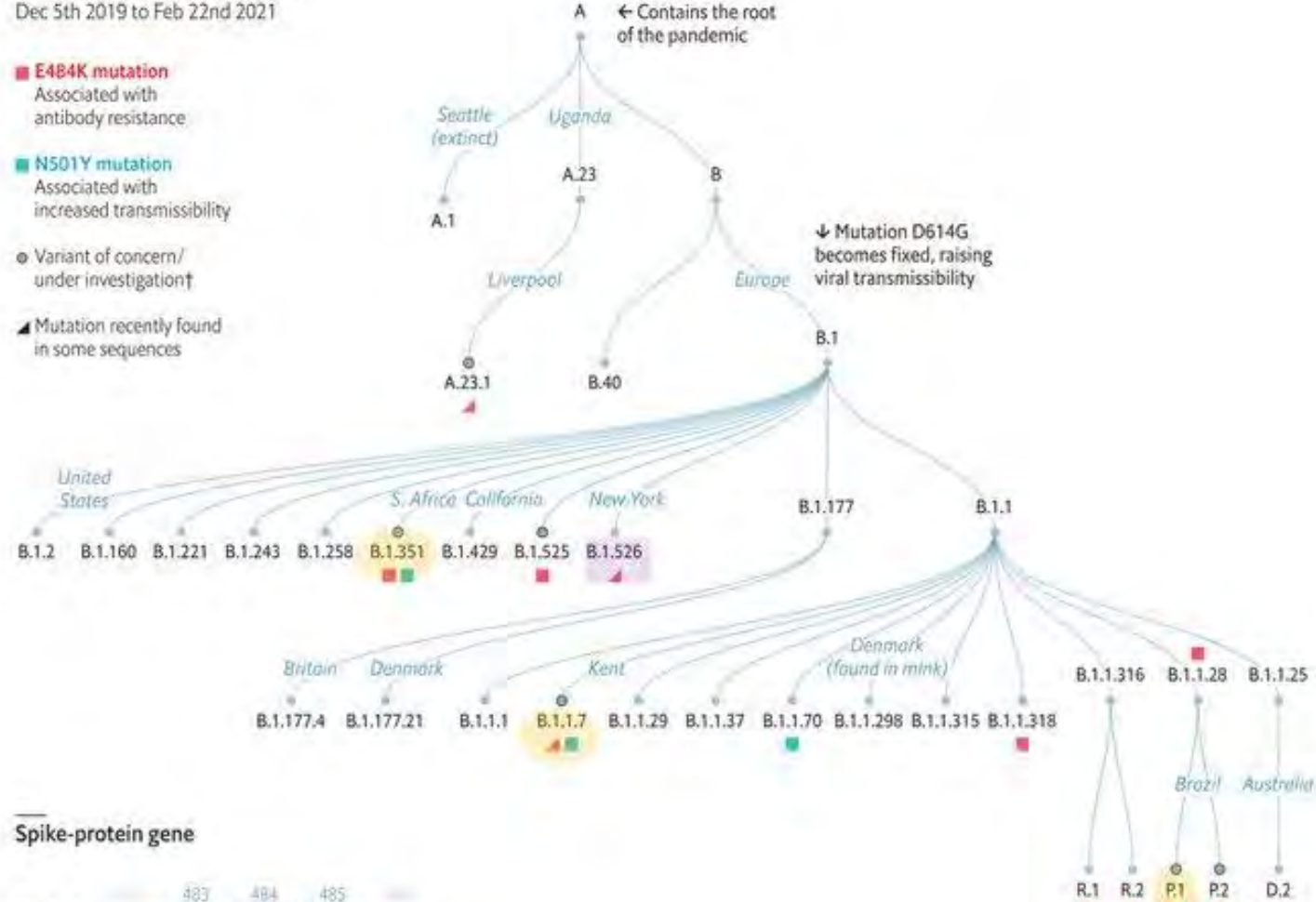


Evolution in action

Selected SARS-CoV-2 lineages*

Dec 5th 2019 to Feb 22nd 2021

- **E484K mutation**
Associated with antibody resistance
- **N501Y mutation**
Associated with increased transmissibility
- Variant of concern/under investigation†
- ▲ Mutation recently found in some sequences



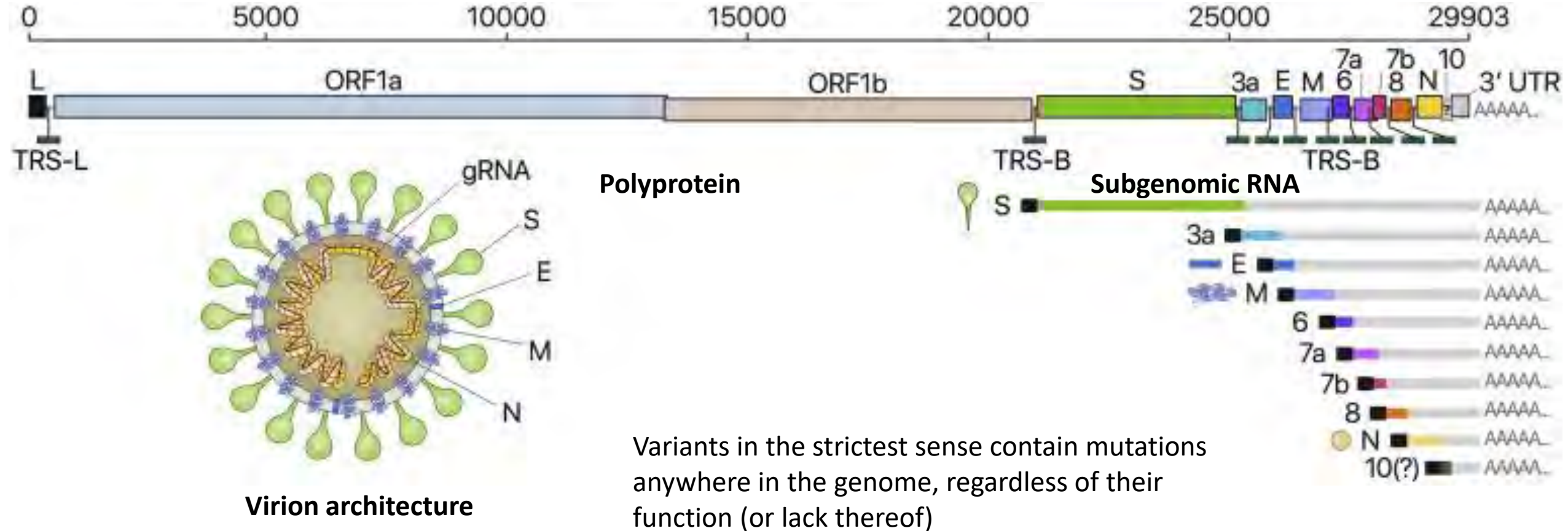
Spike-protein gene

Original
 483 484 485
 U G U U G A A G G U U U
 Code for glutamic acid (E)

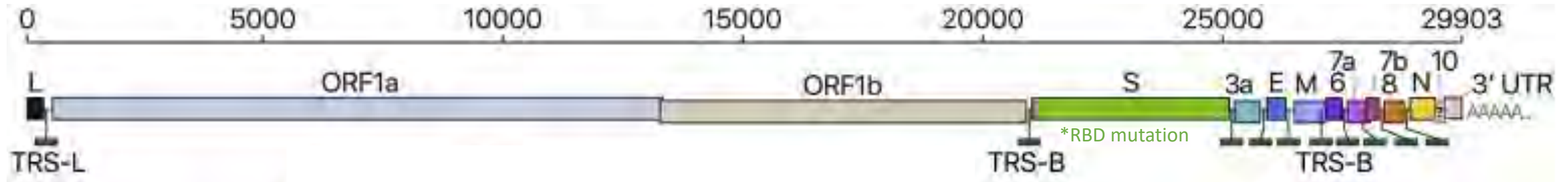
E484K
 U G U U A A A G G U U U
 Code for lysine (K)

*36 of 880 lineages containing 68% of all 560,000 samples deposited by Public Health England

SARS-CoV-2 genome organization



The (for now best studied) variants of concern



B.1.1.7 (501Y.V1)

T1001I (nsp3/PL2pro)
 A1708D (nsp3/PL2pro)
 I2230T (nsp3/PL2pro)
 3675-3677del (nsp6)

P4715L (nsp12/RdRp)

69/70del
 144del
N501Y*
 A570D
D614G

P681H
 T716I
 S982A
 D1118H

Q27Stop
 R52I
 Y73C

D3E
R203K
G204R
 S235F

B.1.351 (501Y.V2)

T265I (nsp2)
H417N (nsp2)
 K1655N (nsp3/PL2pro)
 K3353R (nsp5/3CLpro)

P4715L (nsp12/RdRp)

D80A
 241del
K417N*
E484K*
N501Y*

D614G
 A701V

Q57H P71L

P80A
 T205I

P.1 (501Y.V3)

H417T (nsp2)
 S1188S (nsp3/PL2pro)
 K1795Q (nsp3/PL2pro)
 3675-3677del (nsp6)

P4715L (nsp12/RdRp)
 E5665D (nsp13/Helicase)

L18F
 T20N
 P26S
D80R
 D138Y
 R190S

K417N*
E484K*
N501Y*
D614G
 H655Y
 T1027I
 V1176F

S253P

E92K

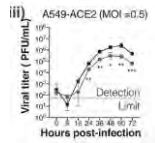
G18F
P80R
 S202C
R203K
G204R

Present in 2/3 variants

Present in 3/3 variants

Possible mechanisms of increased transmissibility

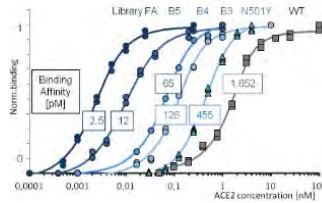
Increased fitness



Increased viral shedding

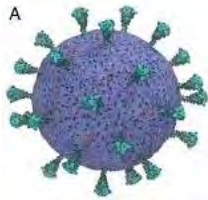
Longer interval of contagiousness

Receptor binding affinity



Increased infectivity

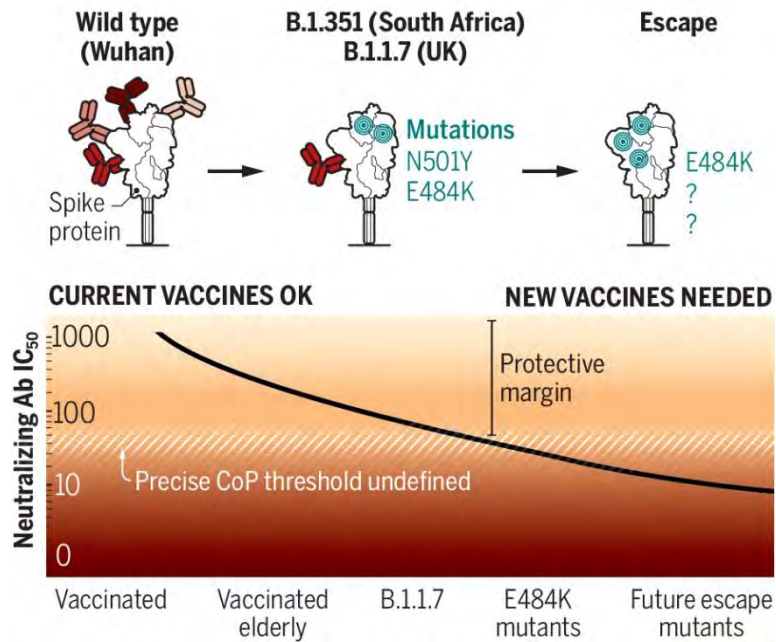
Increased virion stability



Increased environmental stability

Immune evasion

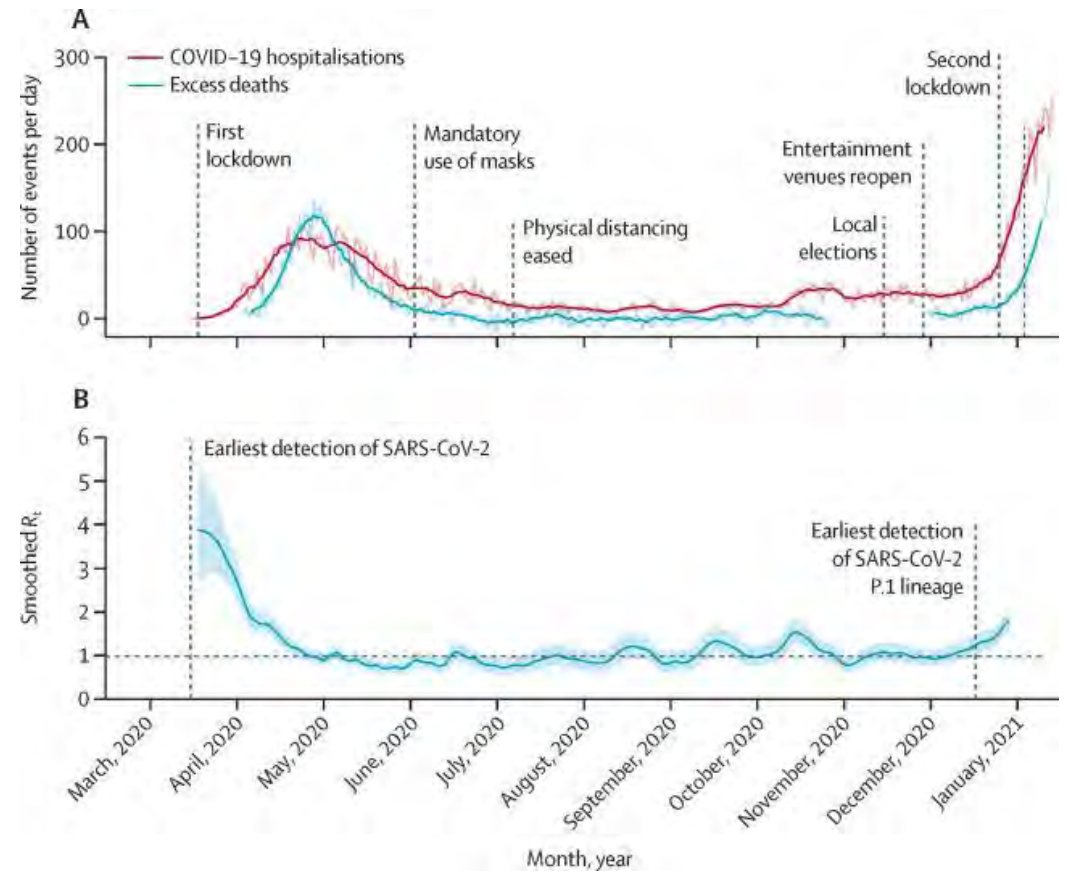
Impact of immune evasion on transmission



Altmann *et al*, *Science*, 2021

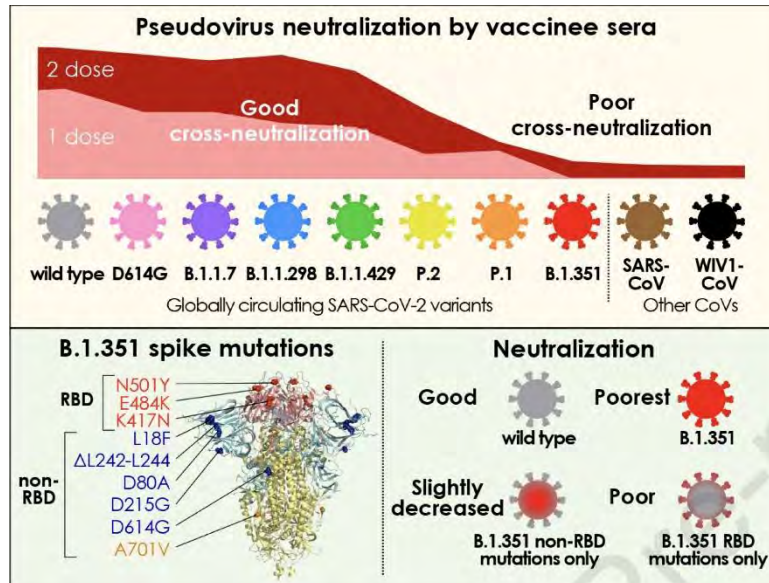
Protection against infection

Protection against disease



Sabino *et al*, *Lancet*, 2021

Antibody neutralization via RBD isn't everything



Garcia-Beltran *et al*, *Cell*, 2021

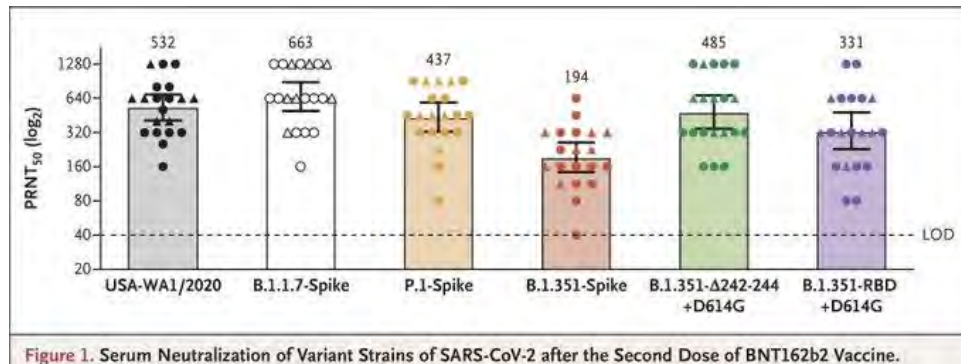
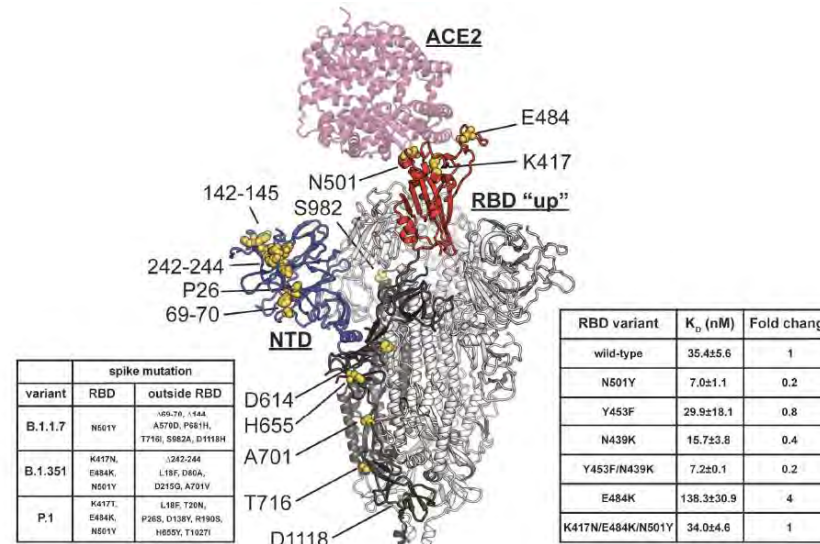
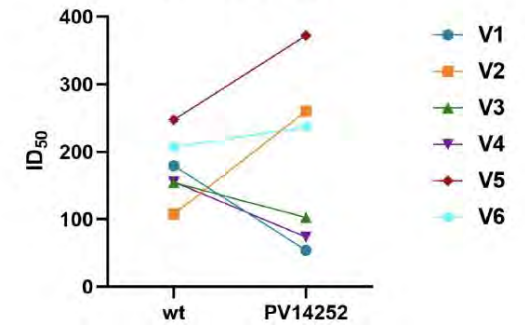


Figure 1. Serum Neutralization of Variant Strains of SARS-CoV-2 after the Second Dose of BNT162b2 Vaccine.

Liu *et al*, *New England Journal of Medicine*, 2021



Vaccinee serum wt versus PV14252 (W64R, L141Y, E484K, D614G, Δ 142-145) neutralization



Amanat *et al*, *medRxiv*, 2021

Some big remaining questions:

- How much does prior immunity (vaccines, convalescent) provide sterilizing protection?
- What impact does this have on viral shedding?
- What is the overall impact on transmission at population level?

Summary of variants

	B.1.1.7	B.1.351	P.1
Alternate name	501Y.V1	501Y.V2	501Y.V3
Country identified	United Kingdom	South Africa	Brazil
Mutations	23	21	17
Spike mutations	8	9	10
Key RBD, spike mutations beyond N501Y in all	E69/70 deletion, P681H 144Y deletion, A570D	E484K, K417N, orf1b deletion	E484K, K417T, orf1b deletion
Other mutations, including N-terminal	T716I, S982A, D1118H	L18F, D80A, D215G, Δ242-244, R264I, A701V	L18F, T20N, P26S, D138Y, R190S, H655Y, T1027I
Transmissibility Δ	>50% increased	No	Not established
Lethality Δ	Not resolved	?	?
Immune evasion	Unclear	Yes	Yes, less than B.1.351
Vaccine efficacy (preserved vs severe infections in all so far)	Modest reduction ~10% point decline in 2 trials (Novavax, AZ)	Yes, reduced in 2 (J&J, Novavax ~20-30% point decline. No efficacy v mild infections w/AZ)	Preserved in J&J trial
Countries reported	94	48	25
US States reported	46	17	5

Disclosures

- Paid consultant for W2O, Edelman, Guidepoint, and IMG Expert Services
- Paid advisor for Siemens Healthineers
- Member of MJH Life Sciences COVID-19 Coalition
- Own stock in Illumina, Pacific Biosciences, ThermoFisher Scientific, & NanoString Technologies
- Research funded by DARPA, DTRA, NIAID, and FastGrants