

Twitter Thread by Billy Bostickson ■■■&■ ■



Billy Bostickson ■■■&■ ■

[@BillyBostickson](#)



@NBA @StephenKissler @yhgrad B.1.1.7 reveals clearly that SARS-CoV-2 is reverting to its original pre-outbreak condition, i.e. adapted to transgenic hACE2 mice (either Baric's BALB/c ones or others used at WIV labs during chimeric bat coronavirus experiments aimed at developing a pan betacoronavirus vaccine)

@EricTopol @NBA @StephenKissler @yhgrad 1. From Day 1, SARS-COV-2 was very well adapted to humansand transgenic hACE2 Mice <https://t.co/TNE4tuLkqN>

1. From Day 1, SARS-COV-2 was very well adapted to humansand transgenic hACE2 Mice

"we generated a mouse model expressing hACE2 by using CRISPR/Cas9 knockin technology. In comparison with wild-type C57BL/6 mice, both young & aged hACE2 mice sustained high viral loads... pic.twitter.com/j94XtSkscj

— Billy Bostickson \U0001f3f4\U0001f441&\U0001f441 \U0001f193 (@BillyBostickson) [January 30, 2021](#)

@EricTopol @NBA @StephenKissler @yhgrad 2. High Probability of serial passaging in Transgenic Mice expressing hACE2 in genesis of SARS-COV-2 <https://t.co/B3eR764c1Z>

1. High Probability of serial passaging in Transgenic Mice expressing hACE2 in genesis of SARS-COV-2!

2 papers:

Human\u2013viral molecular mimicry<https://t.co/irfH0Zgrve>

Molecular Mimicry<https://t.co/yLQoUtfS6s> <https://t.co/lsCv2iMEQz>

— Billy Bostickson \U0001f3f4\U0001f441&\U0001f441 \U0001f193 (@BillyBostickson) [January 2, 2021](#)

@EricTopol @NBA @StephenKissler @yhgrad B.1.1.7 has an unusually large number of genetic changes, ... found to date in mouse-adapted SARS-CoV2 and is also seen in ferret infections.

<https://t.co/9Z4oJmkcKj>

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/959438/Technical_Briefing_VOC_SH_NJL2_SH2.pdf

Variant of concern technical briefing - Gov.uk

Dec 8, 2563 BE — B.1.1.7 has an unusually large number of genetic changes, ... found to date **in mouse-adapted SARS-CoV2 and is also seen in ferret infections.**

[@EricTopol](#) [@NBA](#) [@StephenKissler](#) [@yhgrad](#) We adapted a clinical isolate of SARS-CoV-2 by serial passaging in the ... Thus, this mouse-adapted strain and associated challenge model should be ... (B) SARS-CoV-2 genomic RNA loads in mouse lung homogenates at P0 to P6.
<https://t.co/I90OOCJg7o>

<https://science.sciencemag.org/content/369/6511/1603>

Adaptation of SARS-CoV-2 in BALB/c mice for testing vaccine ...

by H Gu · 2020 · Cited by 87 · Related articles

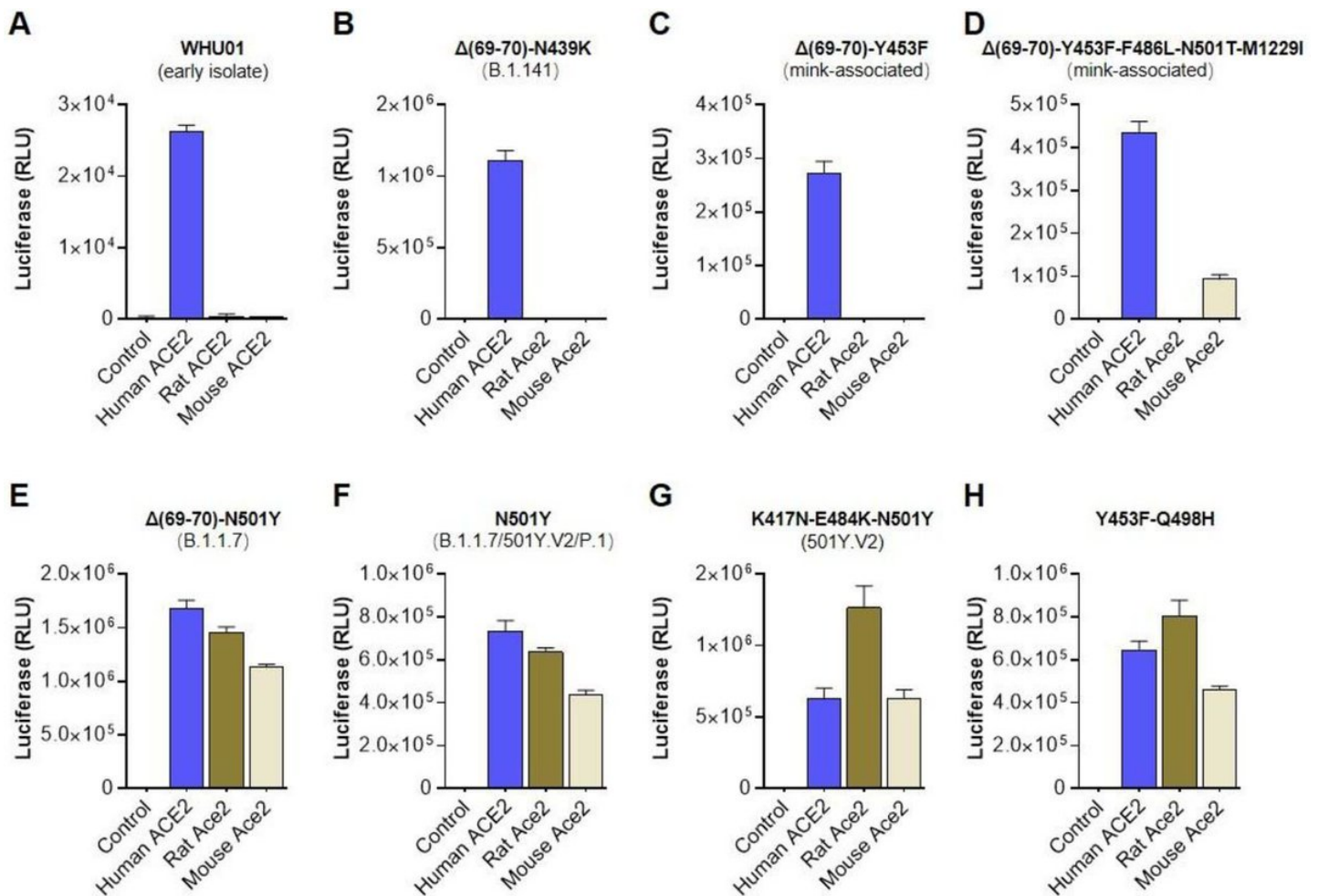
Sep 25, 2563 BE — We **adapted** a clinical isolate of SARS-CoV-2 by serial passaging in the ... Thus, this **mouse-adapted** strain and associated challenge model should be ... (B) SARS-CoV-2 genomic RNA loads in **mouse** lung homogenates at P0 to P6. ... Transmission of SARS-CoV-2 Lineage **B.1.1.7** in England: Insights from ...

[@EricTopol](#) [@NBA](#) [@StephenKissler](#) [@yhgrad](#) Mice!

A mink-associated variant carrying $\Delta(69-70)$ -Y453F-F486L-N501T-M1229I mutations was also able to utilize mouse Ace2. In addition, all variants carrying an N501Y mutation, a shared feature of UK, South Africa, & Brazil VOC strains, efficiently use mouse Ace2 orthologs.

[@EricTopol](#) [@NBA](#) [@StephenKissler](#) [@yhgrad](#) Topolino!

"Moreover, the K417N-E484K-N501Y mutations found in the South Africa variant 501Y.V2 even enable the virus to utilize rat Ace2 more efficiently than using human ACE2. These data suggest that rats and mice may (have) be(en) able to harbor and spread these variants"?



@EricTopol @NBA @StephenKissler @yhgrad Above taken from:

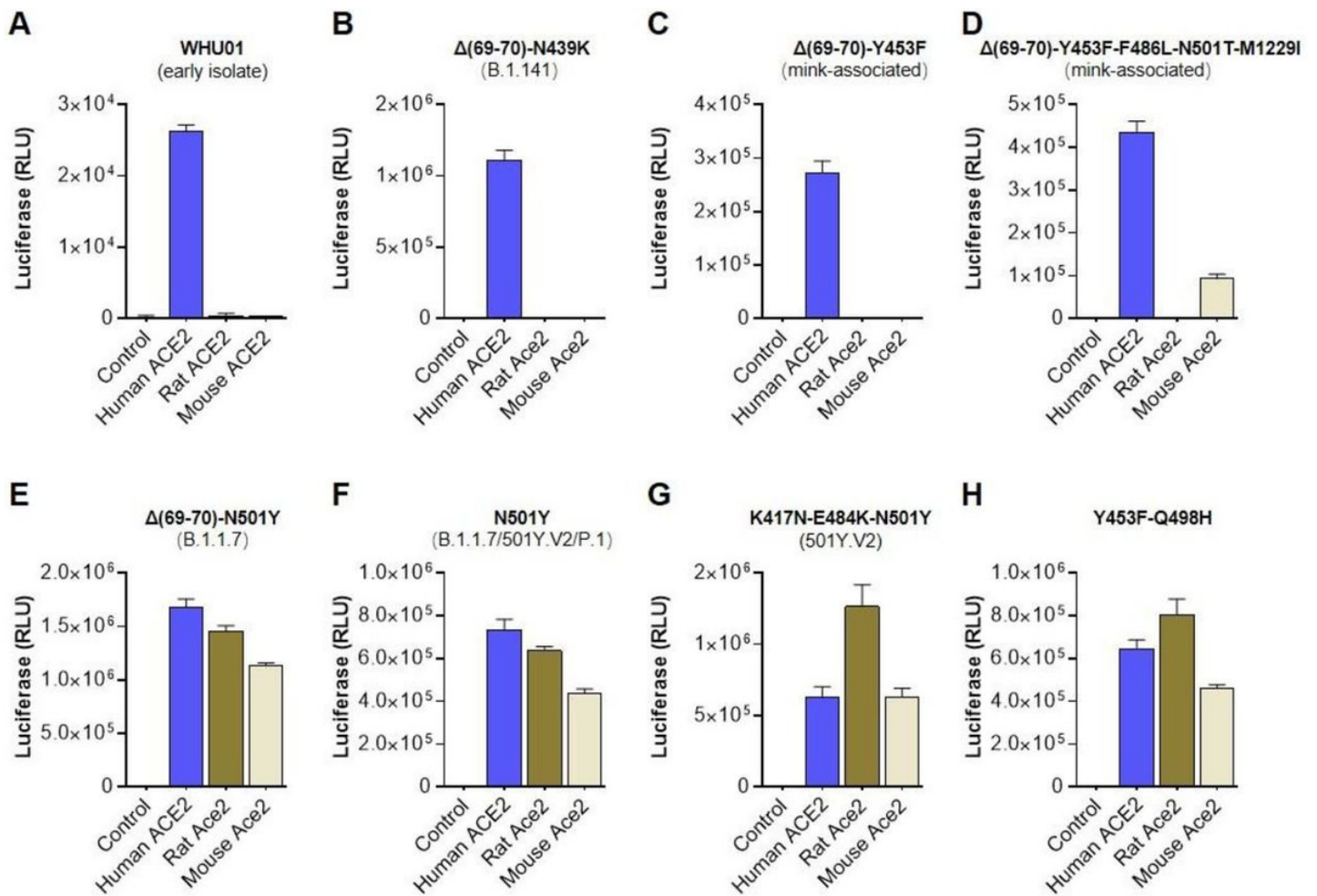
Circulating SARS-CoV-2 variants B.1.1.7, 501Y.V2, and P.1 have gained ability to utilize rat and mouse Ace2 and altered in vitro sensitivity to neutralizing antibodies and ACE2-Ig

<https://t.co/j9qEcUz4ea>

Well worth a read!

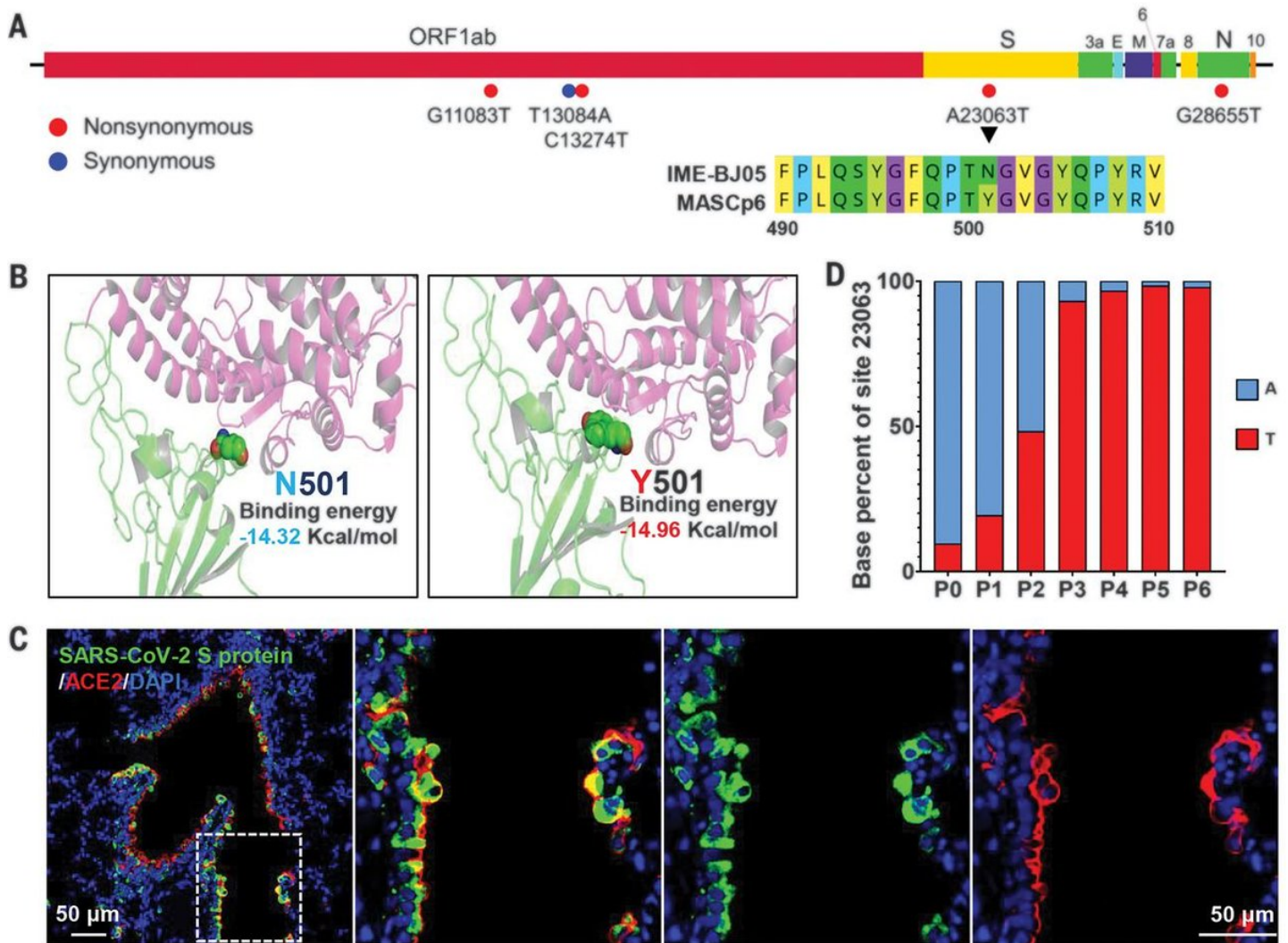
that emerged during the pandemic. We found that, in contrast to an early isolate WHU01, the circulating variants B.1.1.7/501Y.V1, B.1.351/501Y.V2, and P.1/501Y.V3 were able to use rat and mouse Ace2 orthologs as entry receptors, suggesting that rats and mice might ~~be able to~~ **have** harbored **ed** & spread these variants. We

@EricTopol @NBA @StephenKissler @yhgrad even the mink variants were mouse ACE2 adapted, what a surprise...now, who would have expected that?



@EricTopol @NBA @StephenKissler @yhgrad Serial passaging of virus in mouse lungs results in adaptive mutations that increase viral infectivity

MASCP6 genome contains 5 mutations compared to its parental strain IME-BJ05, resulting in four amino acid residue changes in the ORF1ab, S, and N genes, respectively (Fig. 3A)



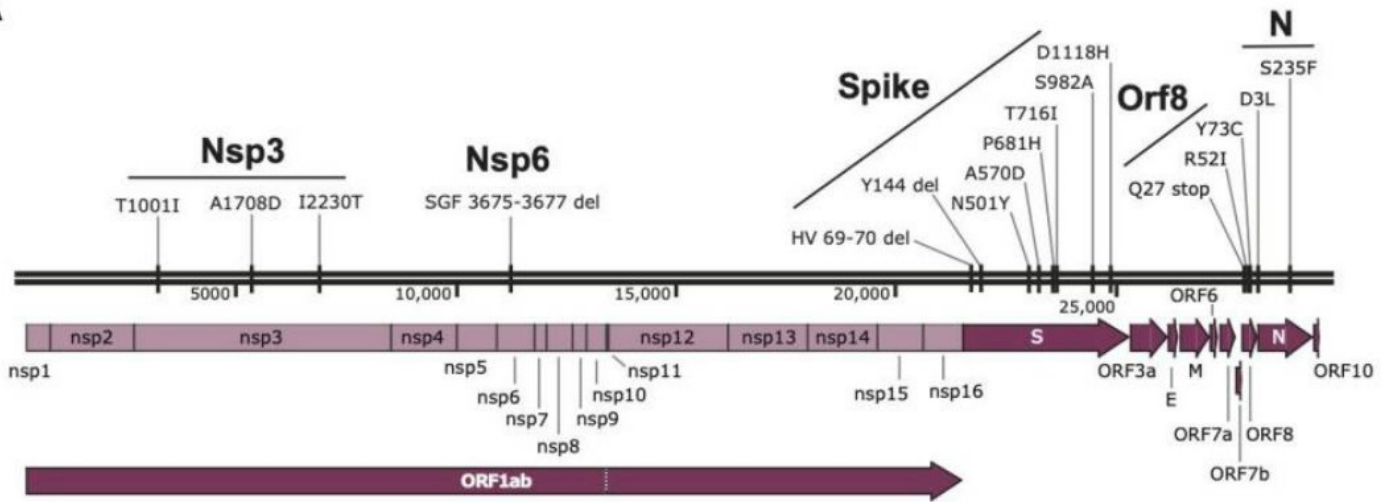
@EricTopol @NBA @StephenKissler @yhgrad The N501Y mutation seems to provide a more favorable interaction with mouse ACE2 for docking and entry, thus leading to the increased virulence phenotype in mice.

Adaptation of SARS-CoV-2 in BALB/c mice

<https://t.co/I90OOCJg7o>

@EricTopol @NBA @StephenKissler @yhgrad Protein-coding mutations in SARS-CoV-2 B.1.1.7 virus variant.

A) open reading frames (dark purple arrows) and proteins resulting from cleavage of ORF1ab polypeptide into non-structural proteins (light purple). 17 protein-coding mutations are annotated (top)

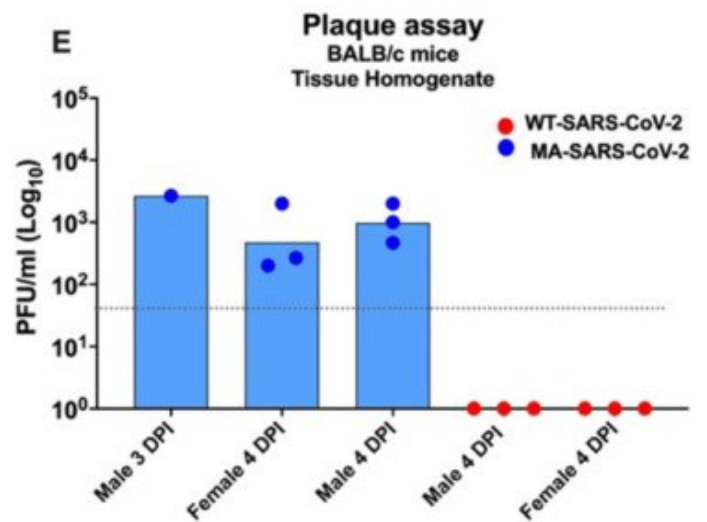
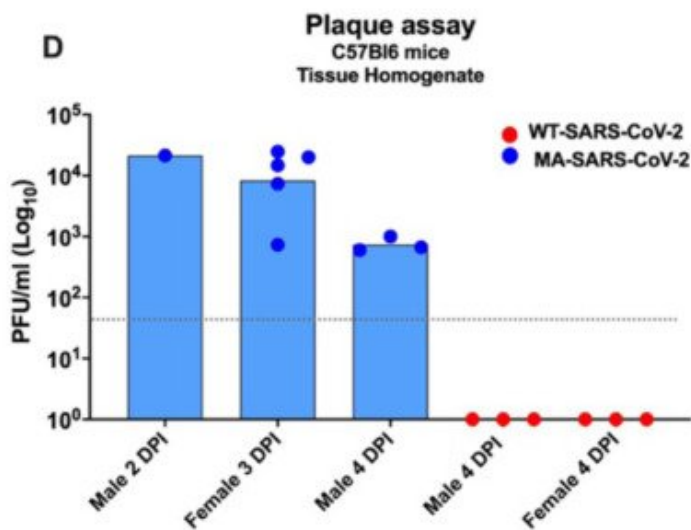
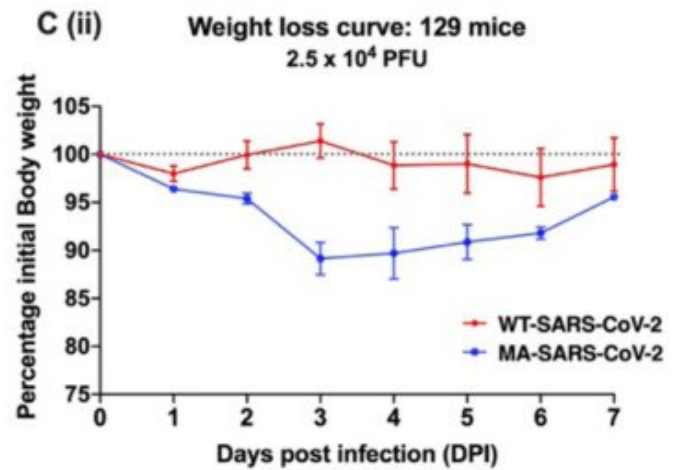
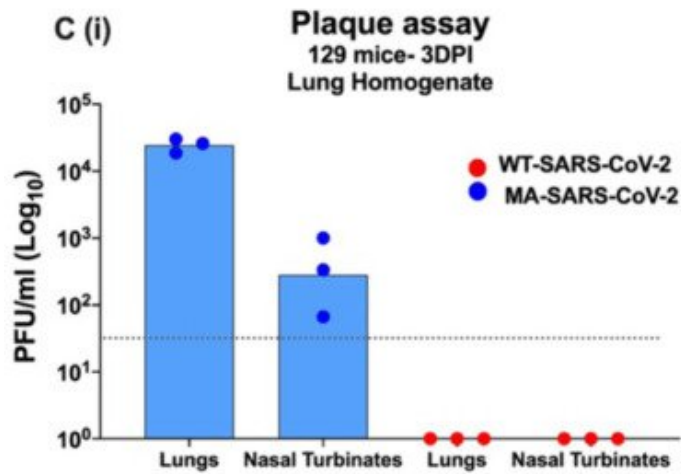
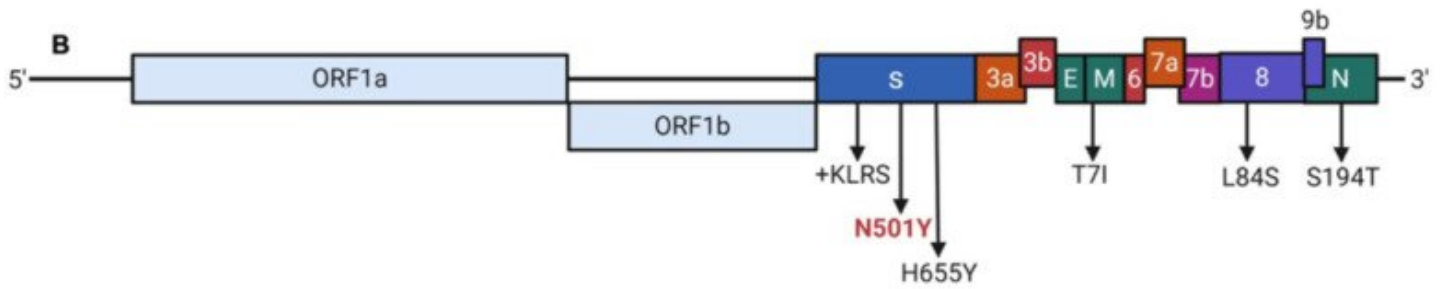
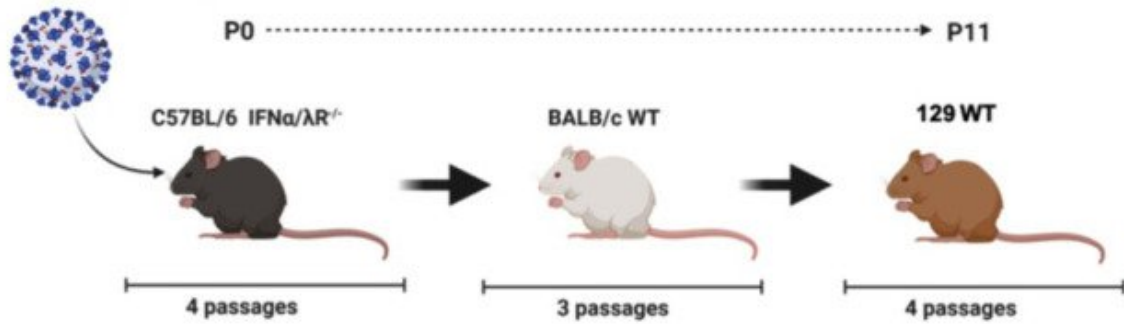
A

[@EricTopol](#) [@NBA](#) [@StephenKissler](#) [@yhgrad](#) which includes 14 non-synonymous mutations and 3 deletions spanning 5 viral proteins. B) Expansion of the genomic region from spike to N protein for visualization purposes.

[@EricTopol](#) [@NBA](#) [@StephenKissler](#) [@yhgrad](#) "N501Y mutation in SARS-CoV-2 spike leads to morbidity in obese and aged mice"

<https://t.co/FOfZq8SiQU>

A SARS-CoV-2-WT (WA1/202)



@EricTopol @NBA @StephenKissler @yhgrad Differential efficiencies to neutralize the novel mutants B.1.1.7 and 501Y.V2 by collected sera from convalescent COVID-19 patients and RBD nanoparticle-vaccinated rhesus macaques
<https://t.co/fBHatIKvJ>

Both 501Y.V2 and B.1.1.7 variants harbor the early epidemic D614G mutation within the spike protein.⁴ Several reports demonstrate that the D614G mutation enhances SARS-CoV-2 infectivity and transmission by increasing the functional spike density on the virion.^{5,6,7,8} However, the D614G mutation does not alter the binding affinity to hACE2 or the susceptibility to neutralizing antibodies.^{5,7,9} The mutant virus with glycine at residue 614 (Spike-G614 virus) also becomes more sensitive to sera from Spike-D614-vaccinated **mice**, nonhuman primates (NHPs) and humans, and convalescent sera as well as from RBD-specific monoclonal antibodies.⁶ Another shared mutation of 501Y.V2 and B.1.1.7 is N501Y within the RBD. Mutational scanning of the RBD and correlated experiments in **mice** indicate that N501F and N501Y enhance ACE2 binding affinity and increase virulence, respectively.^{10,11}

[@EricTopol](#) [@NBA](#) [@StephenKissler](#) [@yhgrad](#) Just to annoy people

Virology: the problem with 'leaky' vaccines

Fresh evidence supports the theory that some vaccines lead to the evolution of more virulent viral strains

<https://t.co/ttyM9J2idl>