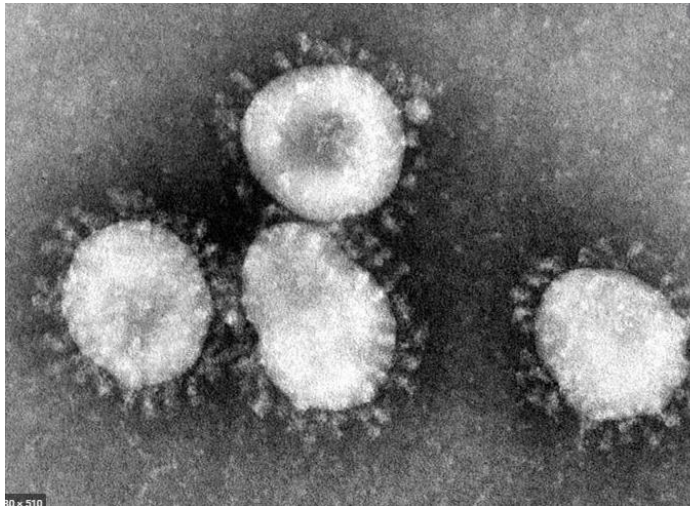
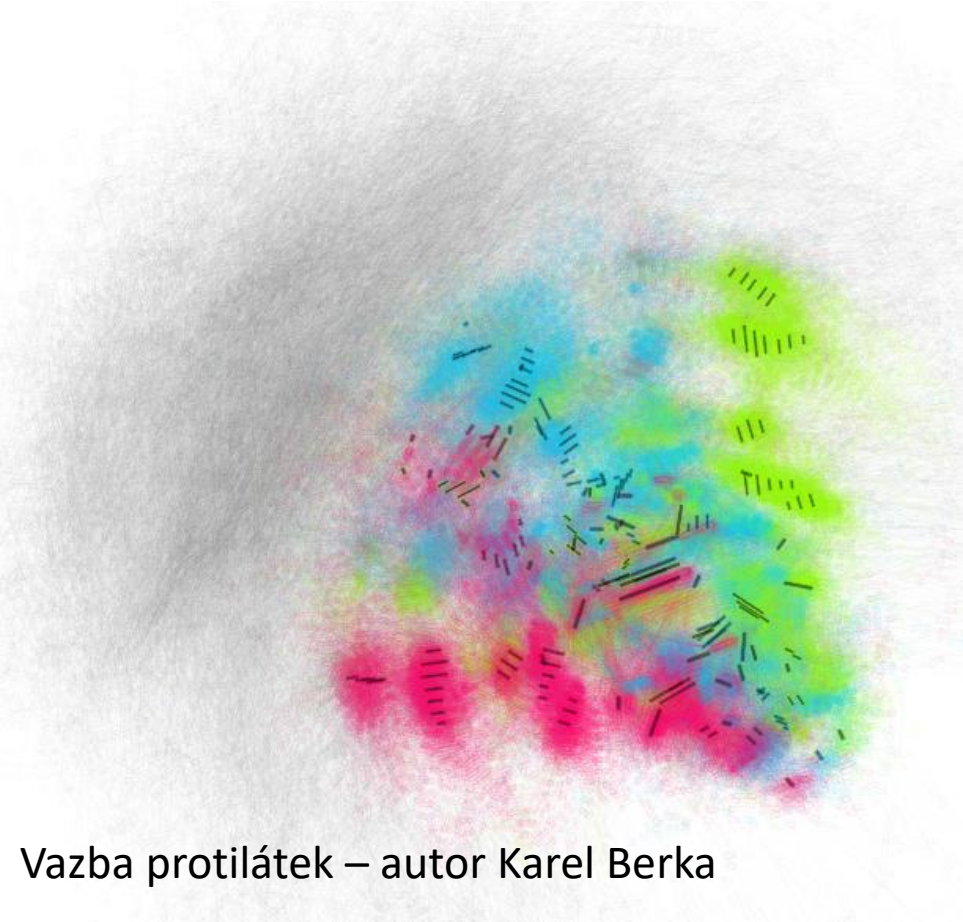
SARS-CoV-2

NRL pro chřipku a nechřipková virová respirační onemocnění

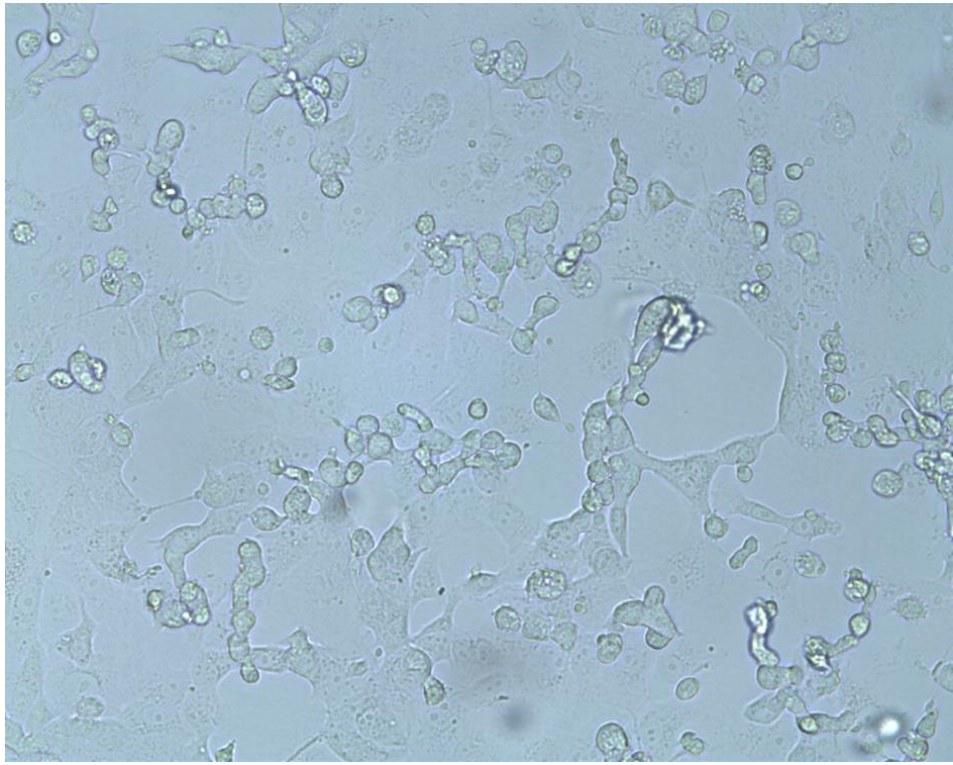


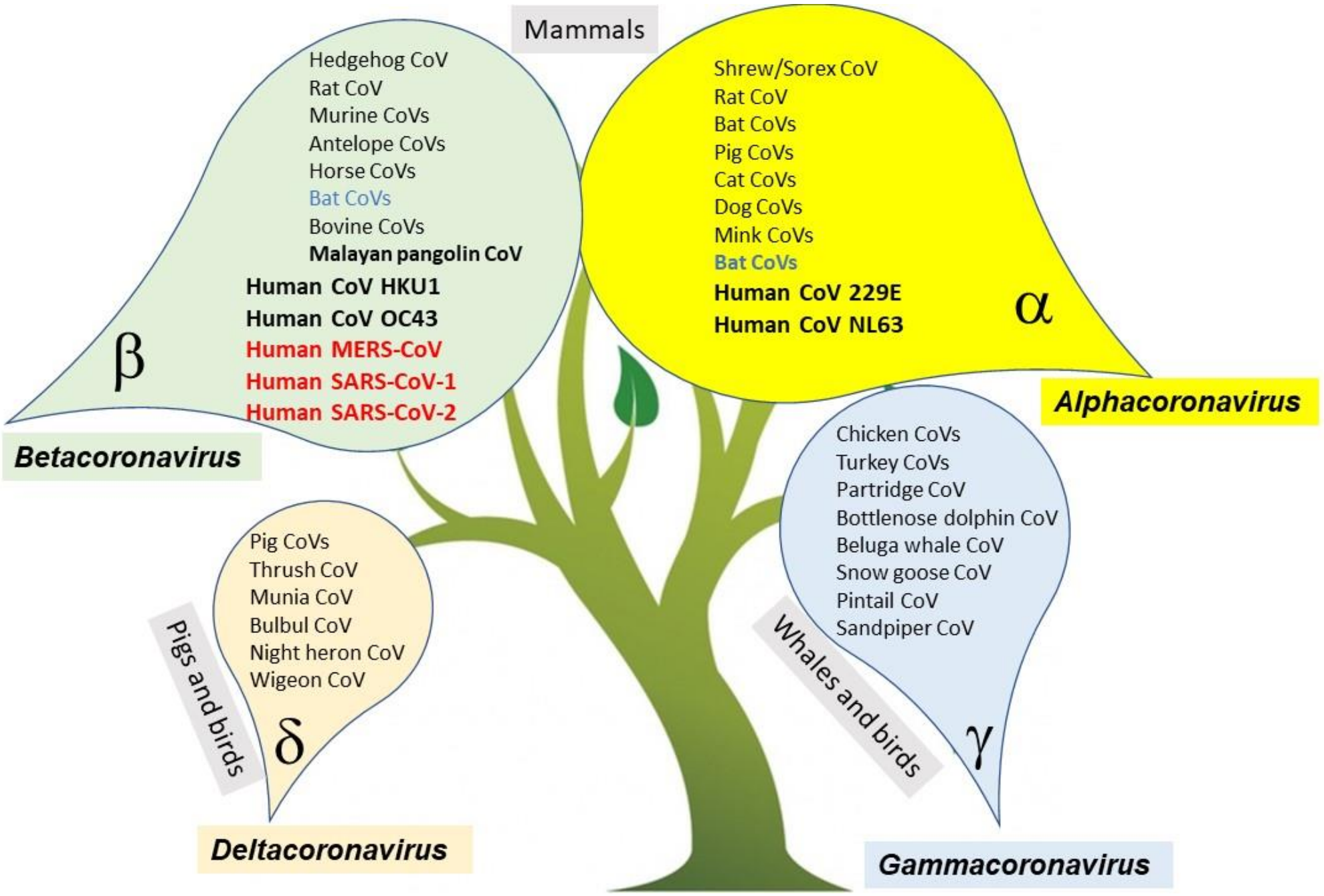
Helena Jiřincová, SZÚ



Vazba protilátek – autor Karel Berka

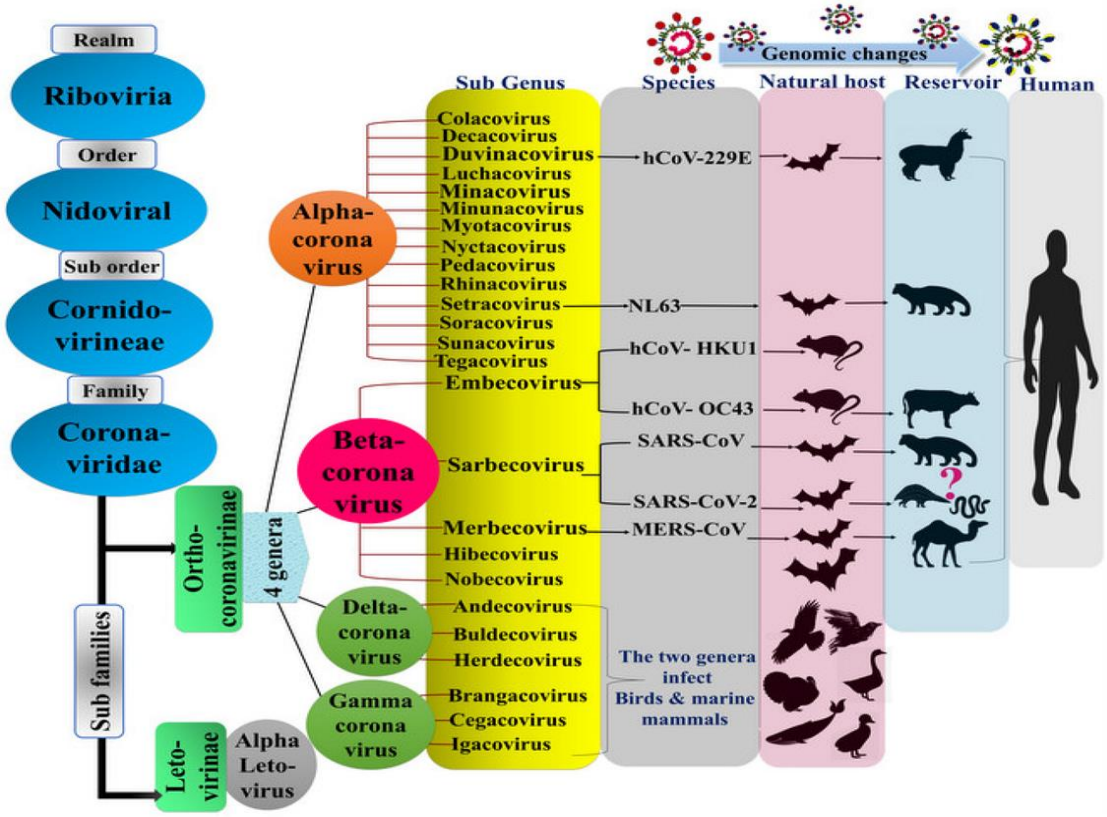
Omicron



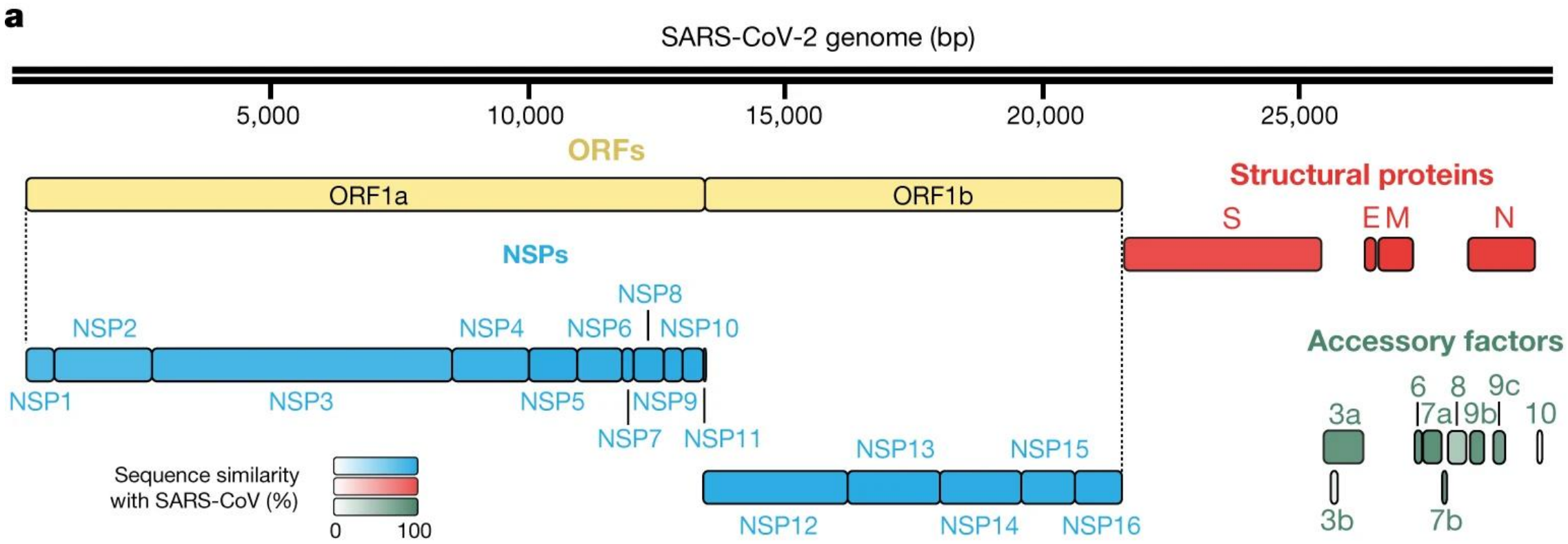

Mammals
Hedgehog CoV
Rat CoV
Murine CoVs
Antelope CoVs
Horse CoVs
Bat CoVs
Bovine CoVs
Malayan pangolin CoV
Human CoV HKU1
Human CoV OC43
Human MERS-CoV
Human SARS-CoV-1
Human SARS-CoV-2
β
Betacoronavirus
Shrew/Sorex CoV
Rat CoV
Bat CoVs
Pig CoVs
Cat CoVs
Dog CoVs
Mink CoVs
Bat CoVs
Human CoV 229E
Human CoV NL63
α
Alphacoronavirus
Pigs and birds
Pig CoVs
Thrush CoV
Munia CoV
Bulbul CoV
Night heron CoV
Wigeon CoV
δ
Deltacoronavirus
Whales and birds
Chicken CoVs
Turkey CoVs
Partridge CoV
Bottlenose dolphin CoV
Beluga whale CoV
Snow goose CoV
Pintail CoV
Sandpiper CoV
γ
Gammacoronavirus

Specifické vlastnosti SARS-CoV-2

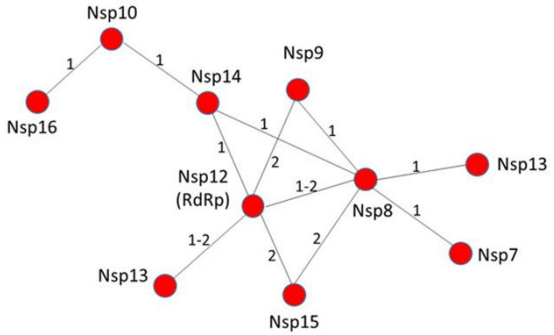
- Ribosomal frame shift
- Exonukleasová aktivita
- Inhibice MHC I prezentace
- Inhibice produkce IFN gamma – inátní imunitní obrana
- Inhibice IFN alfa dráhy – tehtherin (brání odštěpení viru z buňky)
- Furinové štěpné místo – specifiky vstup do buňky + aktivace tvorby syncitií



SARS-CoV-2 – strukturální a nestrukturální proteiny



Nature (Nature) ISSN 1476-4687 (online) ISSN 0028-0836 (print)



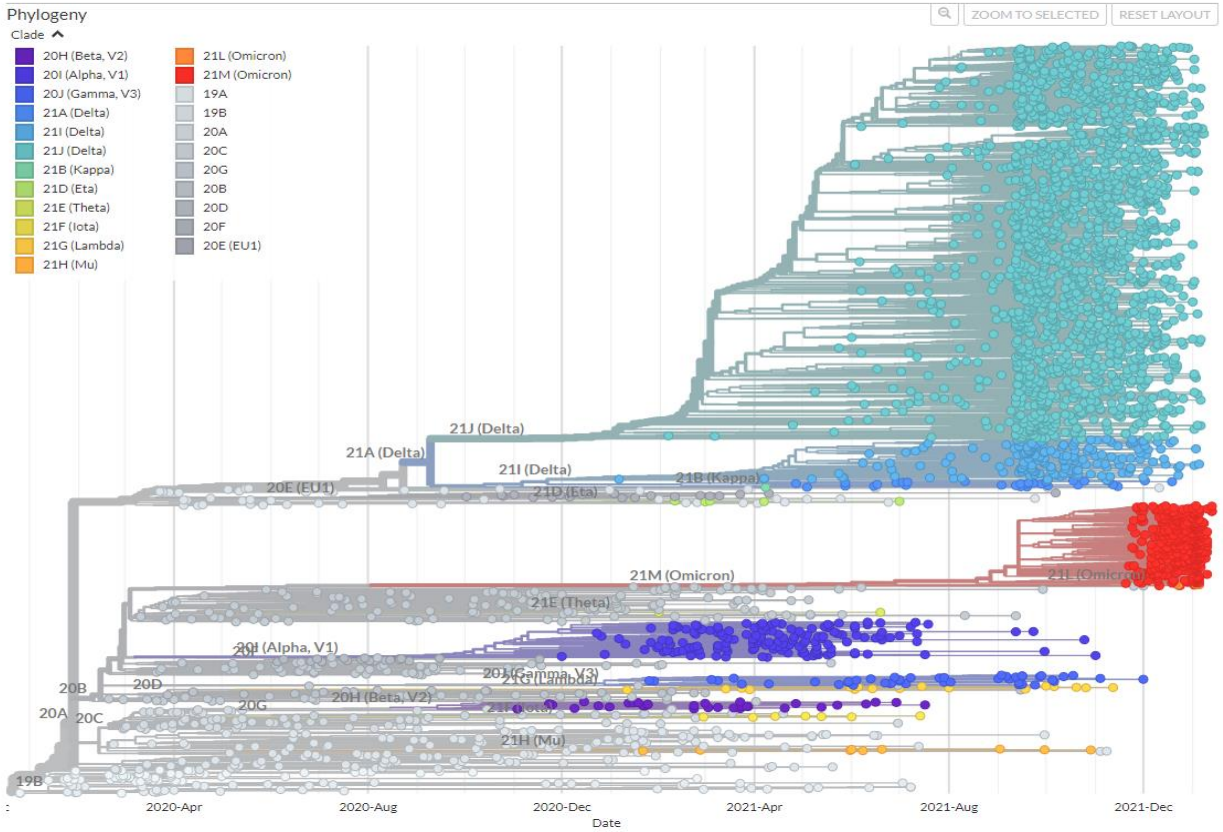
NSP 14 – proofreading exonuclease

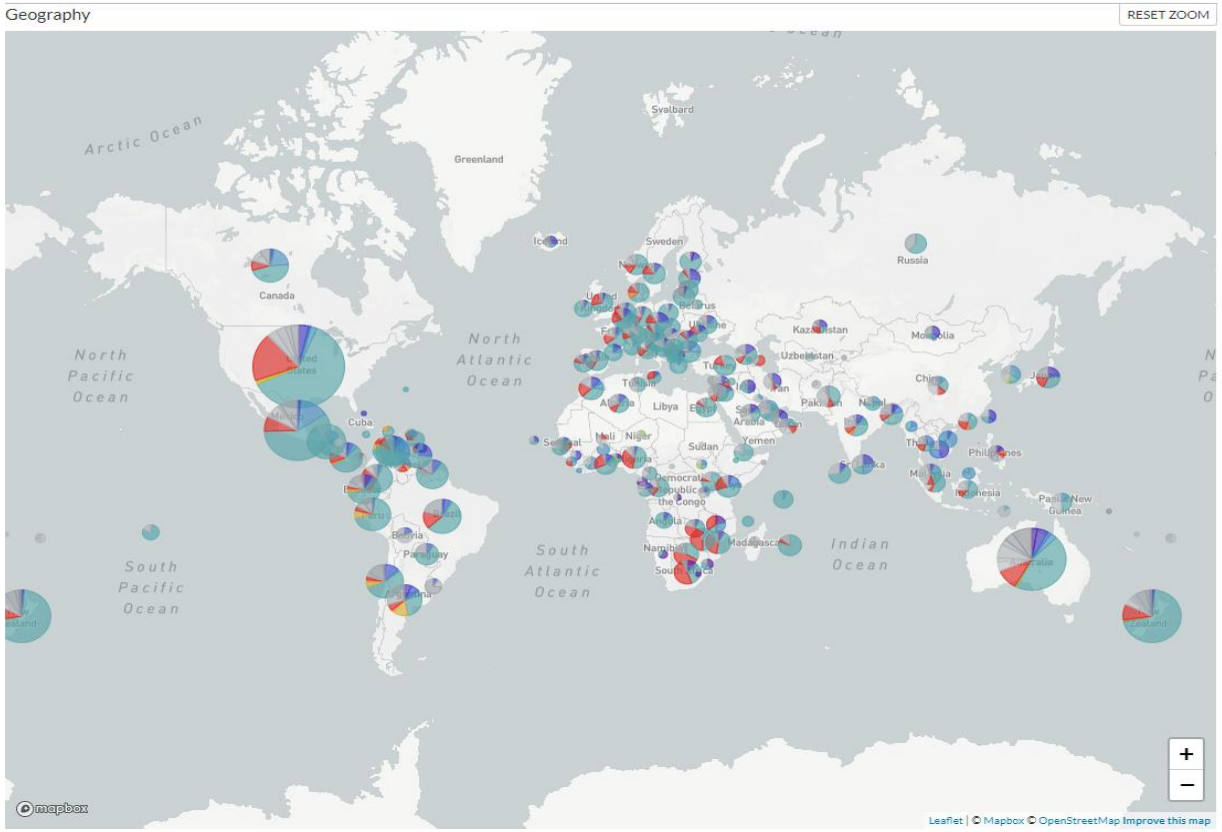
Cells **2020**, *9*(5), 1267; https://doi.org/10.3390/cells9051267

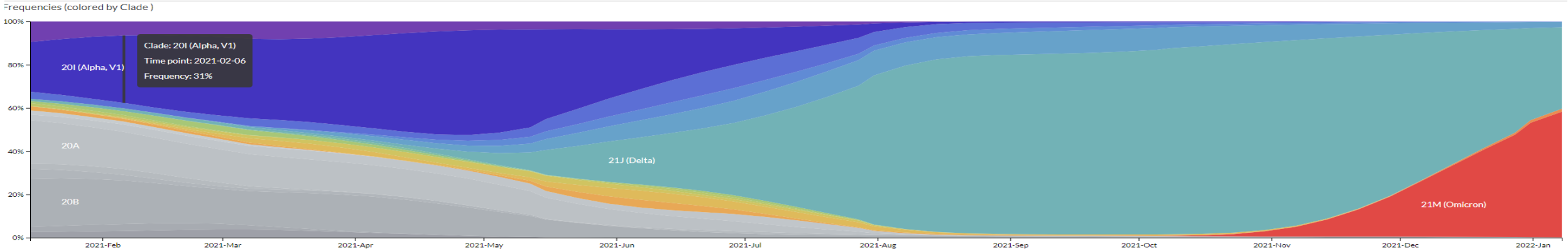
Genomic epidemiology of novel coronavirus - Global subsampling

Built with nextstrain/ncov. Maintained by the Nextstrain team. Enabled by data from GISAID.

Showing 3270 of 3270 genomes sampled between Dec 2019 and Jan 2022.



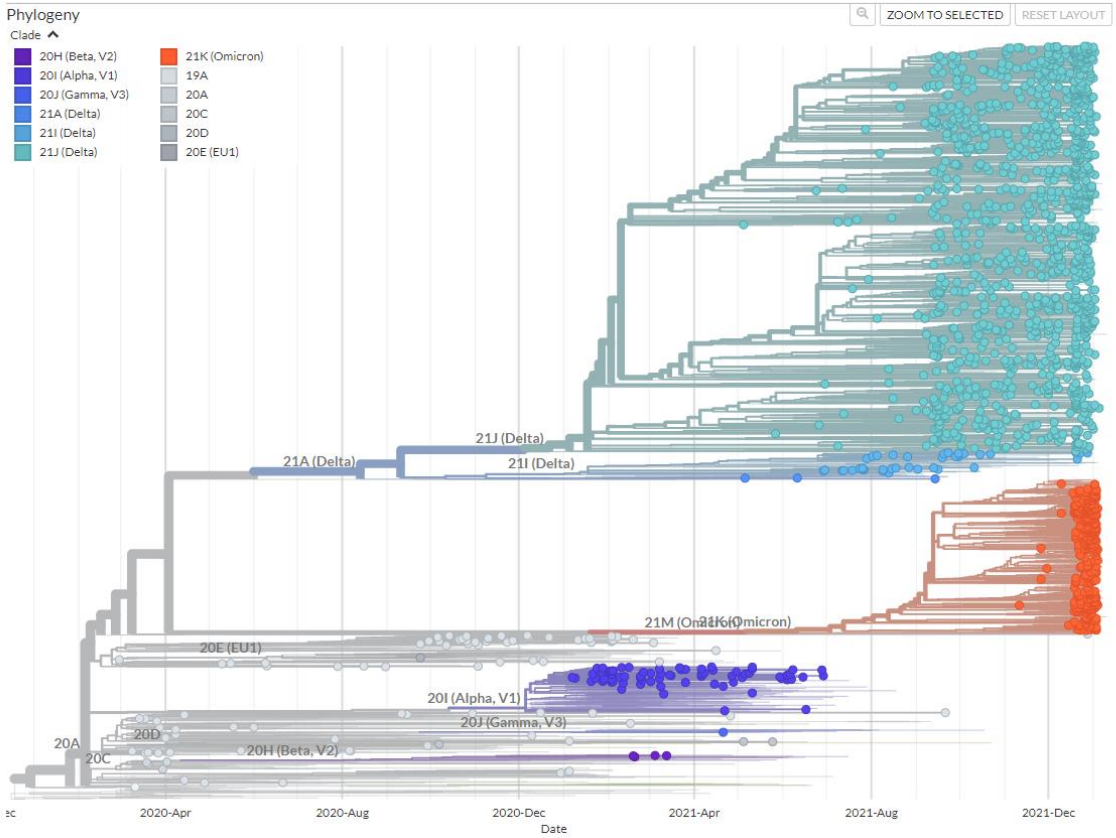


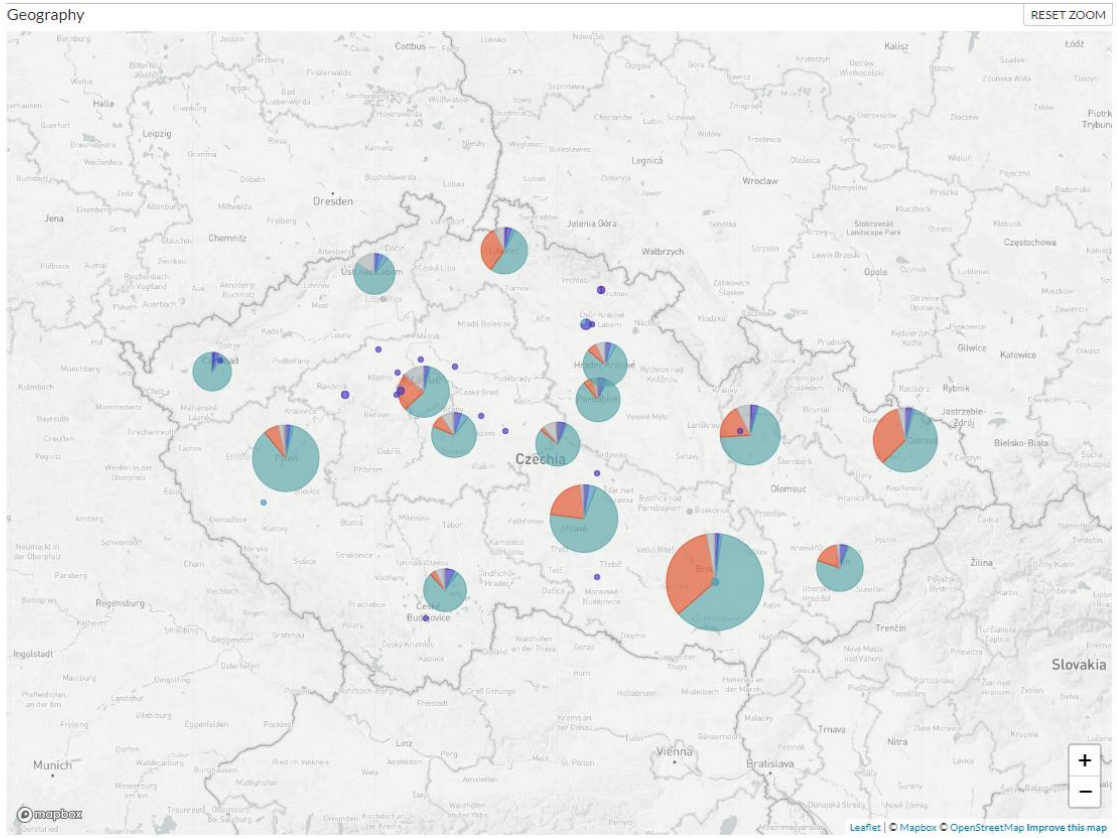


SARS-CoV-2 phylogeny

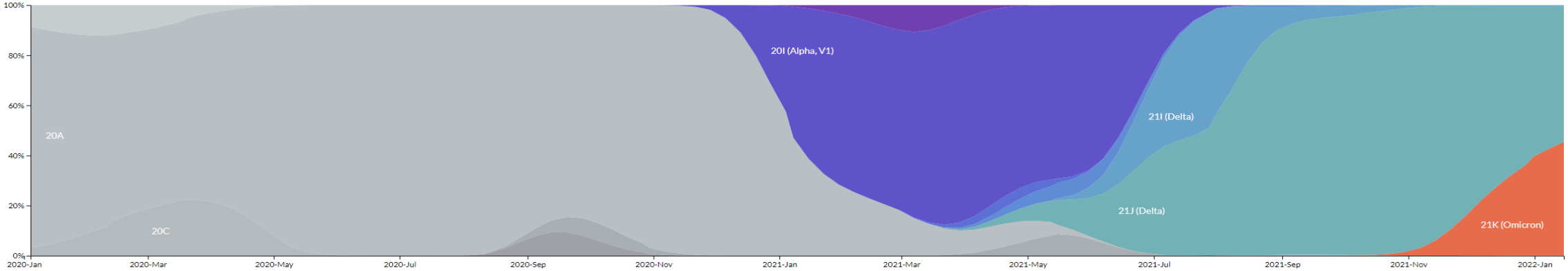
Built with neherlab/ncov-simple. Maintained by Cornelius Roemer and Richard Neher. Enabled by data from GISAID.

Showing 1761 of 3640 genomes sampled between Feb 2020 and Jan 2022. Filtered to Czech Republic (1761).





Frequencies (colored by Clade and normalized to 100% at each time point for 1761 out of a total of 3640 tips)



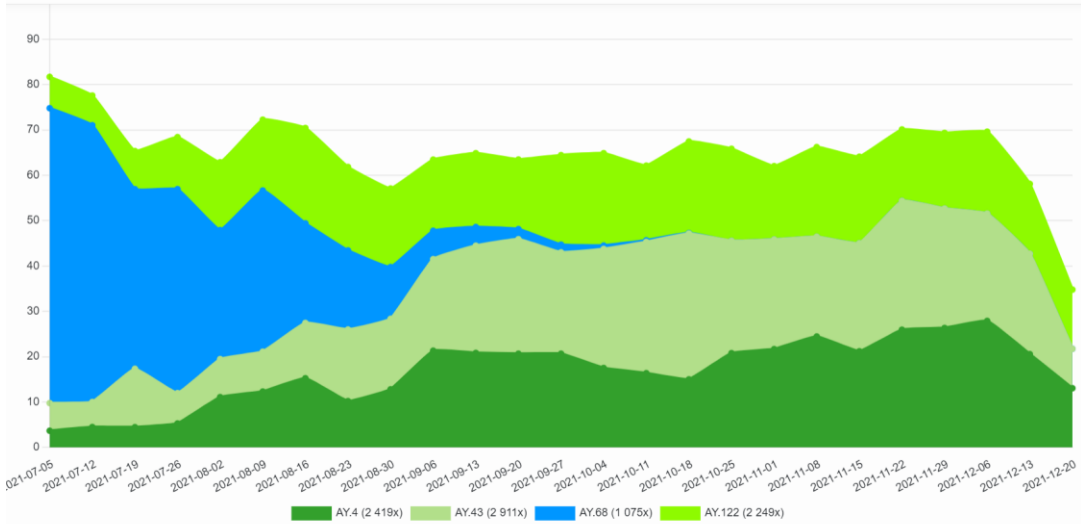
Datum odběru (prosím vložte obě hodnoty)

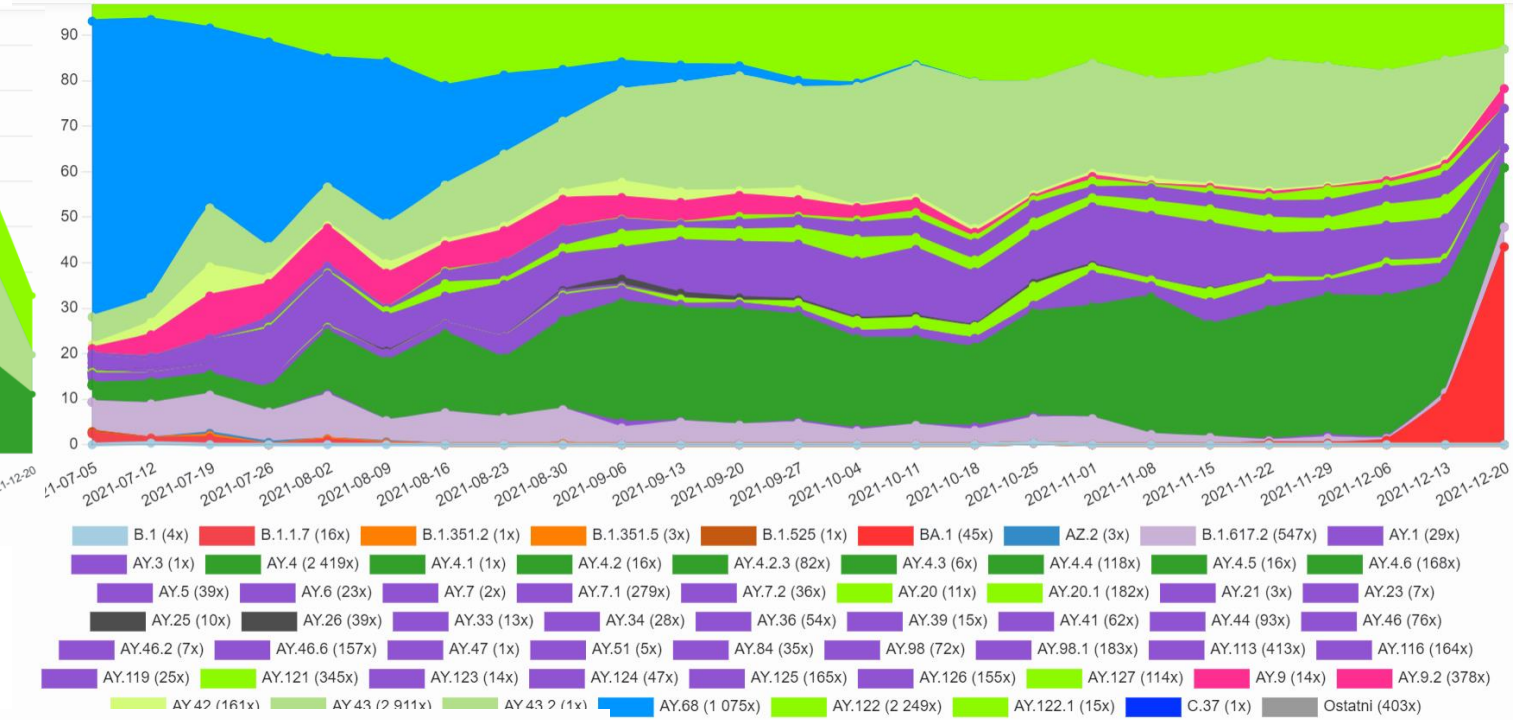
1. 7. 2021	17. 1. 2022

Zastoupení linii

Vše Minimálně 1% Minimálně 5%

AY.4, AY.43. AY.68, AY.122 + B.1.1.529





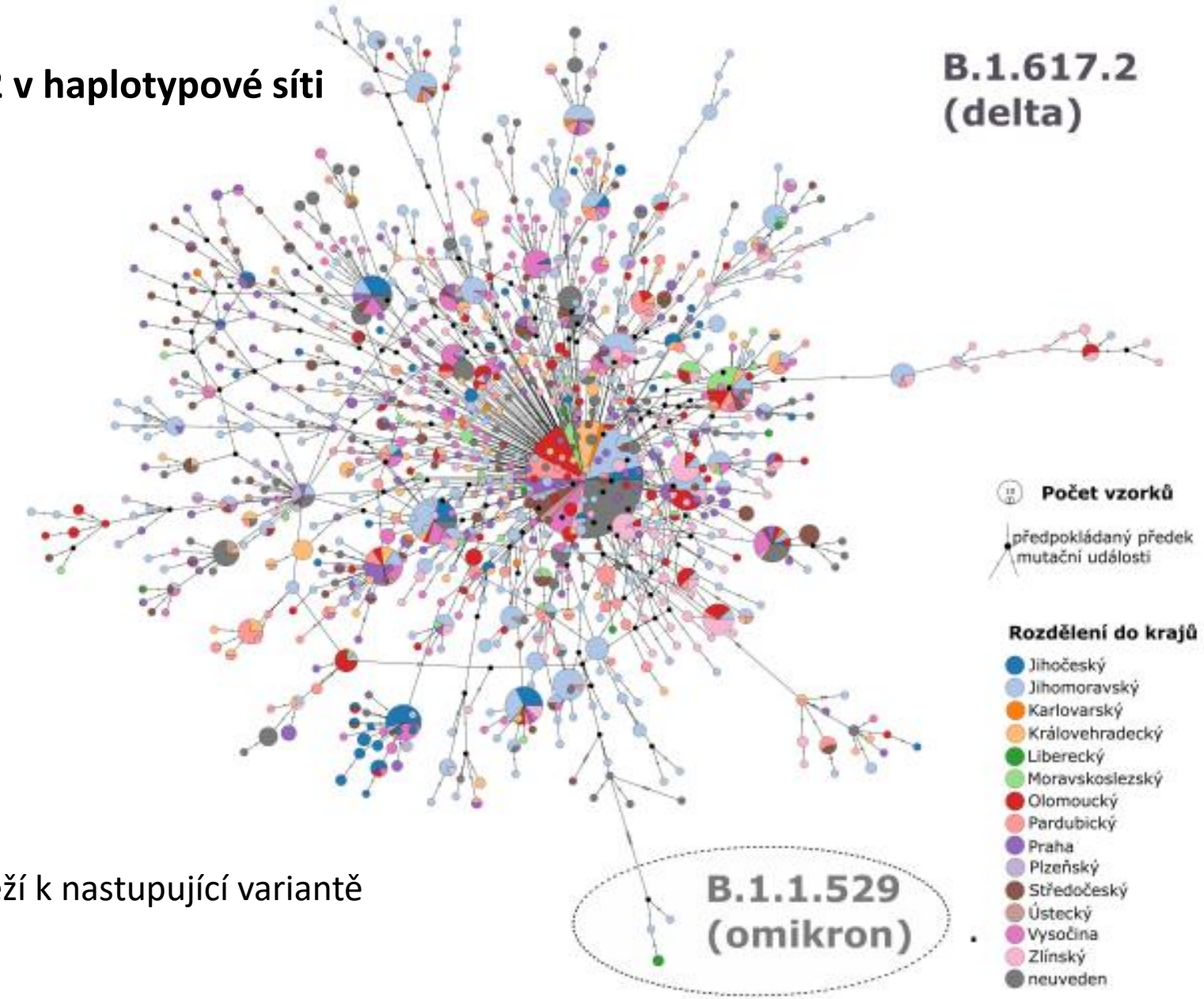
Linie SARS-CoV-2 detekované v Česku (celé období)

COG CZ: https://virus.img.cas.cz/

Znázornění variant SARS-CoV-2 v haplotypové síti

Výběr sekvencí 2093 vzorků
22. 10. – 18. 12. 2021.

Velikost uzlů – dle počtu vzorků
s identickou sekvencí.
Spojnice naznačují pravděpodobné
příbuzenské vztahy,
počet krátkých kolmých úseček
odpovídá počtu mutačních



Tři sekvence v dolní části grafu náleží k nastupující variantě
Omicron (B.1.1.529)

Autor: Vladimír Hampl

Vyhodnocení dat z diskriminační PCR 9. 1. do 16. 1. 2022 (dle data odběru) - 40 468 provedených testů diskriminační PCR z 89 laboratoří.

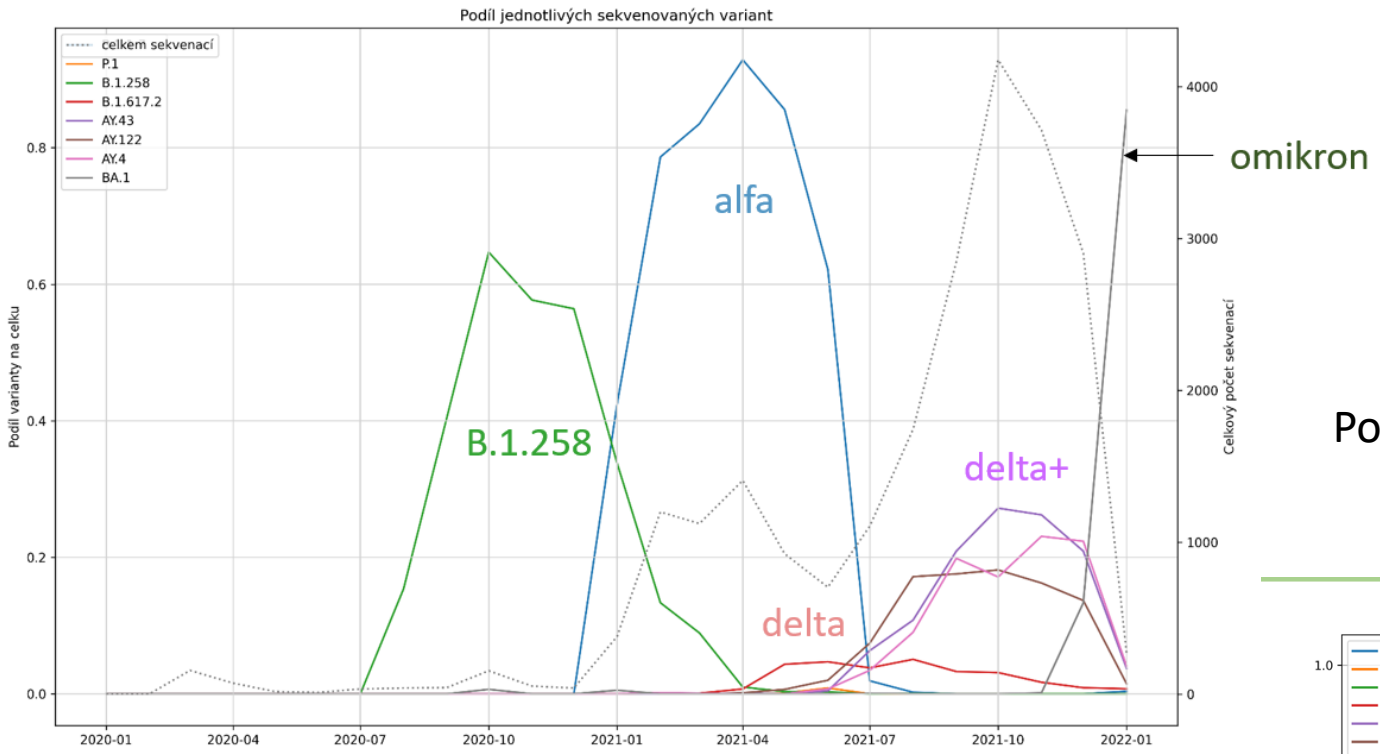
Tabulka 1: **Přehled zachycených mutací - 8denní průměr**

Mutace	Pozitivních	Celkem	Procento	Interpretace (pouze susp. varianta)
A570D+	6	5 731	0,10 %	alfa, delta + A570D
E484K+	366	11 540	3,17 %	beta, gama, alfa E484K+, delta+
L452R+	5 261	24 895	21,13 %	delta, delta+
L452R- a K417+ a N501Y+ a del69_70+ nebo Y505H, nebo S371L nebo S373P nebo T547K	29 367	40 468	72,57 %	Suspektní omikron

Tabulka 2: **Procento suspektních případů omikronu z celkového počtu diskriminačních PCR v ČR (aktualizovaná data k 17. 1.) vztažená k danému dnu odběru**

Datum	Suspektní omikron	Celkový počet případů SARS-CoV-2 vyšetřených diskriminační PCR	Procento záchytů varianty omikron
16. 1. 2022	481	574	83,80 %
15. 1. 2022	2 188	2 557	85,57 %
14. 1. 2022	5 311	6 470	82,09 %
13. 1. 2022	5 891	7 777	75,75 %
12. 1. 2022	4 852	6 875	70,57 %
11. 1. 2022	5 355	7 858	68,15 %
10. 1. 2022	4 243	6 767	62,70 %
9. 1. 2022	1 045	1 589	65,76 %

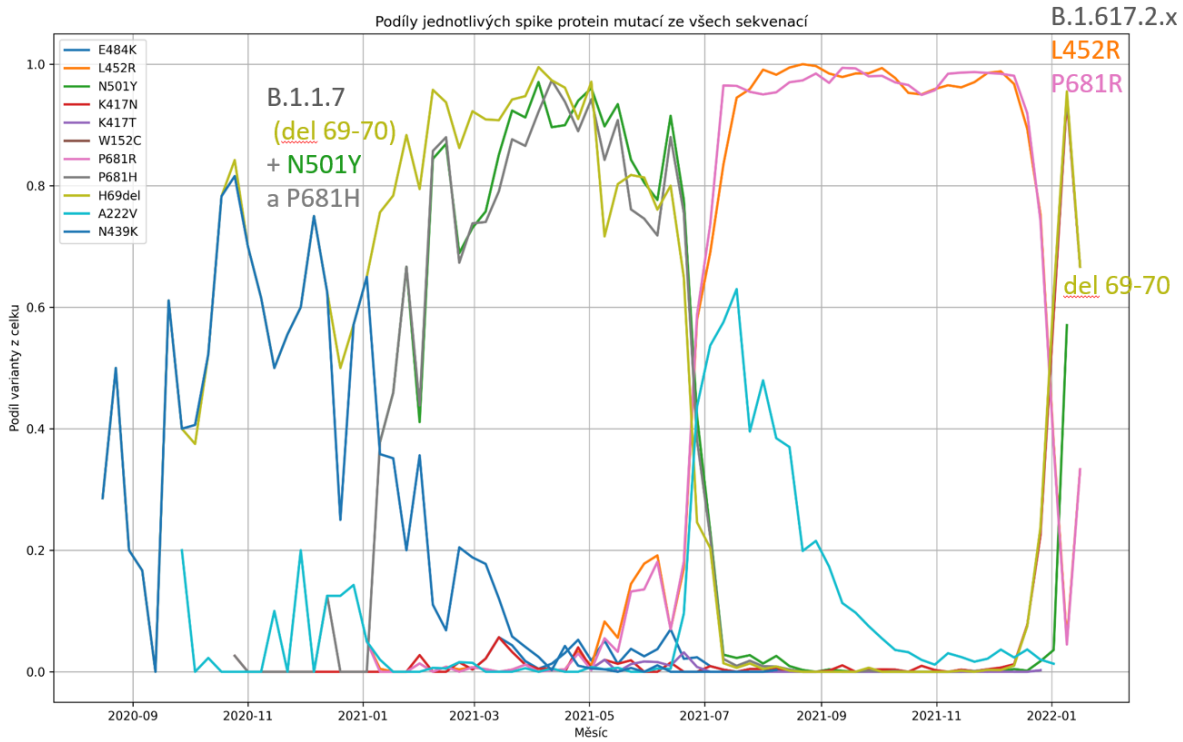
WGS – přehled ČR



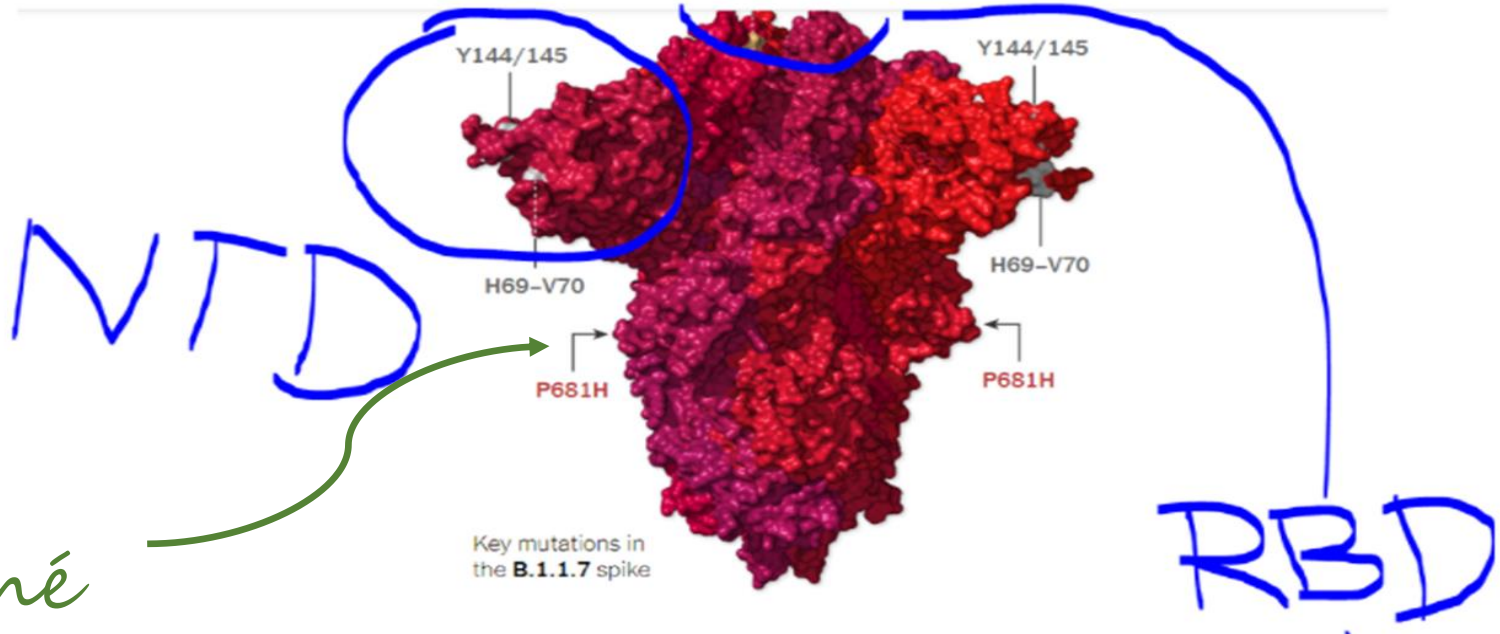
Podíl sekvenovaných variant SARS-CoV-2 dominantních v ČR od ledna 2021 do prosince 2021

Podrobnější heat maps: COG CZ: https://virus.img.cas.cz/

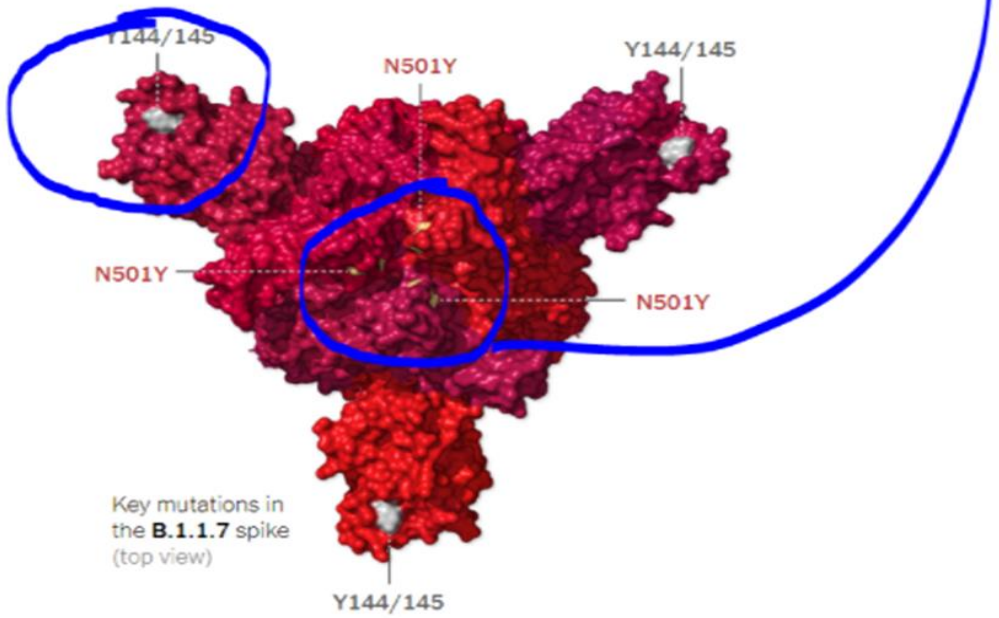
Podíl dominantních mutací ve spike genu SARS-CoV-2 od března 2020



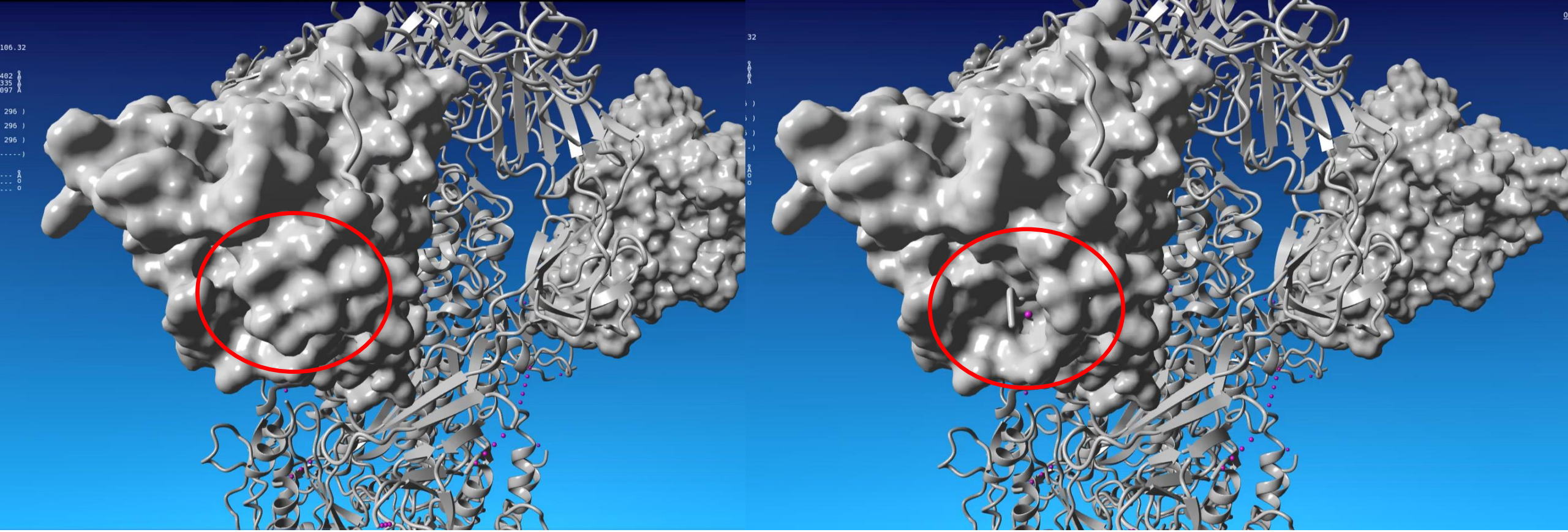
Furinové štěpné místo



It takes three spike proteins to form one spike, so each mutation appears in three places:

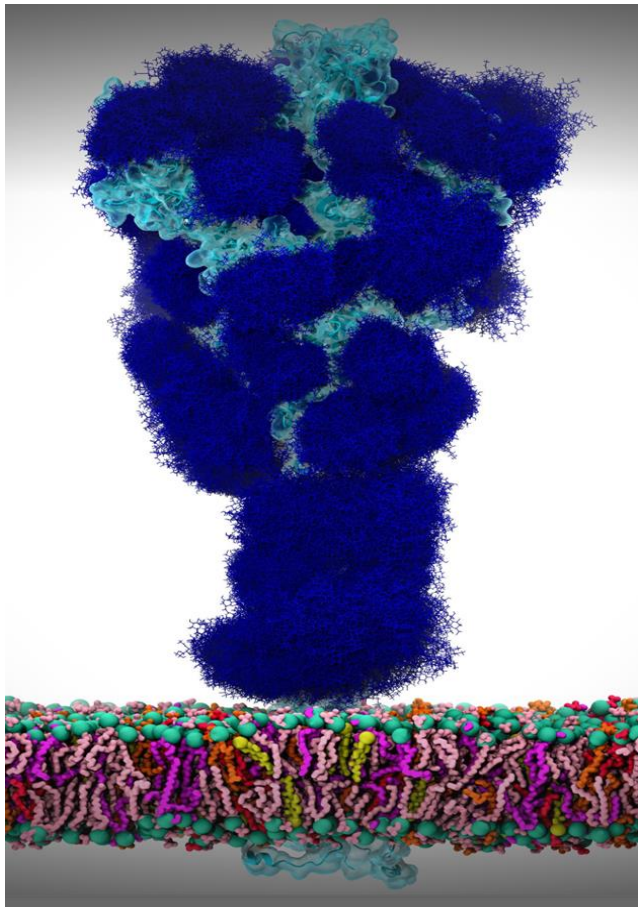


For more on the B.1.1.7 mutations, see: Inside the B.1.1.7

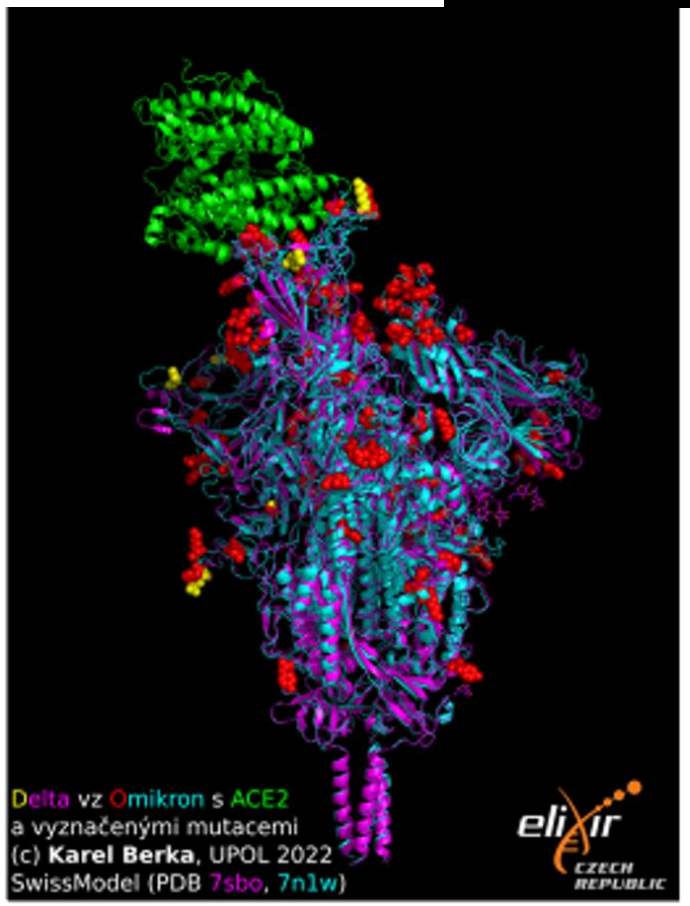


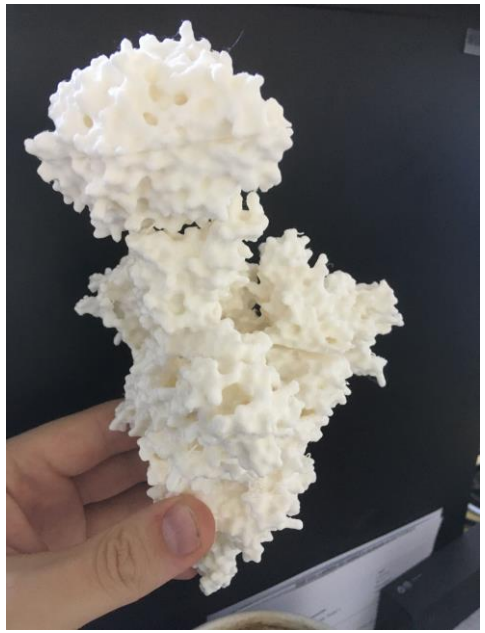
Delece 6 nukleotidů, tedy 2 aminokyselin (69 histidin, 70 valin) v N-terminální doméně spike proteinu - boční pohled (model dle rentgenostrukturní analýzy – SVU+SZU)

V hlavní roli spike

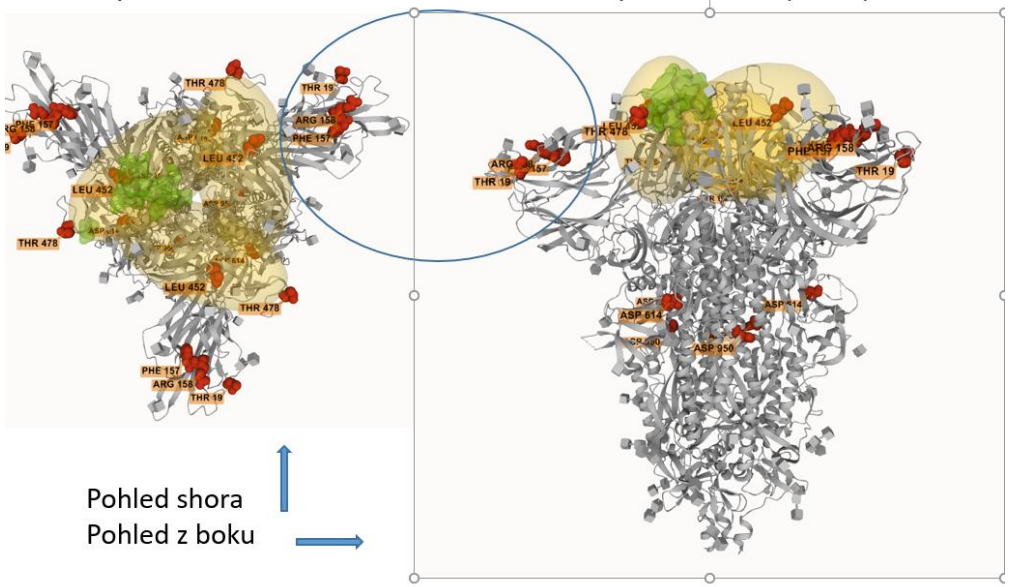


omikron





Aminokyselinové substituce charakteristické pro B.617.2 (delta)



Pohled shora
Pohled z boku

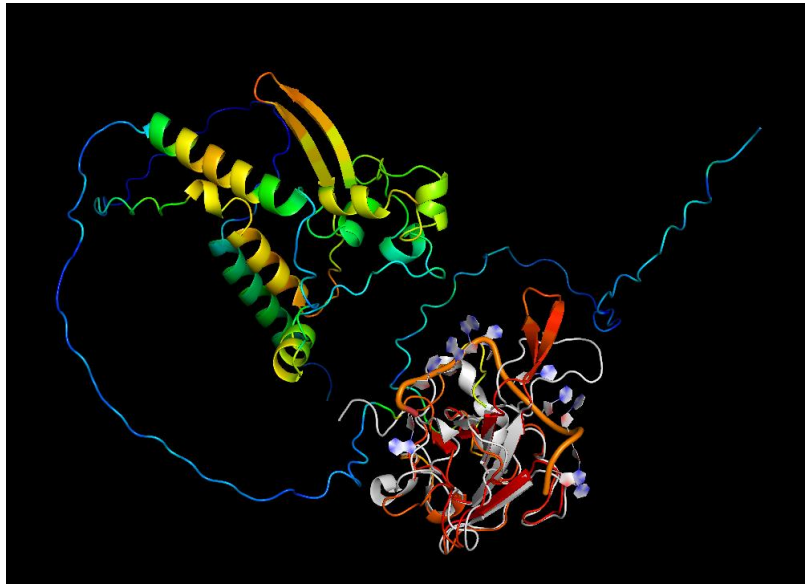
Modře označena N terminální doména
Žlutě vazebné místo

https://molstar.org/

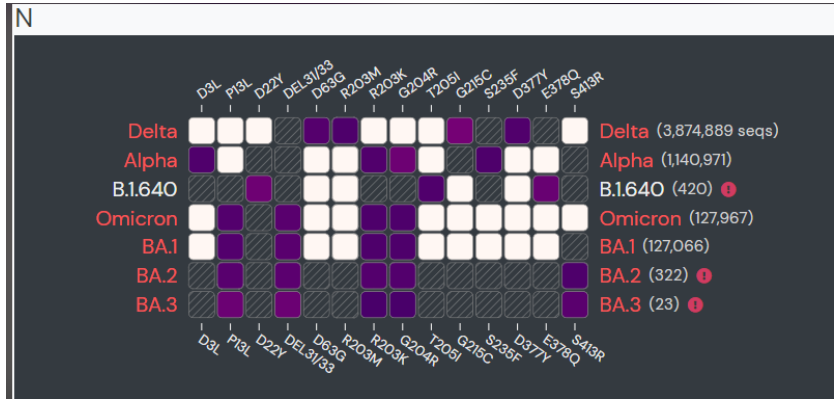
Strukturní modely glykosylace spike a spike omikronu
autor Karel Berka

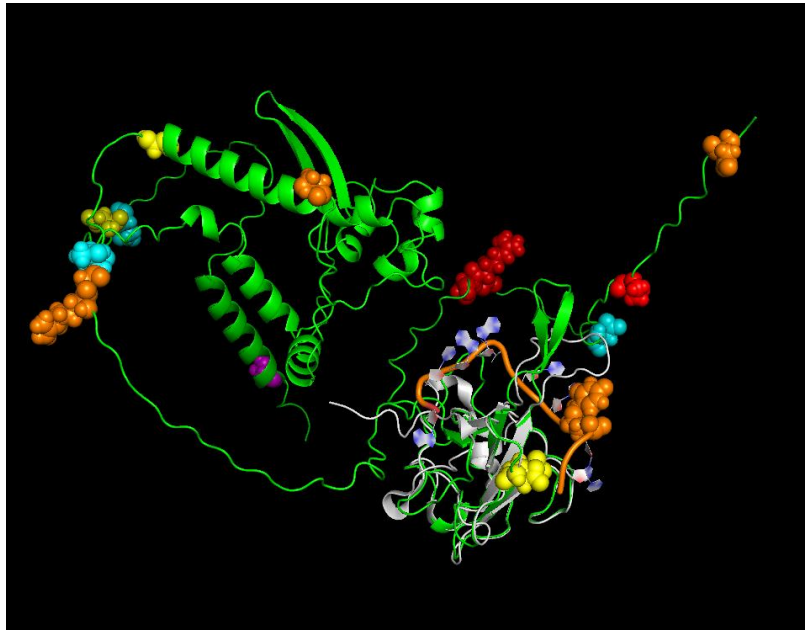
Ve vedlejší roli nukleokapsiodvý protein Jsou Ag testy funkční?

N-term domain binds RNA
C-term domain binds other N proteins
monoclonal IG-light lambda binds to N-term domain
IG-heavy bind to both domains
MHC binds to both and to unstructured linker
HLA binds to N-term domain



Bílá
struktura z s navázaným RNA
barvy označující lokální kvalitu modelu
(AlphaFold)



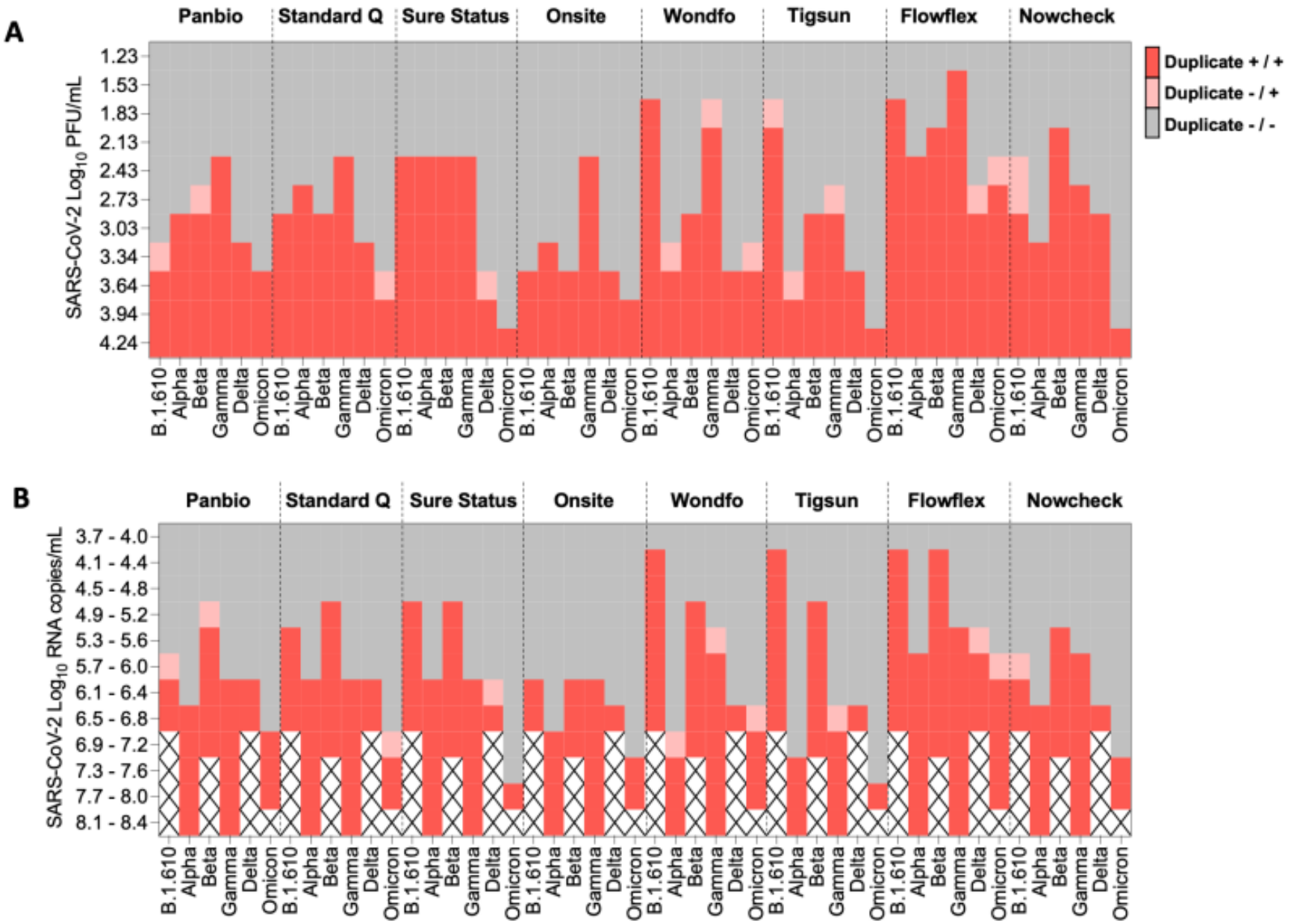


N - 2 domény propojené flexibilními linkery.
Na jednu doménu je navázána ssRNA
(Václav Veverka – UOCHB)

Delta - žlutá
B.1.640 - bledě modrá
Alpha - oranžová
Omikron - červená
(+ dost těch oranžových z Alfy)
BA.2 - fialová (+červená Omikronu)

Strukturní modely a popis
autor Karel Berka

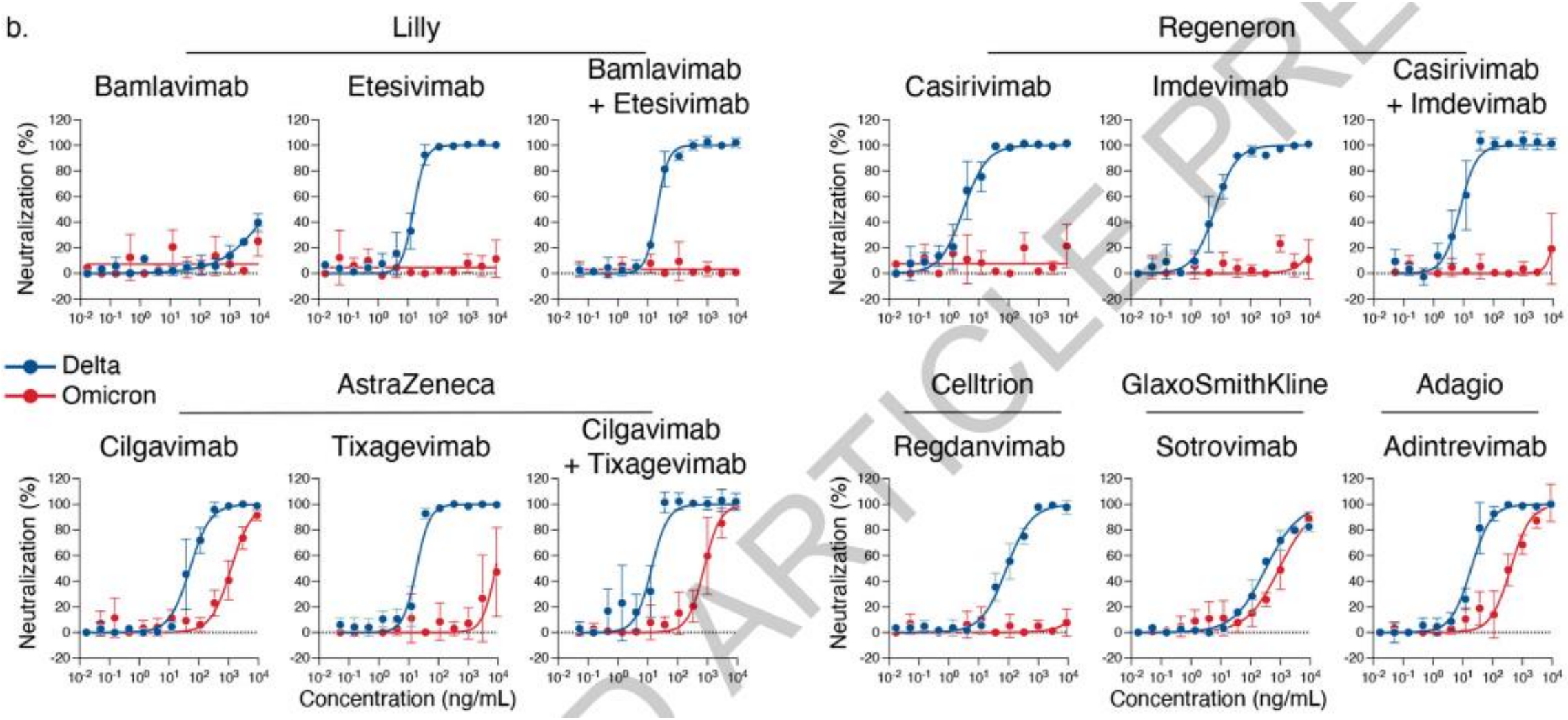
AG testy x VOC



medRxiv preprint doi: https://doi.org/10.1101/2021.12.18.21268018; this version posted January 17, 2022. The copyright holder for this preprint **(which was not certified by peer review)** is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.

nature
https://doi.org/10.1038/s41586-021-04389-z
Accelerated Article Preview

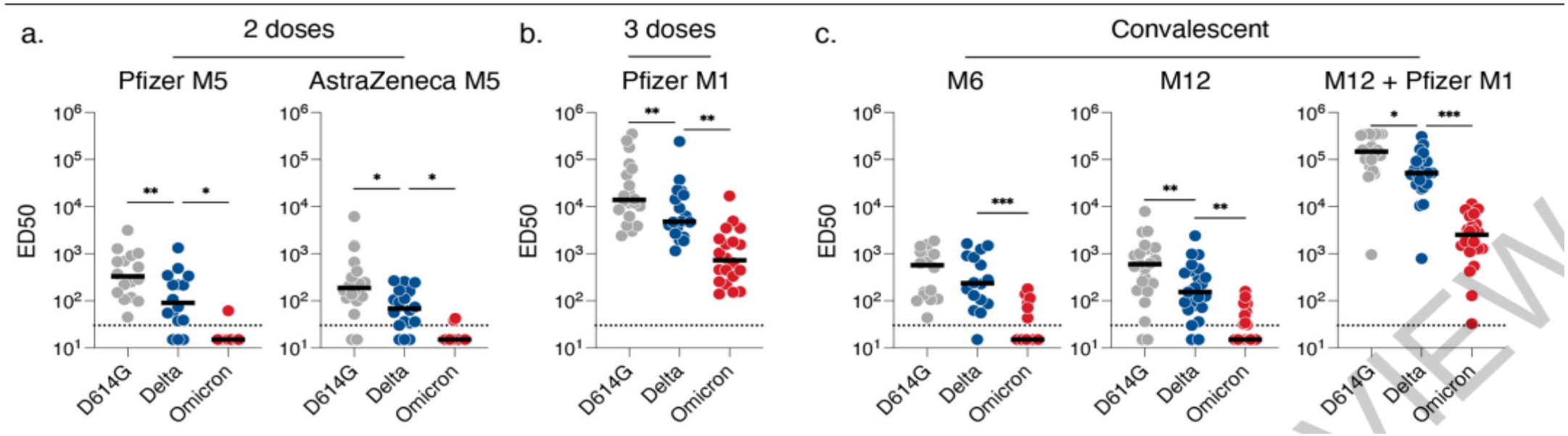
Considerable escape of SARS-CoV-2 Omicron to antibody neutralization



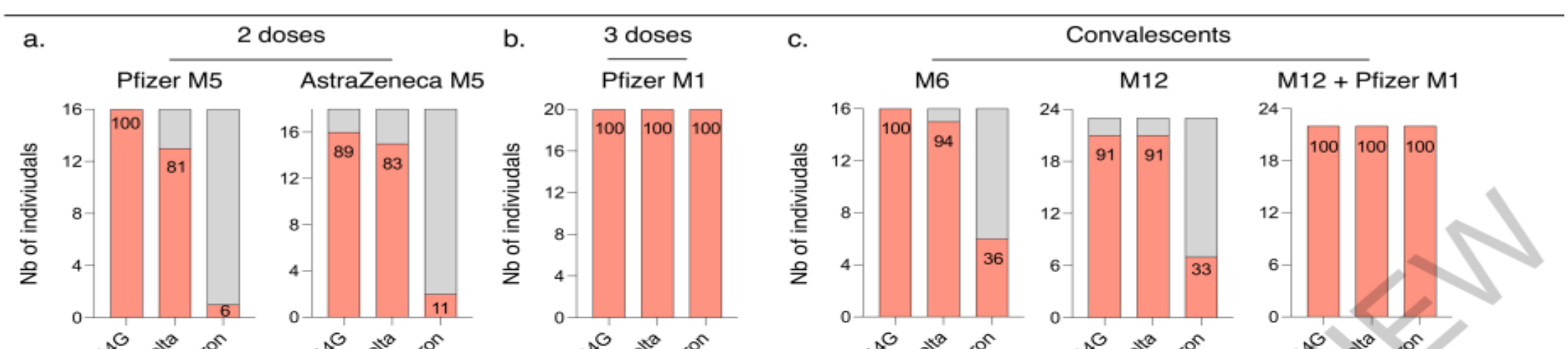
ARTICLE PREVIEW

nature
https://doi.org/10.1038/s41586-021-04389-z
Accelerated Article Preview

Considerable escape of SARS-CoV-2 Omicron to antibody neutralization



VNT



Podíl osob s dostatečným VNT ED50 > 30

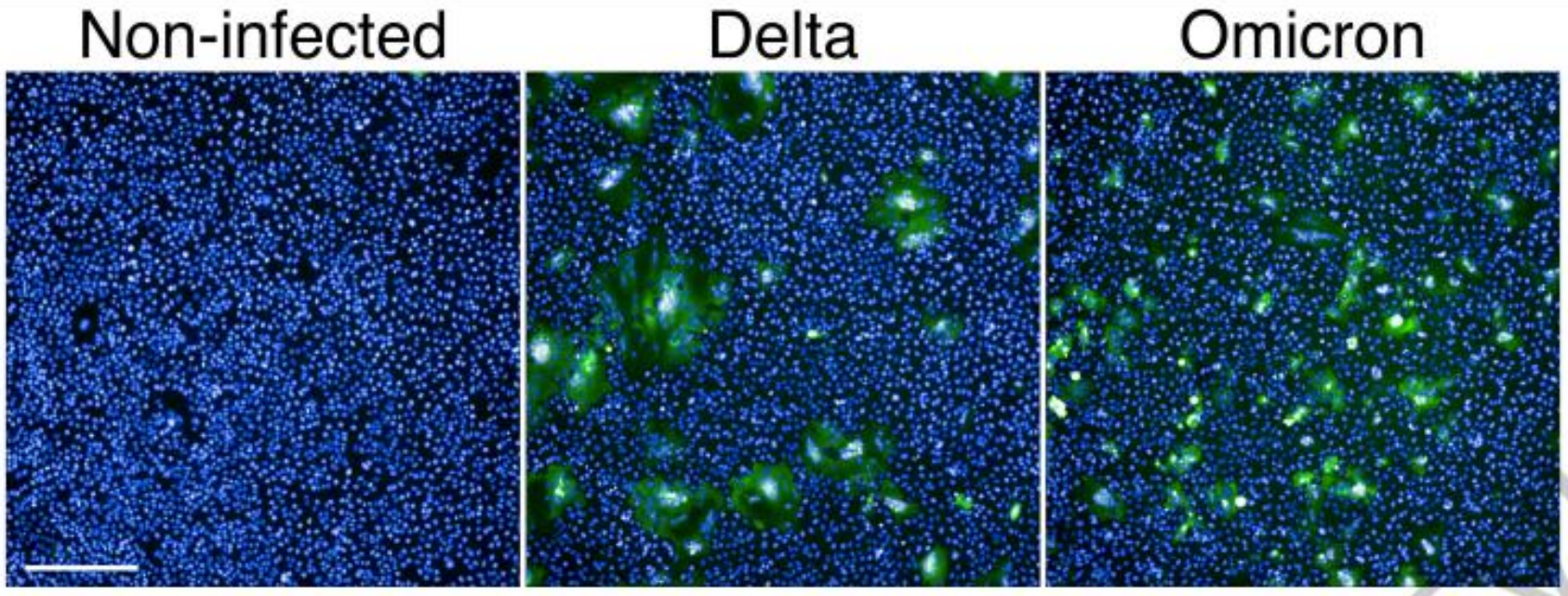
nature

https://doi.org/10.1038/s41586-021-04389-z

Accelerated Article Preview

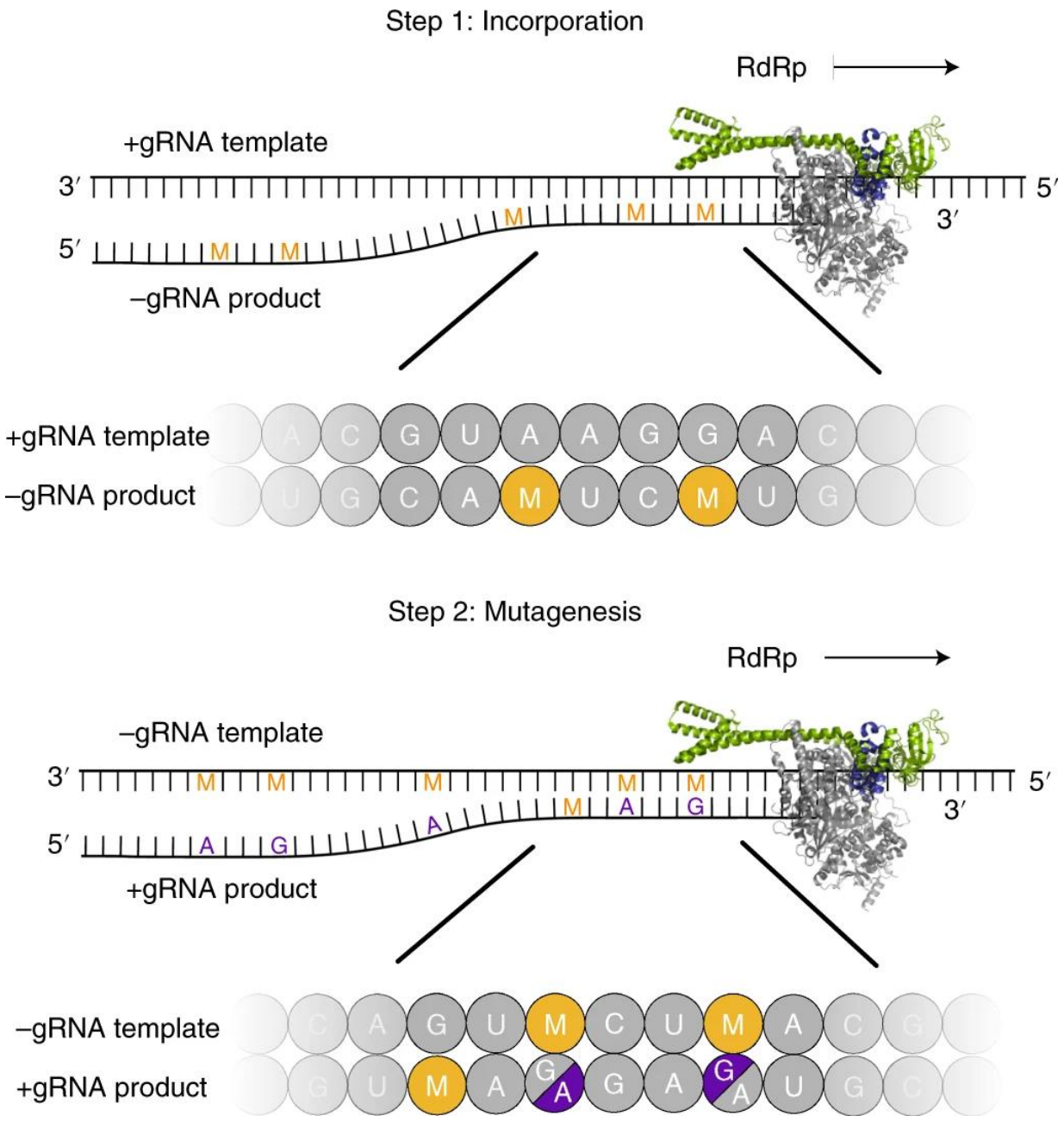
Considerable escape of SARS-CoV-2 Omicron to antibody neutralization

Article



Extended Data Fig. 1 | SARS-CoV-2 variants induce syncytia in S-Fuse cells. S-Fuse cells were exposed to the indicated SARS-CoV-2 strains, at a multiplicity of infection (MOI) of 10^{-3}. The cells become GFP+ when they fuse together. After 20 h, infected cells were stained with Hoechst to visualize nuclei (green) and nuclei (blue) are shown. Representative images from three independent experiments are shown. Scale bar, 500 µm.

Mechanism of molnupiravir-induced SARS-CoV-2 mutagenesis

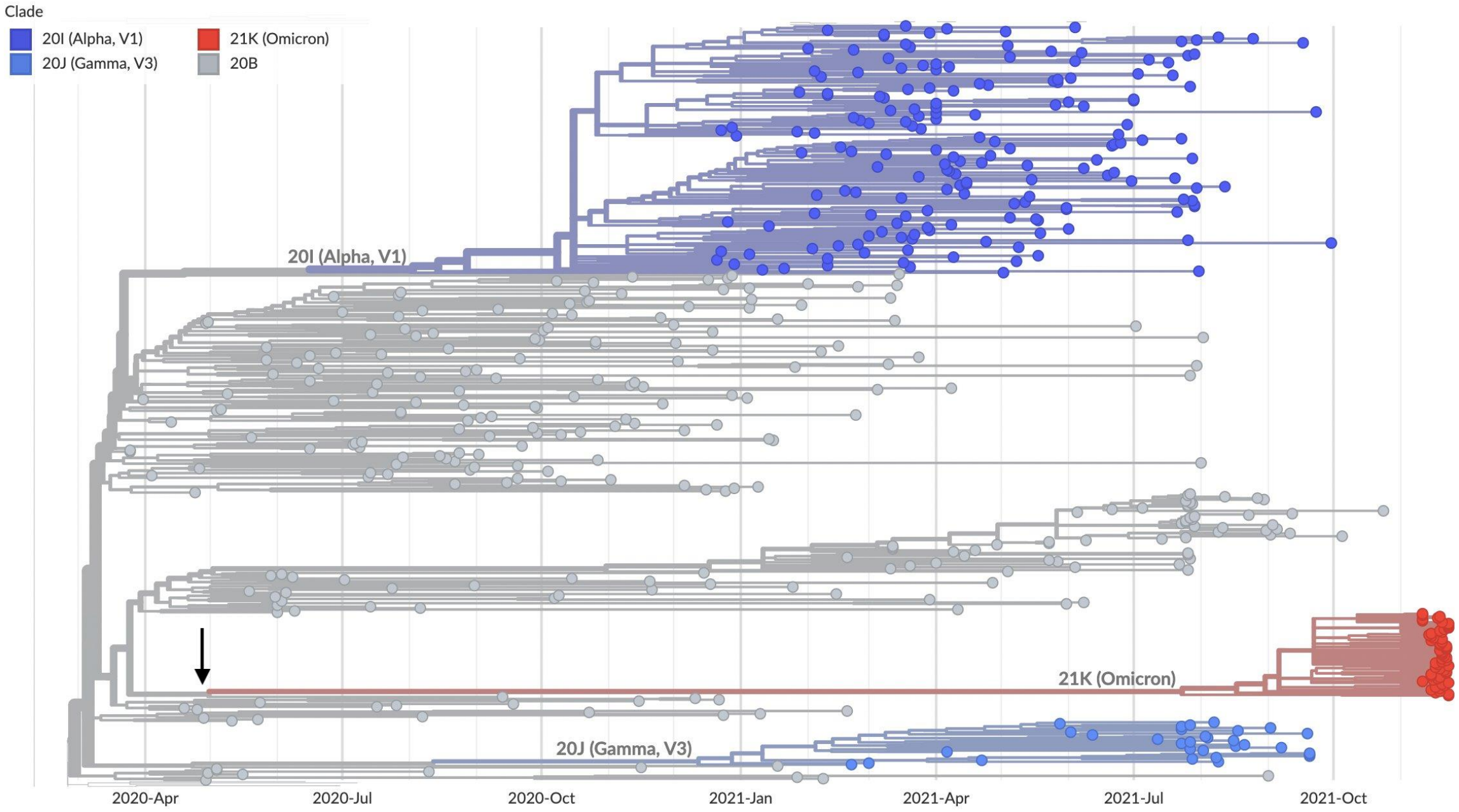


In the presence of NTPs and MTP, M nucleotides can be incorporated by SARS-CoV-2 RdRp instead of C or U into the negative-strand genomic (−gRNA) or subgenomic RNA (−sgRNA) during copying of the positive-strand genomic RNA template (+gRNA). The obtained M-containing negative-strand RNAs can then be used as a template for the production of mutagenized +gRNA and positive-strand subgenomic mRNA (+sgmRNA). These RNA products are predicted to be mutated and not to support formation of functional viruses. RNA of random sequence is shown, with M and mutated residues indicated as orange and violet letters, respectively.

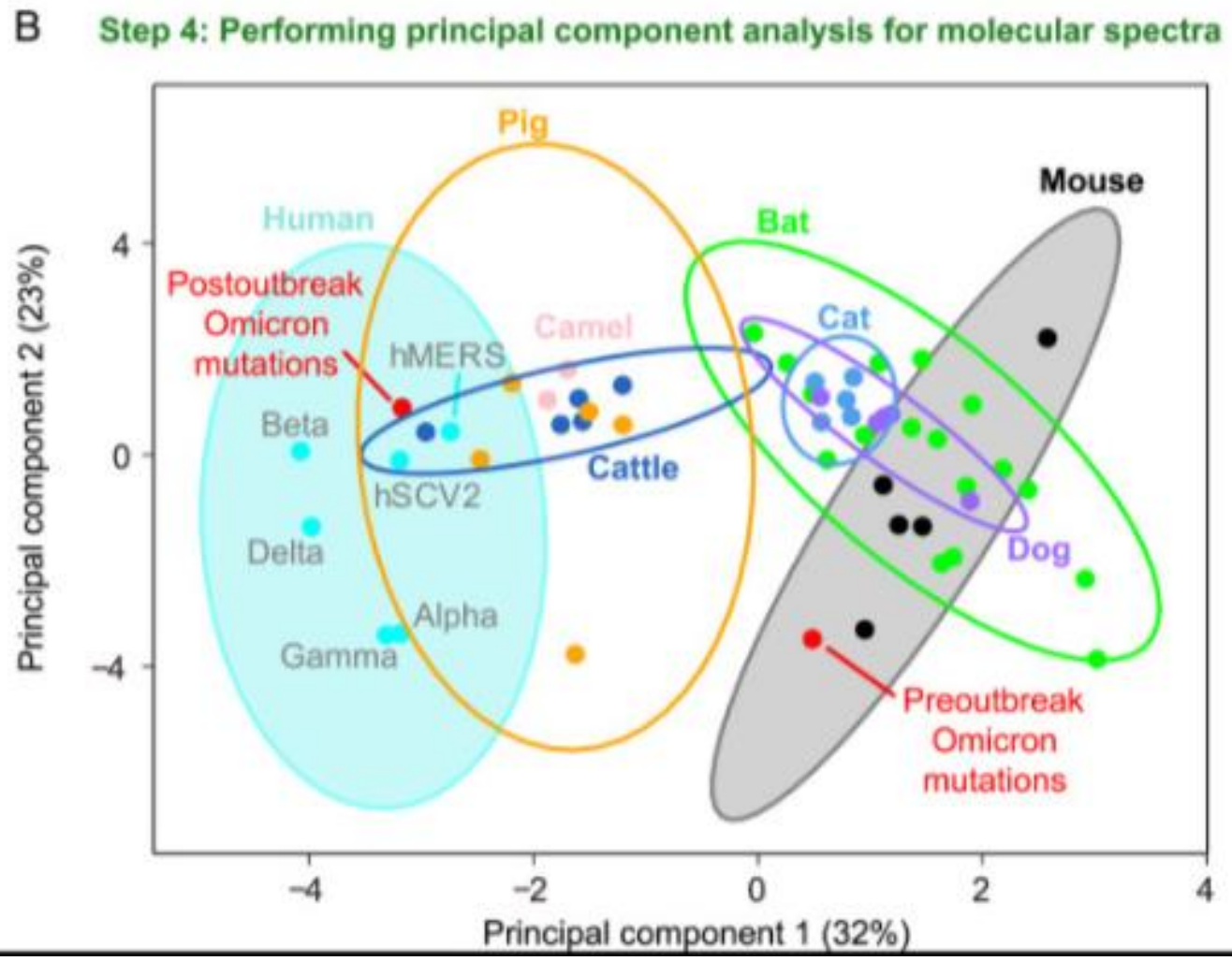
Nature Structural & Molecular Biology (*Nat Struct Mol Biol*) ISSN 1545-9985 (online) ISSN 1545-9993 (print)

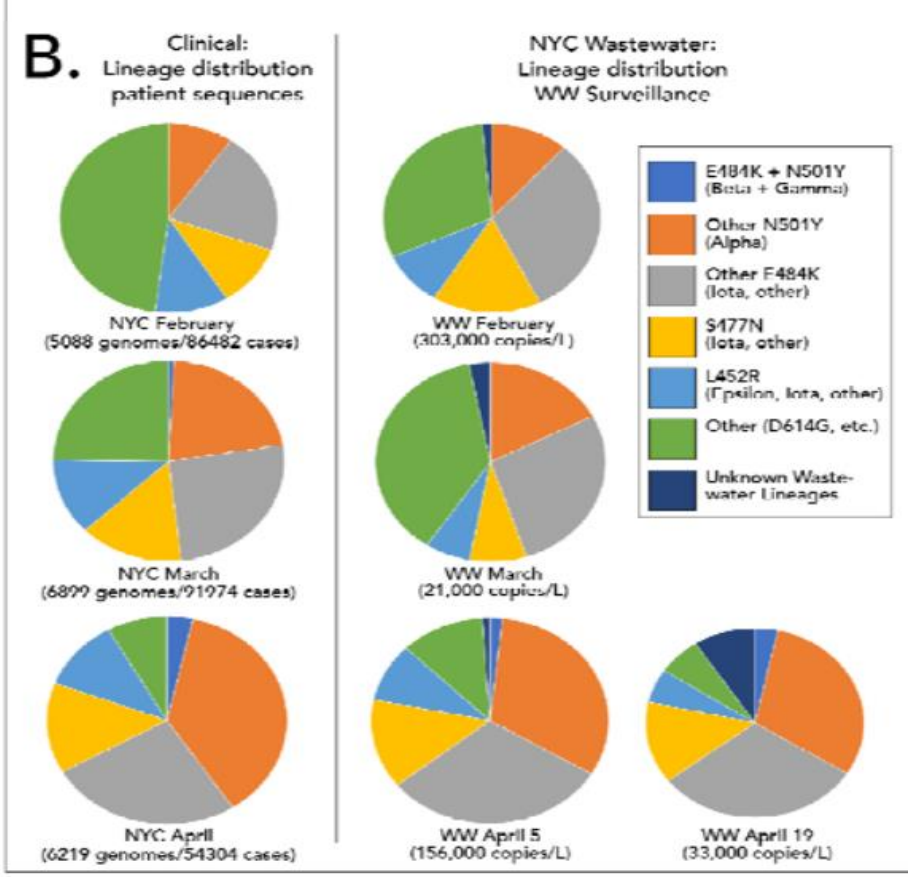
- Můžeme predikovat další vlnu/y?
- Omikron – původ- reintrodukce?
- Zoonotické rozšíření?
- Jsou ohroženy další druhy?

Omikron – původ?



Omikron – původ – reintrodukce – myš?





NY – monitoring odpadních vod

od února atypické mutace: Q493K, Q498Y, H519N and T572N.

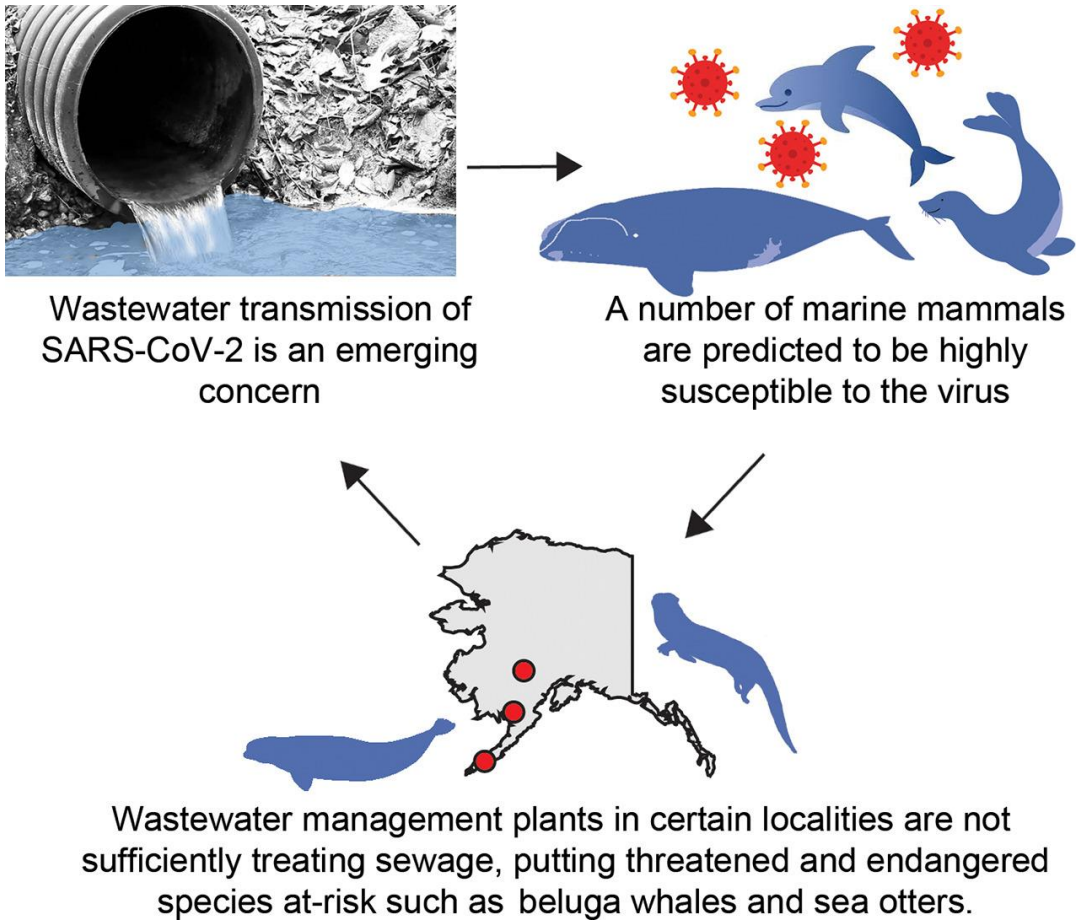
Rozšíření tropismu SARS-CoV-2 pseudoviru – infekce buněk s lidským/myším/krysím ACE2.

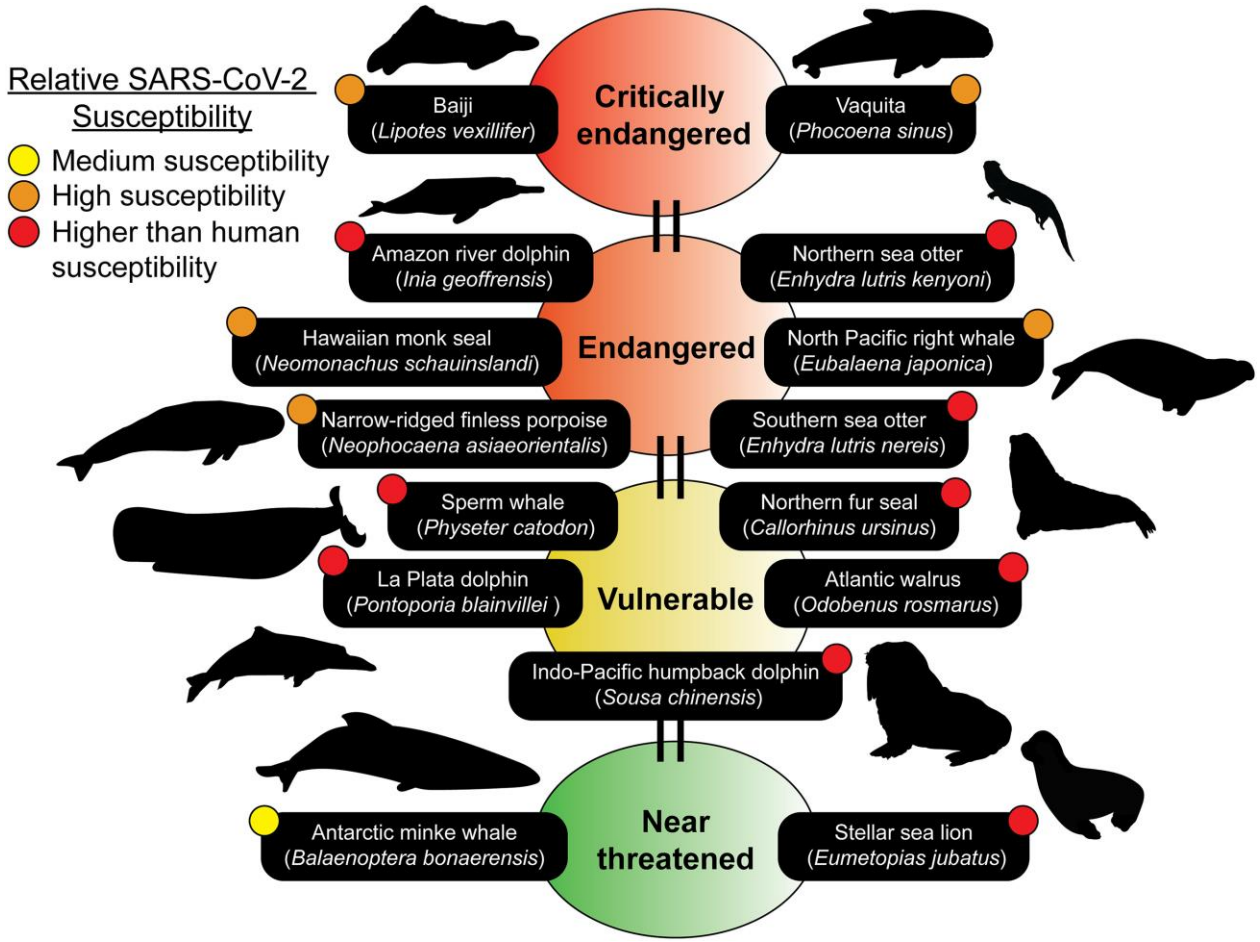
Rezistence vůči MAB

Wei C, Shan KJ, Wang W, Zhang S, Huan Q, Qian W. Evidence for a mouse origin of the SARS-CoV-2 Omicron variant. J Genet Genomics. 2021 Dec 24:S1673-8527(21)00373-8. doi: 10.1016/j.jgg.2021.12.003. Epub ahead of print. PMID: 34954396; PMCID: PMC8702434.

medRxiv preprint doi: https://doi.org/10.1101/2021.07.26.21261142; this version posted July 29, 2021.

Odpadní vody a možnost šíření SARS-CoV-2





https://doi.org/10.1016/j.scitotenv.2020.143346

NY TIMES https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html

Enabled by hCoV-19 data shared via GISAID

GISAID
ECDC/CDC/WHO
PROMEDMAIL
PANGO-LINEAGES
NEXSTSTRAIN
NEXTCLADE
OUTBREAK.INFO
COVPSECTRUM
COVARIANTS

ZPRÁVY Z NRL – JEN ČÁST: http://www.szu.cz/tema/prevence/laboratore

Info k SARS/chřipka : Alena Janypková – alena.janypkova@szu.cz
Helena Jiřincová – helena.jirincova@szu.cz

Tel. Kontakt NRL – 724 362 602

Děkuji za pozornost

Smích je z hlediska možné náhlazy nebezpečnější než kašel.
My už se postaráme o to, aby vás brzy přešel.

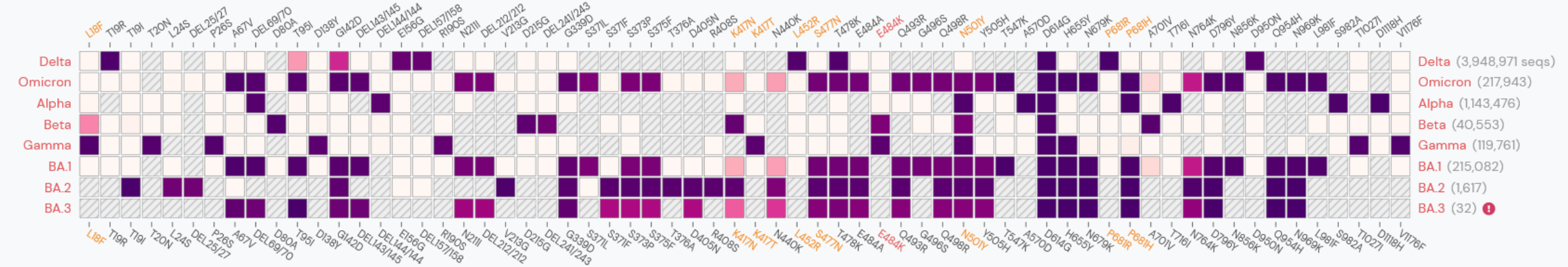
Odborná doporučení NRL. Diskriminační PCR

Diskriminační PCR:

- Dle mimořádného opatření MZČR všechny symptomatické pozitivní případy SARS-CoV-2 musí být konfirmovány diskriminační PCR
- Pro první orientaci je možno vycházet pouze z negativity L452R, v tomto případě je třeba pamatovat, že vzorky vykazující vyšší Ct hodnoty mohou být ve stanovovaní L452R falešně negativní.
- V případě indikace léčby monoklonálními protilátkami je nutné přesnější určení varianty omikron, nestačí jen vyloučení pozitivity L452R a E484K.
- Pouze negativita delece 69_70 nemusí znamenat vyloučení varianty omikron, ale může se jednat o subvariantu BA.2.
- Suspektní omikron doporučujeme určovat na základě negativity L452R a jedné z těchto pozitivních mutací: N501Y, P681H, Del69_70, K417N nebo S371L pozitivní S373P, E484A pozitivní, Y505H pozitivní, T547K pozitivní.

Matice mutací: jsou zahrnuty i varianty BA.1, BA.2, BA.3

Zdroj: outbreak.info



Project „Enhancing Whole Genome Sequencing (WGS) and/or Reverse Transcription Polymerase Chain Reaction (RT-PCR) national infrastructures and capacities to respond to the Covid-19 pandemic in the European Union and European Economic Area“ had received funding from the European Centre for Disease Prevention and Control under the Grant Agreement number ECDC/HERA/2021/004 ECD.12218.

EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

More information about the project: http://www.szu.cz/ecdc-1

NOTE:

Information included reflects only the authors‘ view and the Centre (ECDC) is not responsible for any use that may be made of the information it contains.