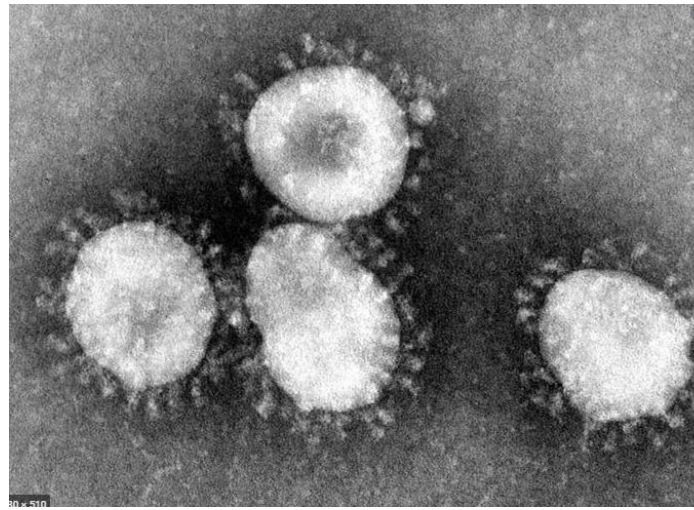
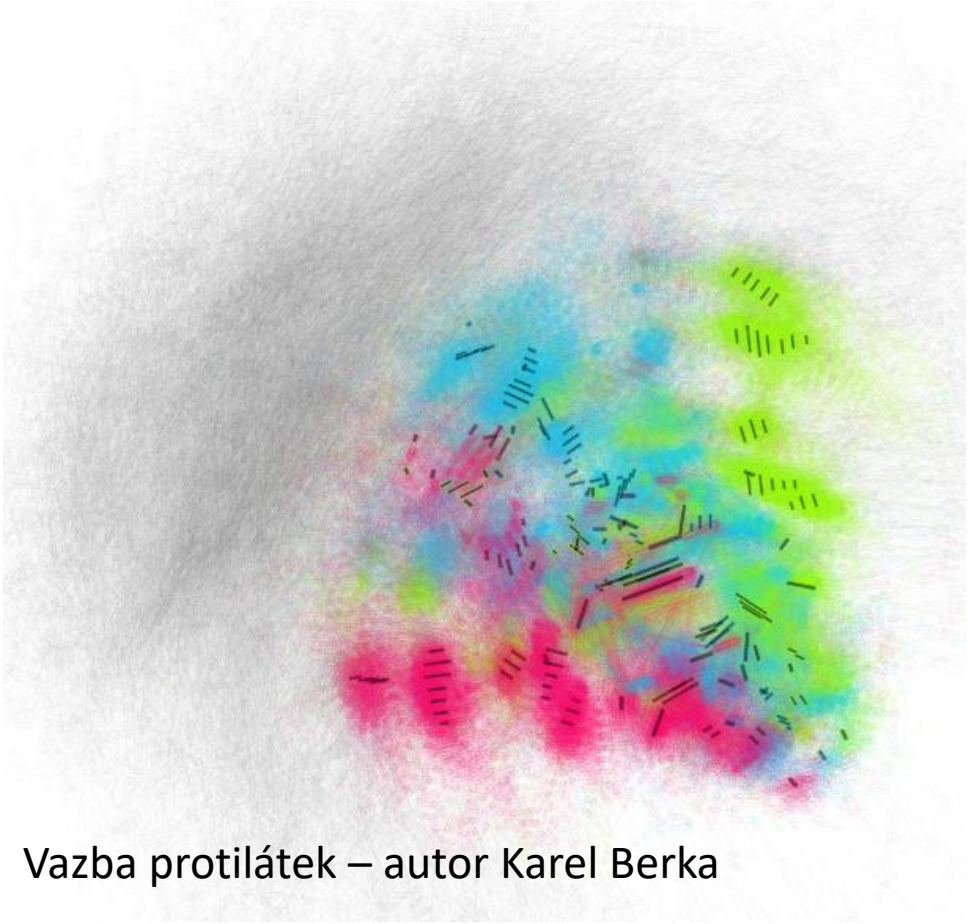
SARS-CoV-2

NRL pro chřipku a nechřipková virová respirační onemocnění

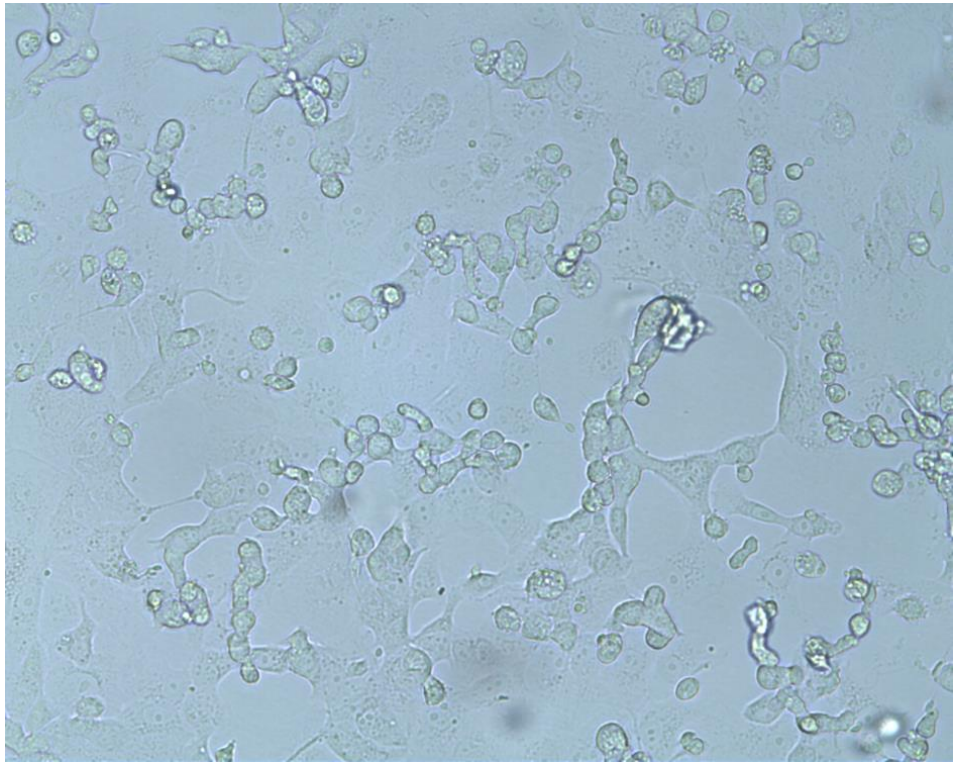
Helena Jiřincová, SZÚ

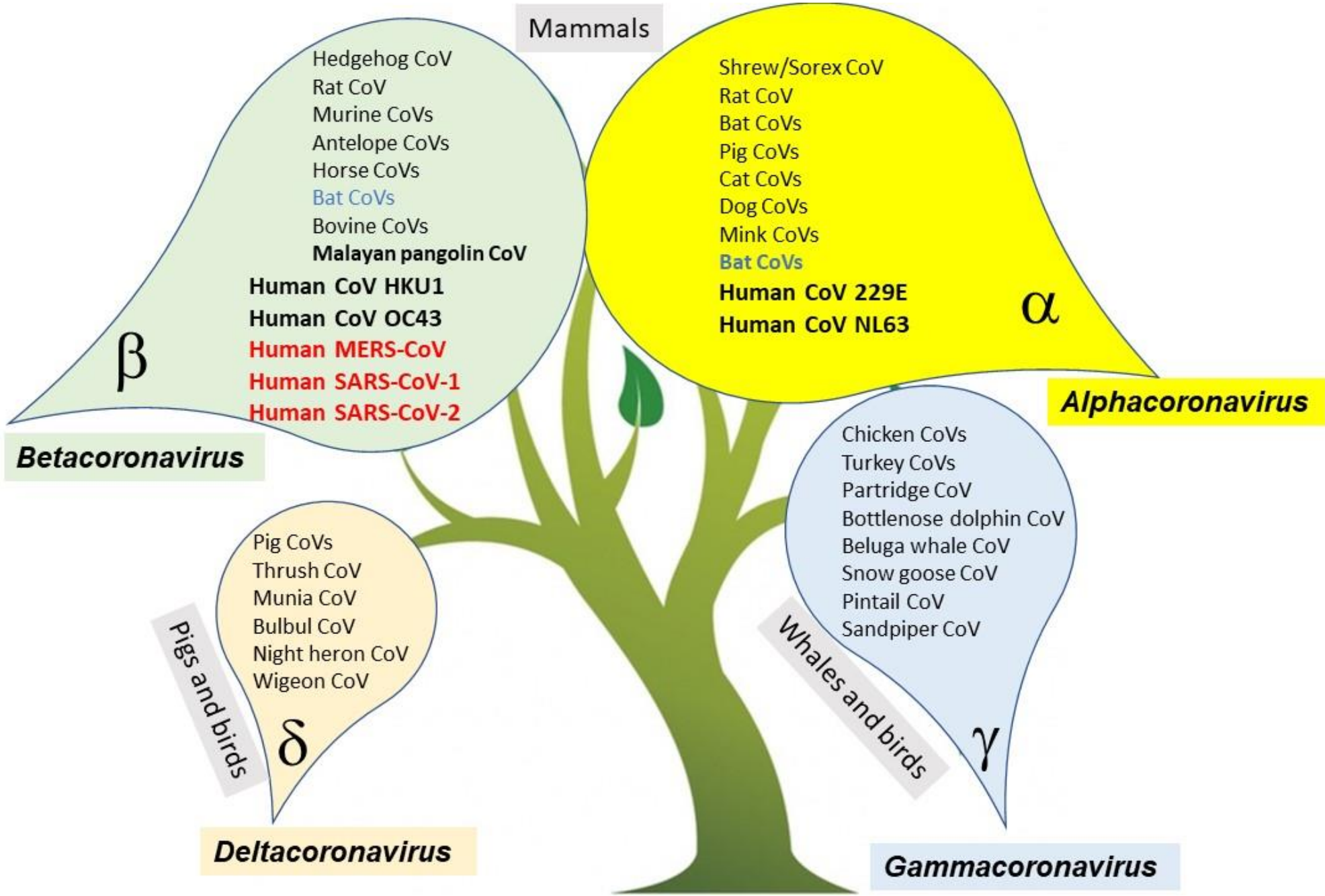




Vazba protilátek – autor Karel Berka

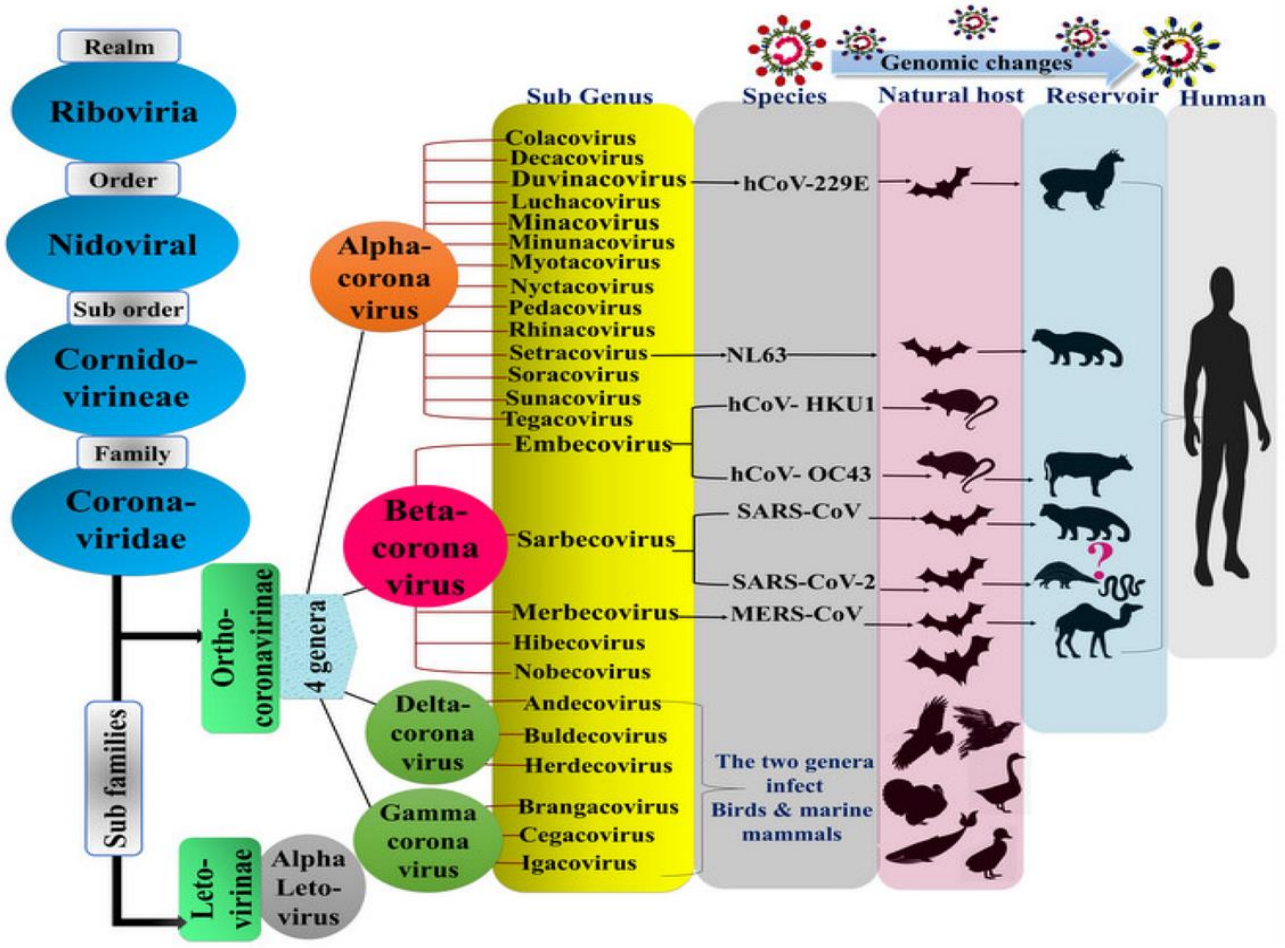
Omicron



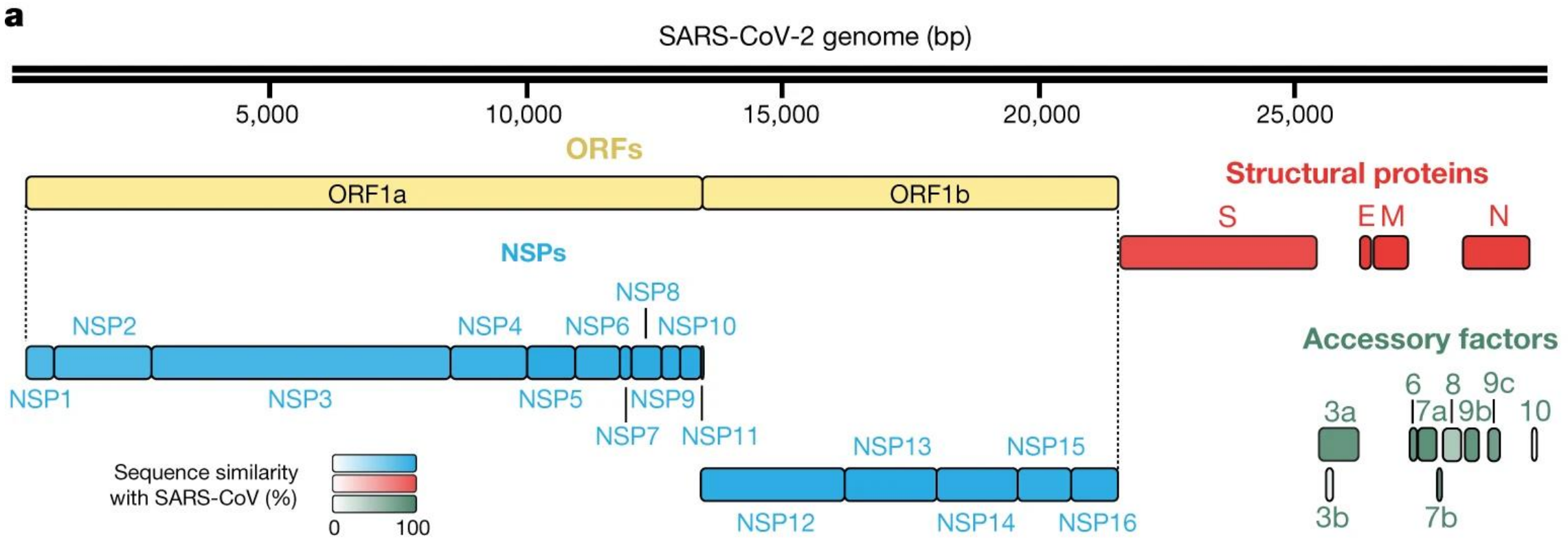

Mammals
Hedgehog CoV
Rat CoV
Murine CoVs
Antelope CoVs
Horse CoVs
Bat CoVs
Bovine CoVs
Malayan pangolin CoV
Human CoV HKU1
Human CoV OC43
Human MERS-CoV
Human SARS-CoV-1
Human SARS-CoV-2
β
Betacoronavirus
Shrew/Sorex CoV
Rat CoV
Bat CoVs
Pig CoVs
Cat CoVs
Dog CoVs
Mink CoVs
Bat CoVs
Human CoV 229E
Human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

Specifické vlastnosti SARS-CoV-2

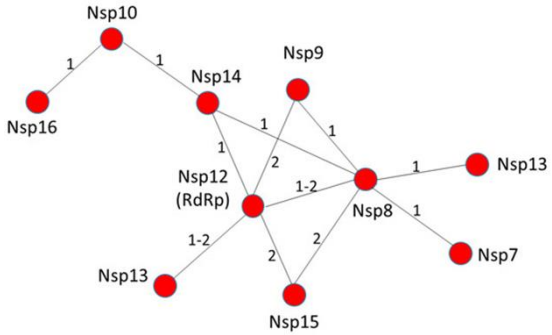
- Ribosomal frame shift
- Exonukleasová aktivita
- Inhibice MHC I prezentace
- Inhibice produkce IFN gamma – inátní imunitní obrana
- Inhibice IFN alfa dráhy – tehtherin (brání odštěpení viru z buňky)
- Furinové štěpné místo – specifiky vstup do buňky + aktivace tvorby syncitií



SARS-CoV-2 – strukturální a nestrukturální proteiny



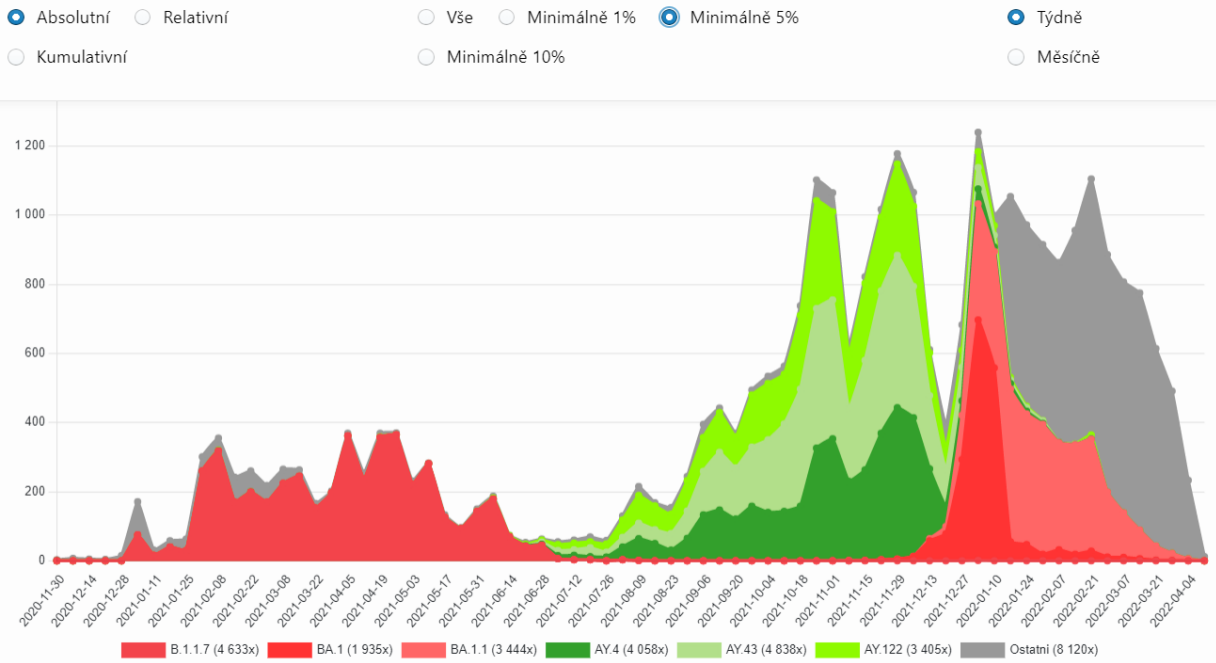
Nature (Nature) ISSN 1476-4687 (online) ISSN 0028-0836 (print)

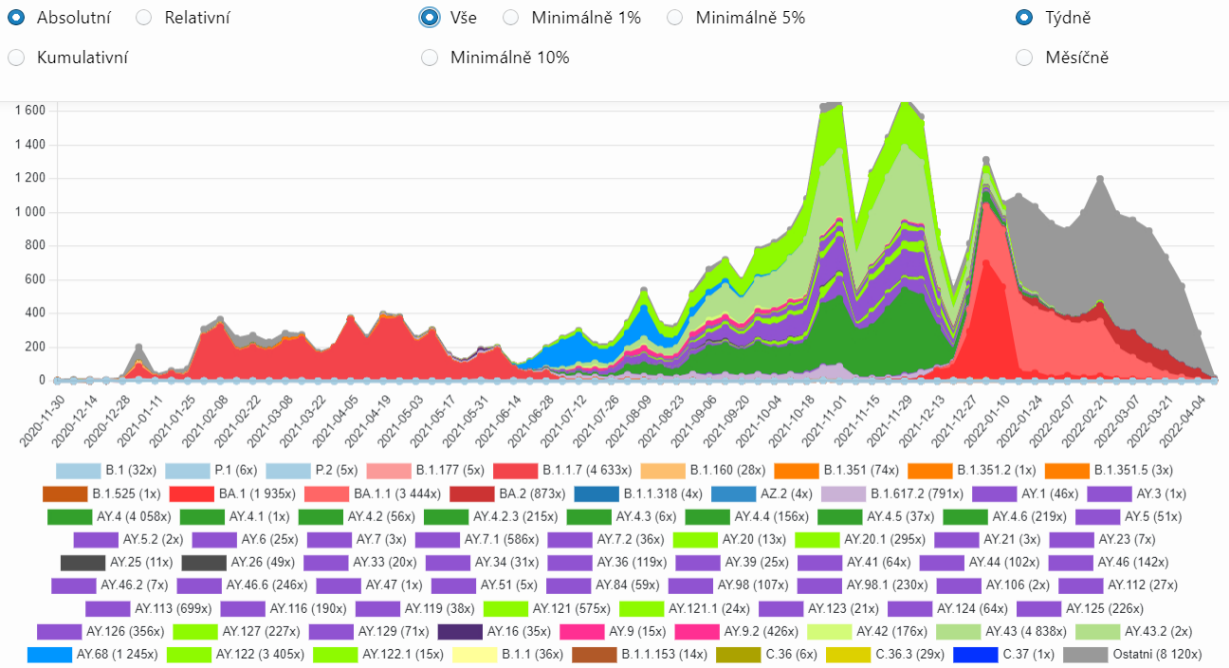


NSP 14 – proofreading exonuclease

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

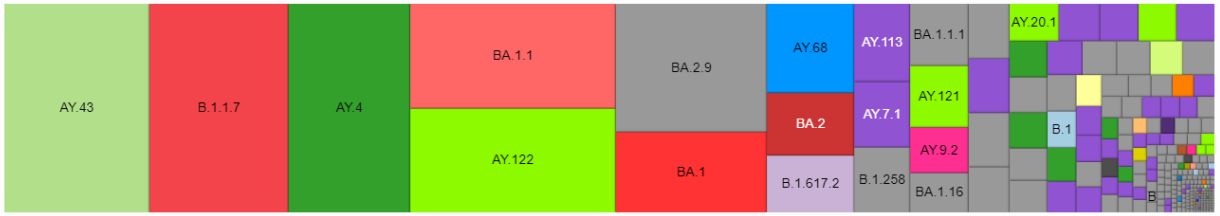
Evoluce SARS – CoV-2 za období 1. 12. 2020 až 28. 5. 2022





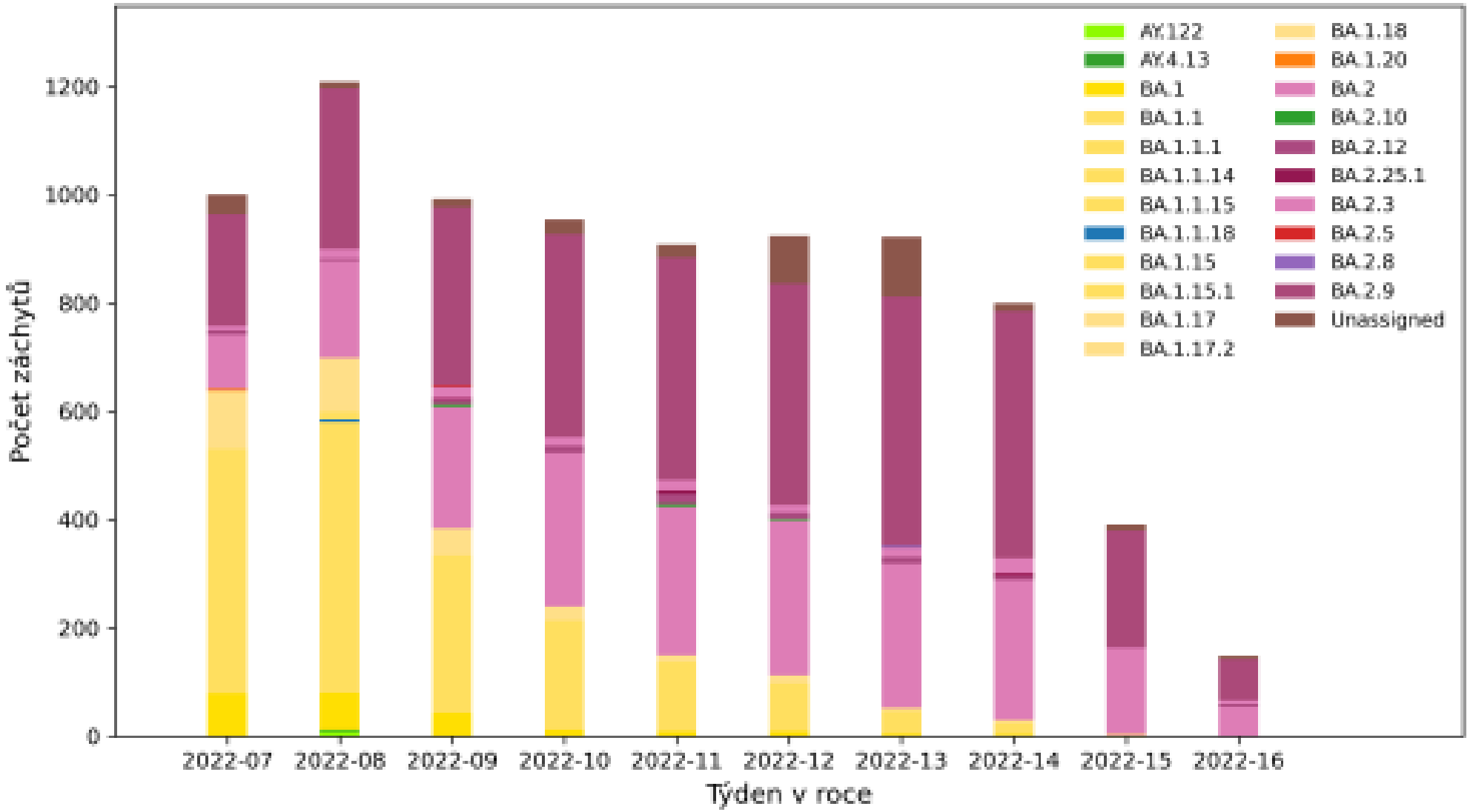
Linie SARS-CoV-2 detekované v Česku (celé období)

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

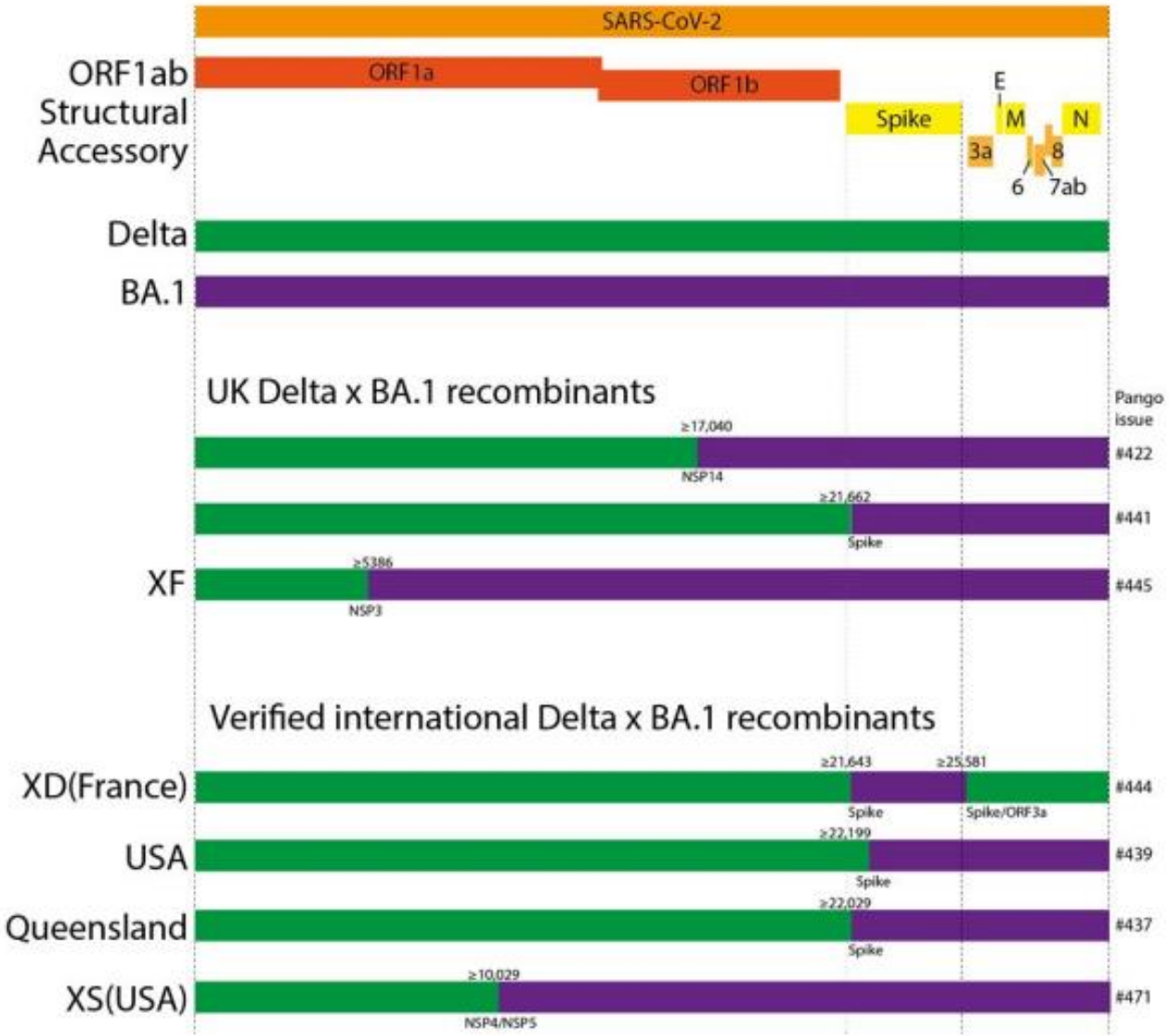


COG CZ: https://virus.img.cas.cz/

Časový vývoj viru SARS-CoV-2 na území ČR od 7. do 18. týdne 2022



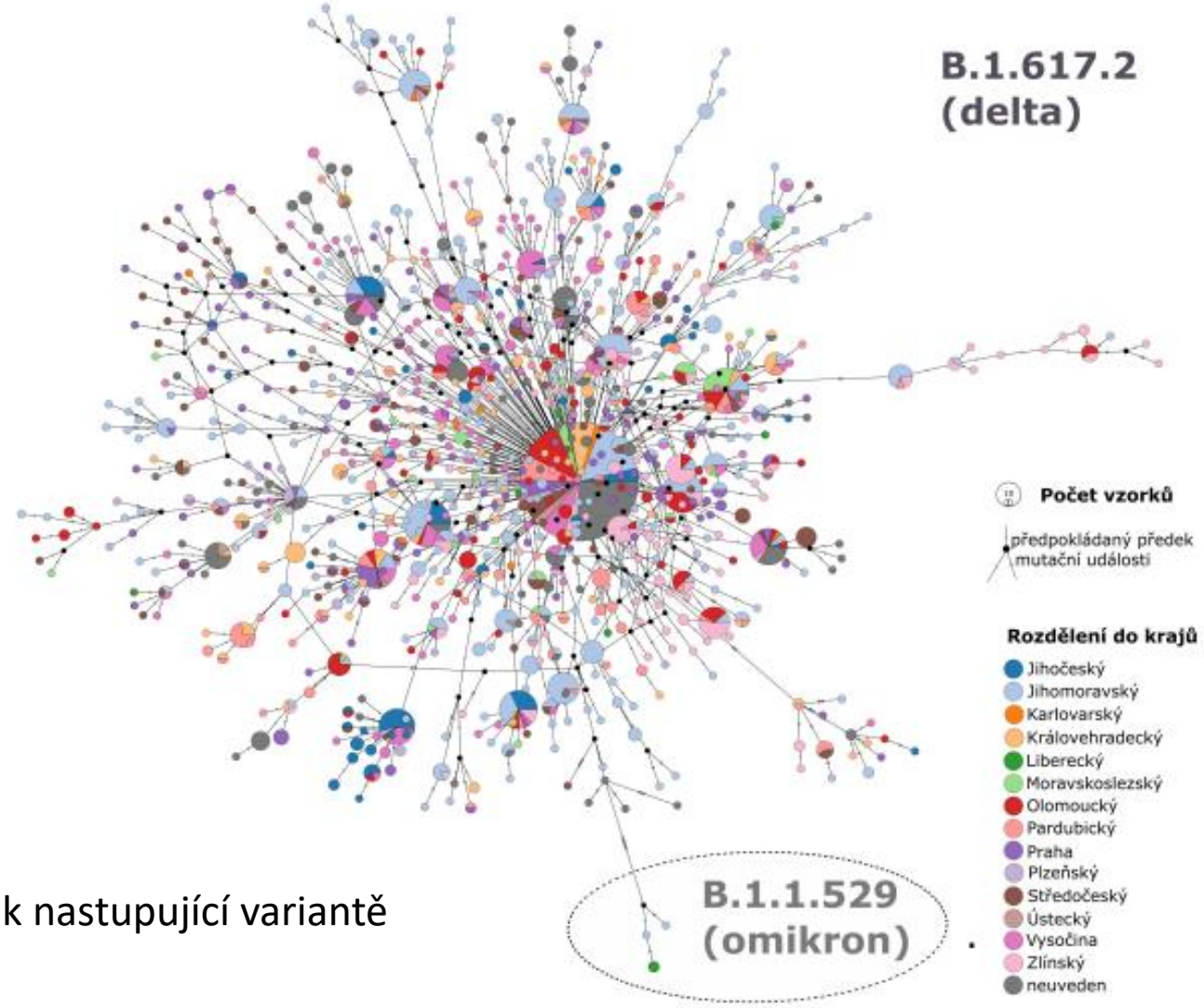
Rekombinantní varianty



Znázornění variant SARS-CoV-2 v haplotypové síti

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

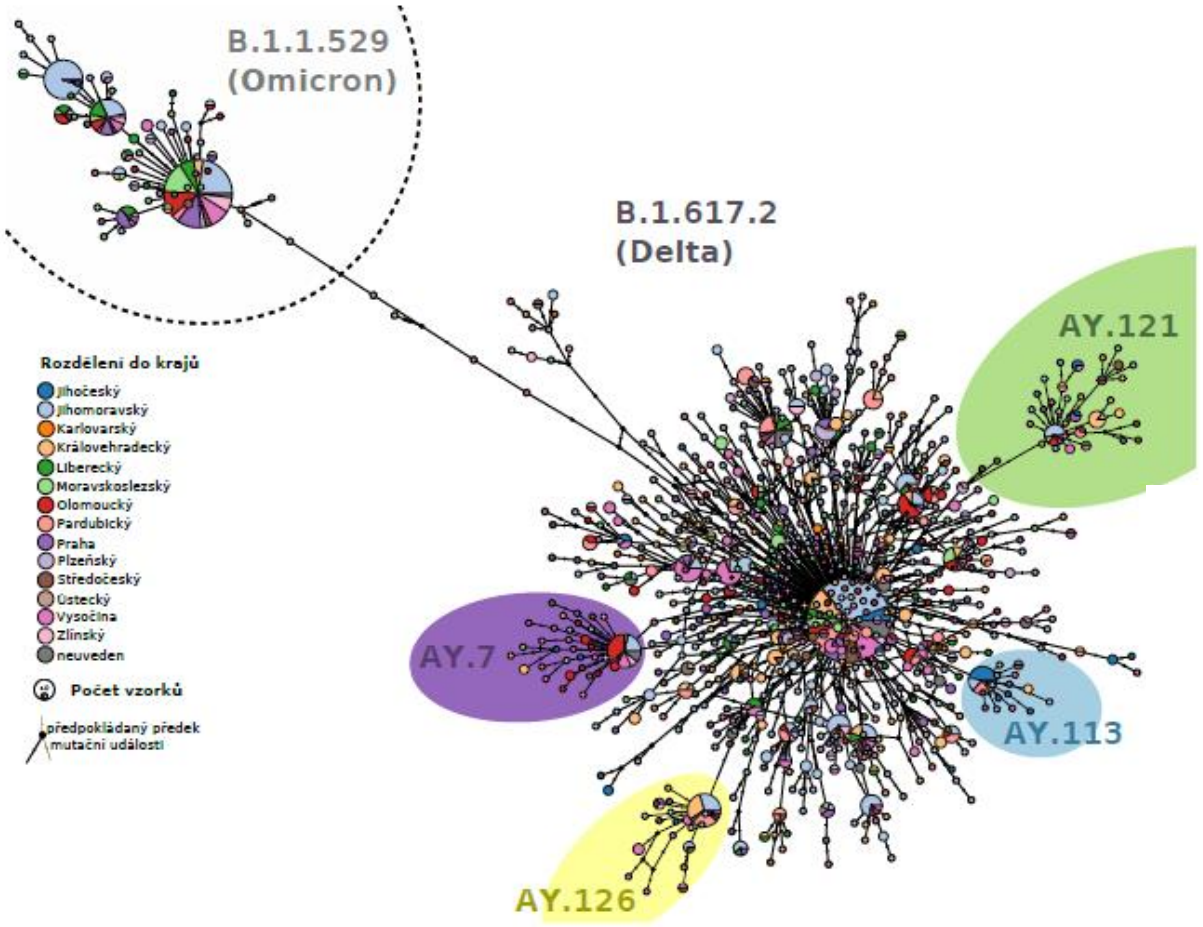
Velikost uzlů – dle počtu vzorků
s identickou sekvencí.
Spojnice naznačují pravděpodobné
příbuzenské vztahy,
počet krátkých kolmých úseček
odpovídá počtu mutačních



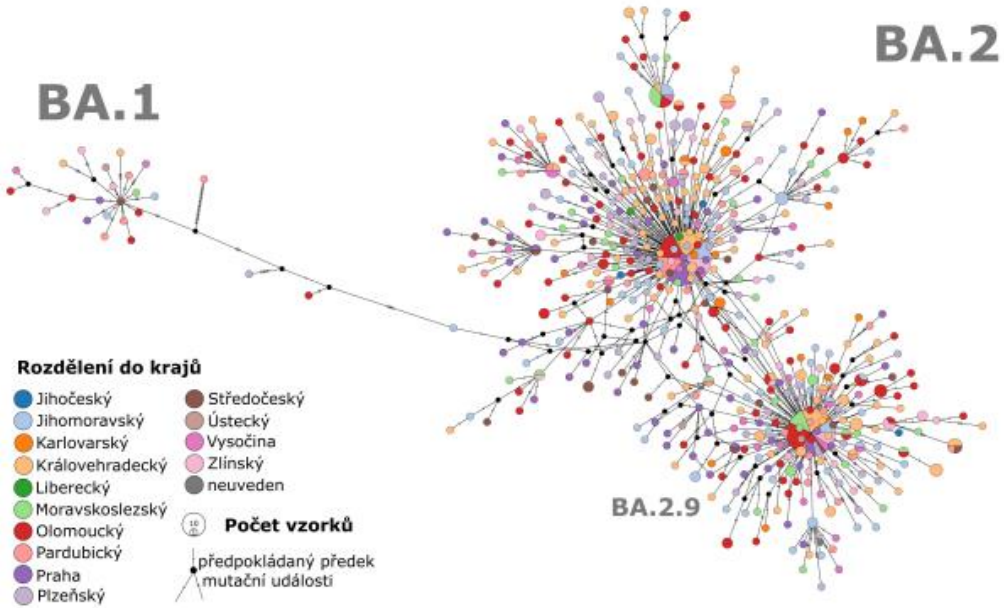
Tři sekvence v dolní části grafu náleží k nastupující variantě
Omicron (B.1.1.529)

Autor: Vladimír Hampl

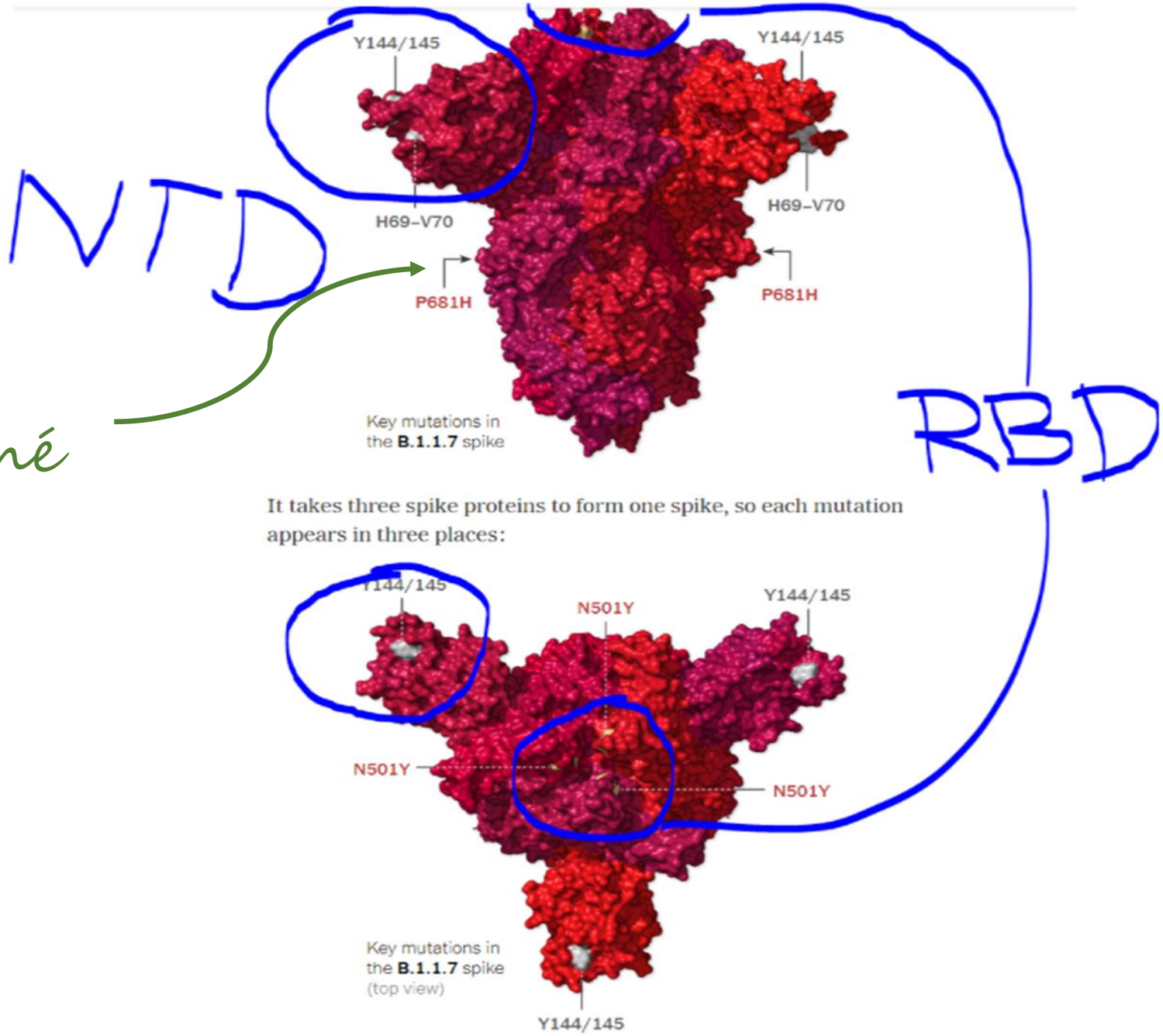
Haplotypoá analýza 1 796 WGS



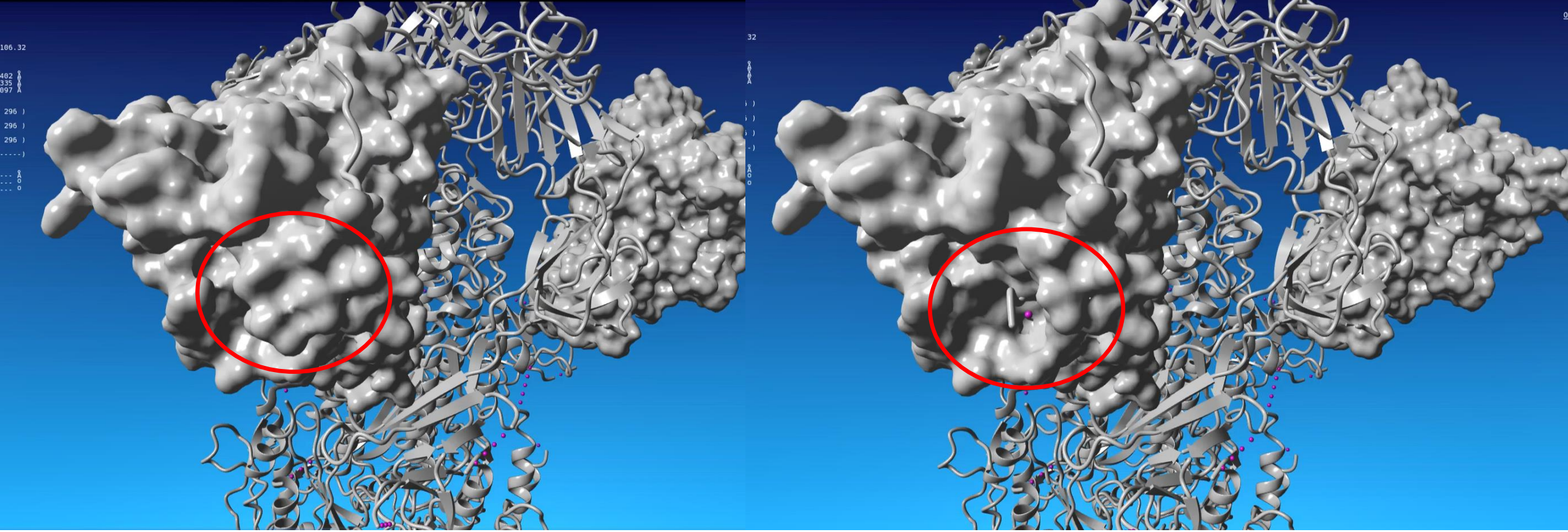
700 vzorků z České republiky shromážděných od 1. 4. 2022.



Furinové štěpné místo

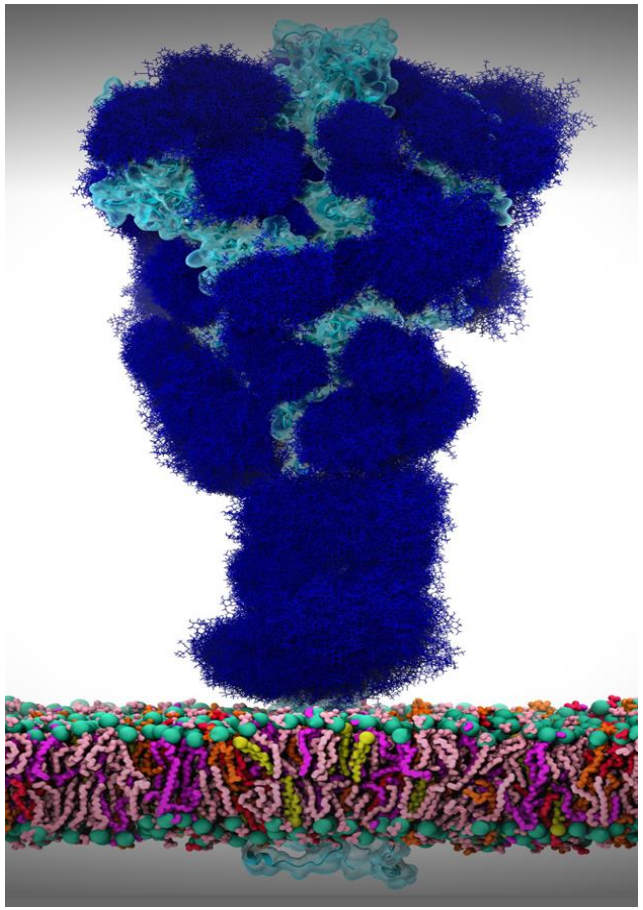


For more on the B.1.1.7 mutations, see: Inside the B.1.1.7

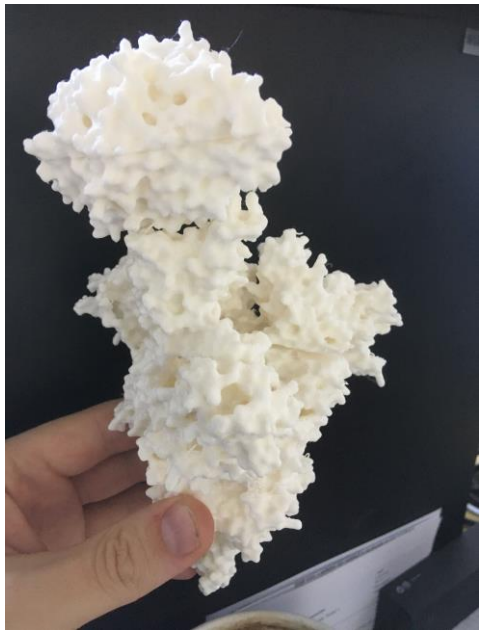


Delece 6 nukleotidů, tedy 2 aminokyselin (69 histidin, 70 valin) v N-terminální doméně spike proteinu - boční pohled (model dle rentgenostrukturní analýzy – SVU+SZU)

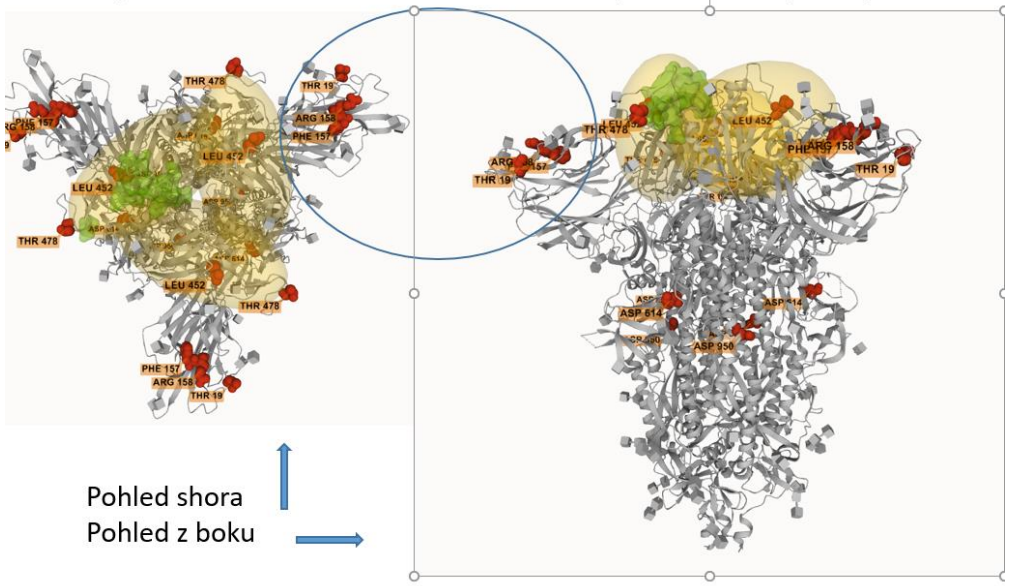
V hlavní roli spike



omikron



Aminokyselinové substituce charakteristické pro B.1.617.2 (delta)



Modře označena N terminální doména
Žlutě vazebné místo

https://molstar.org/

Strukturní modely glykosylace spike a spike omikronu
autor Karel Berka

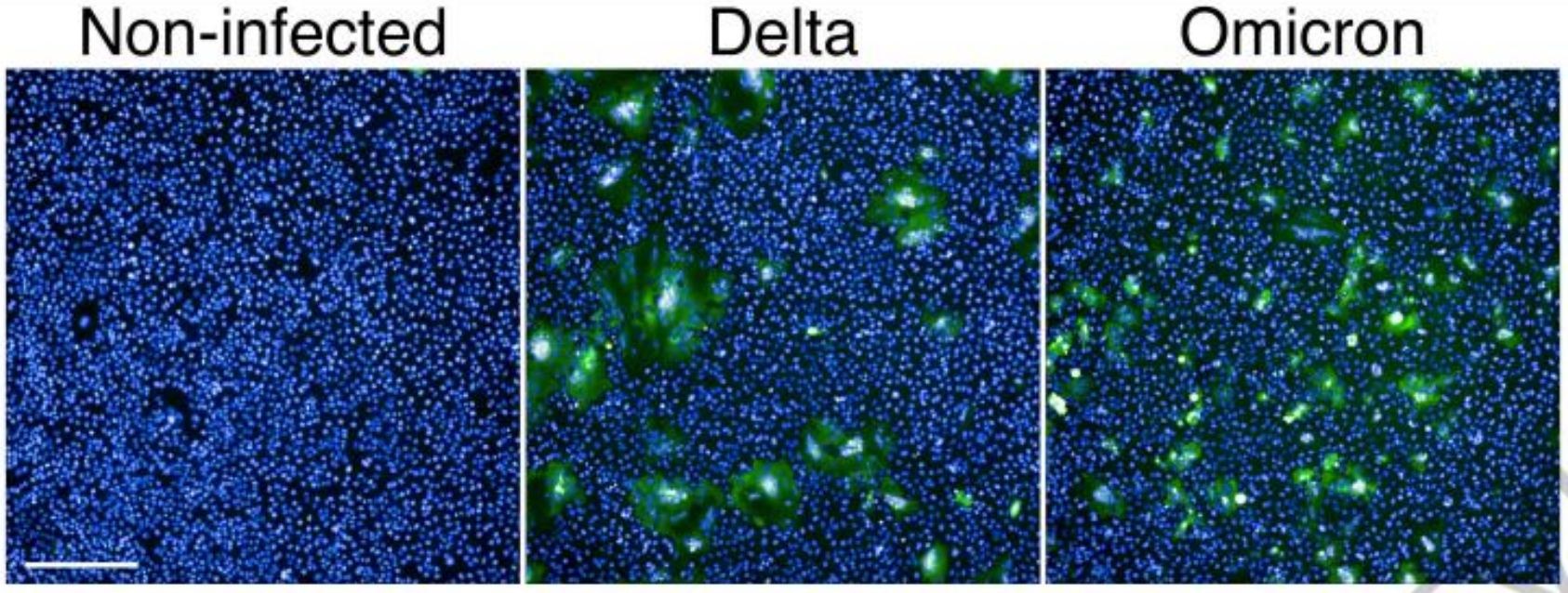
nature

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

Accelerated Article Preview

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

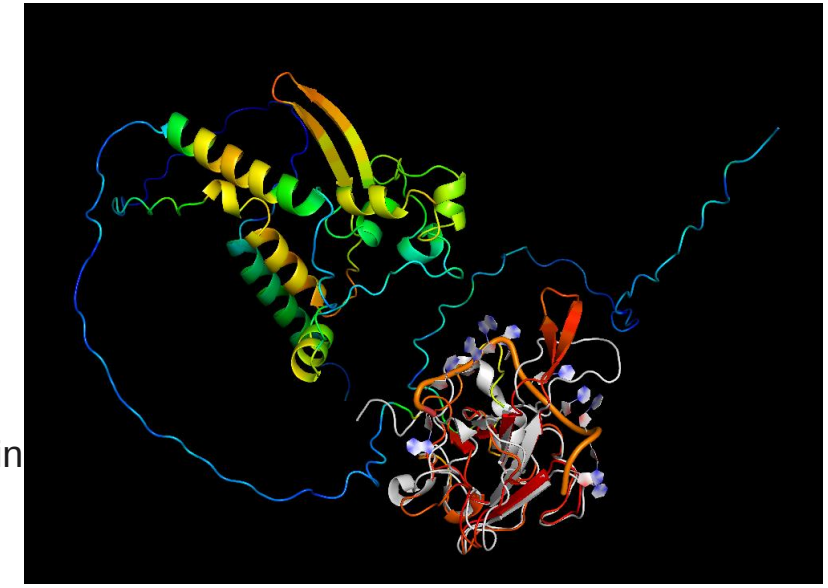
Article



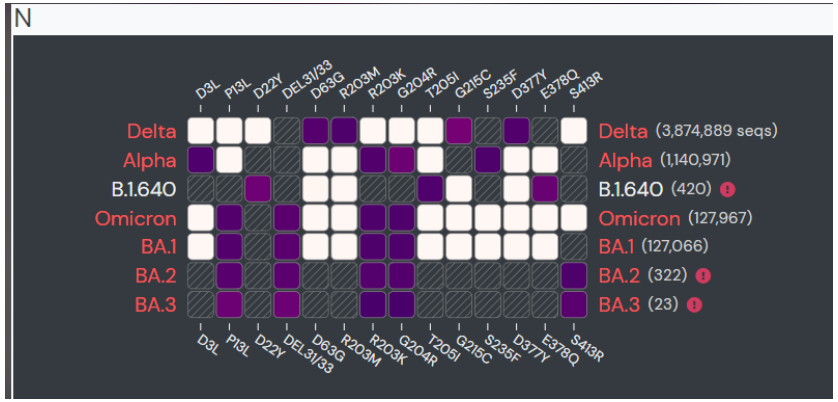
Extended Data Fig. 1 | SARS-CoV-2 variants induce syncytia in S-Fuse cells. S-Fuse cells were exposed to the indicated SARS-CoV-2 strains, at a multiplicity of infection (MOI) of 10^{-3}. The cells become GFP+ when they fuse together. After 20 h, infected cells were stained with Hoechst to visualize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

Ve vedlejší roli nukleokapsiodvý protein
Jsou Ag testy funkční?

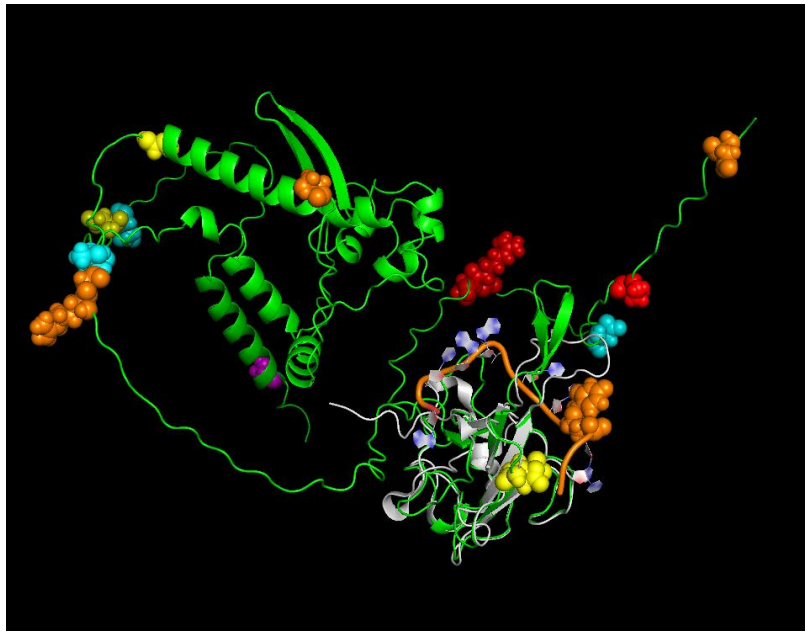
N-term domain binds RNA
C-term domain binds other N proteins
monoclonal IG-light lambda binds to N-term domain
IG-heavy bind to both domains
MHC binds to both and to unstructured linker
HLA binds to N-term domain



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



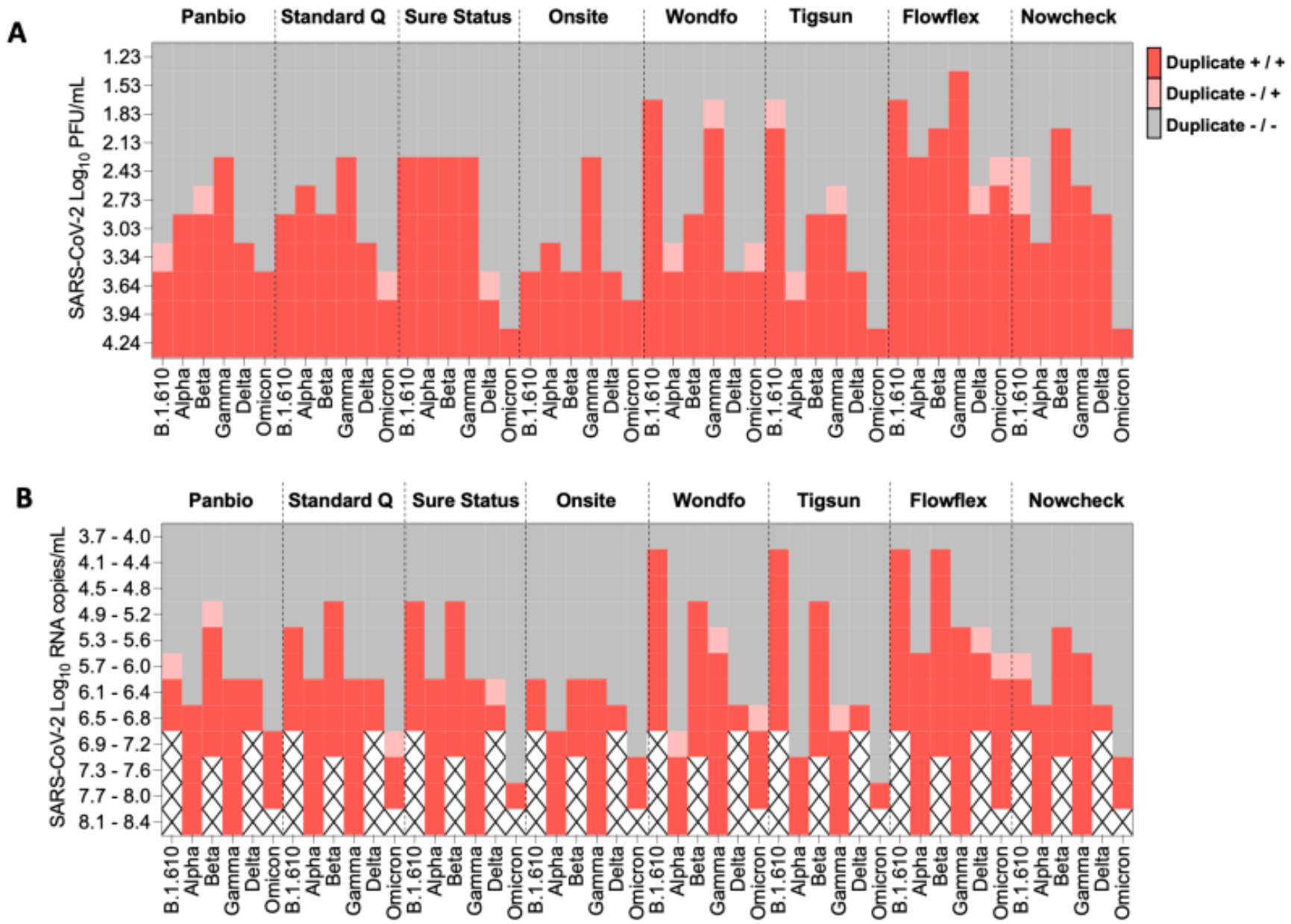
Strukturní modely a popis
autor Karel Berka



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)

AG testy x VOC



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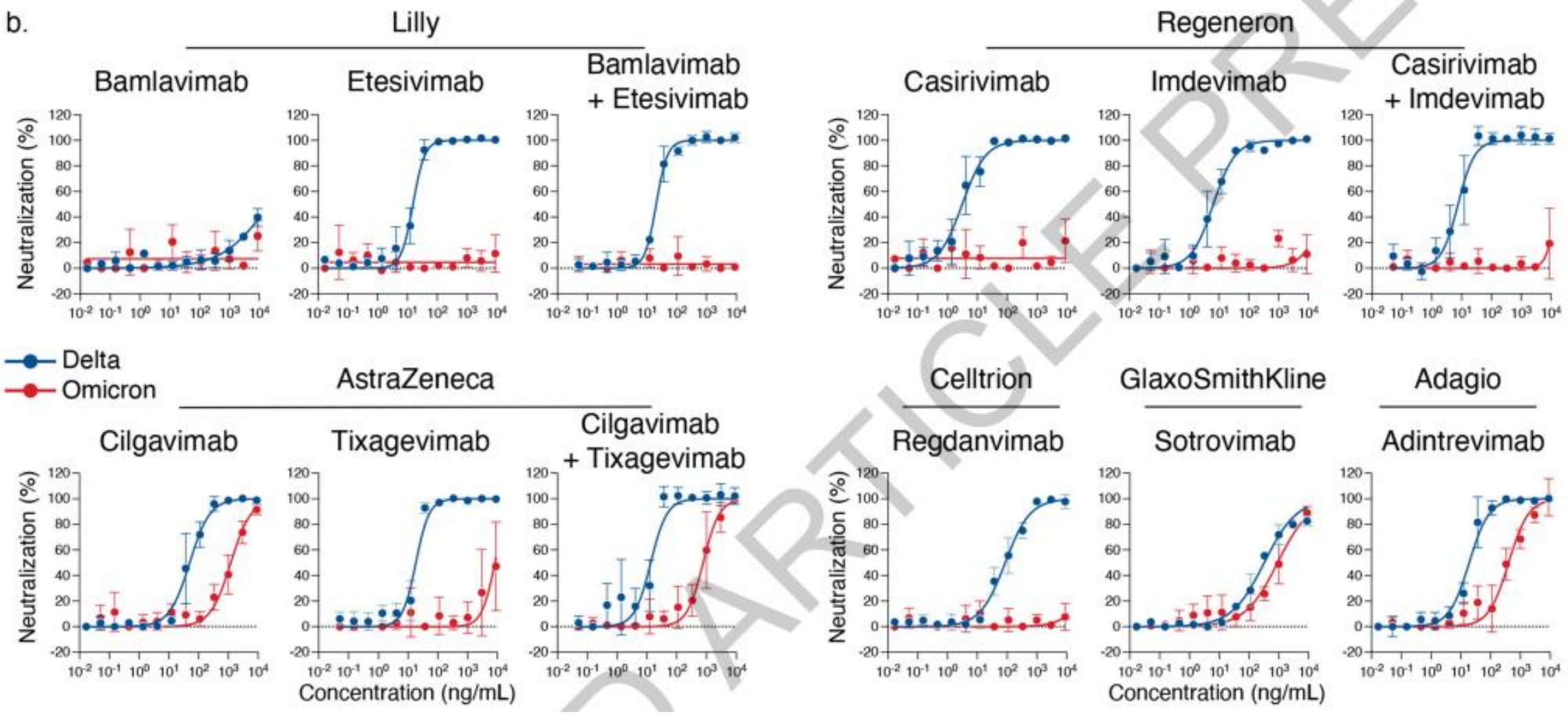
nature

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

Accelerated Article Preview

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



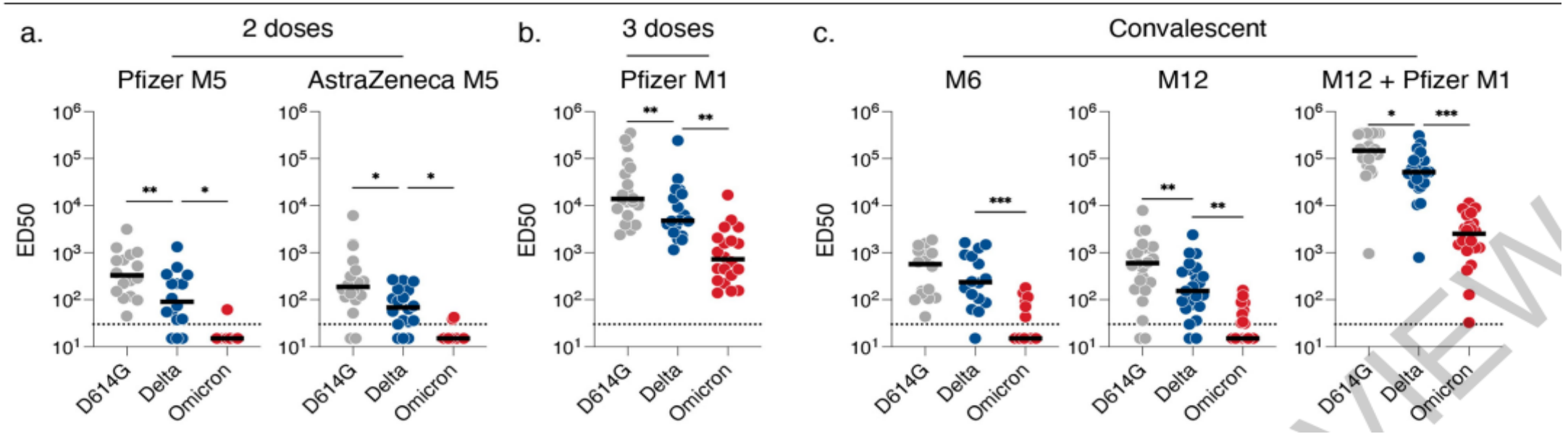
ARTICLE PRE

nature

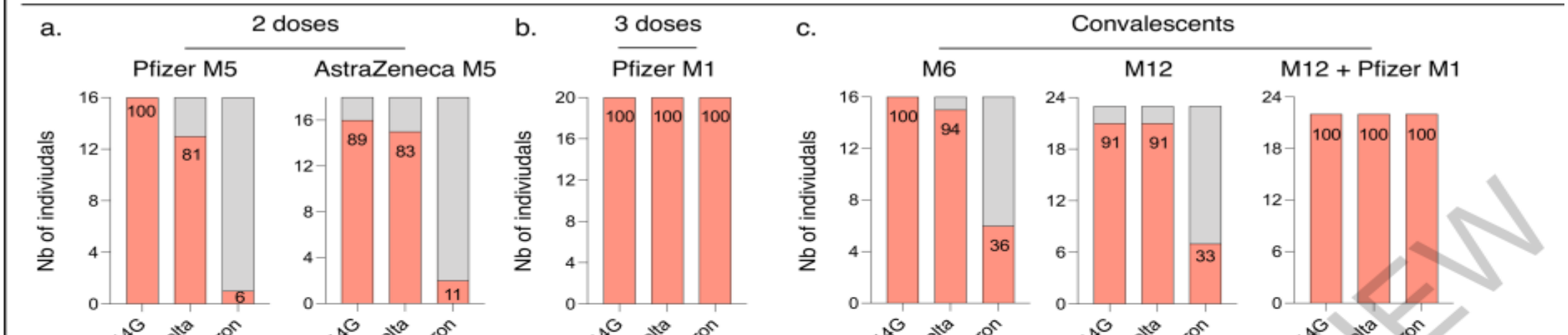
https://doi.org/10.1038/s41586-021-04389-z

Accelerated Article Preview

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



VNT



Podíl osob s dostatečným VNT
ED50 > 30

Serologie v časech escape variant a antivax hnutí

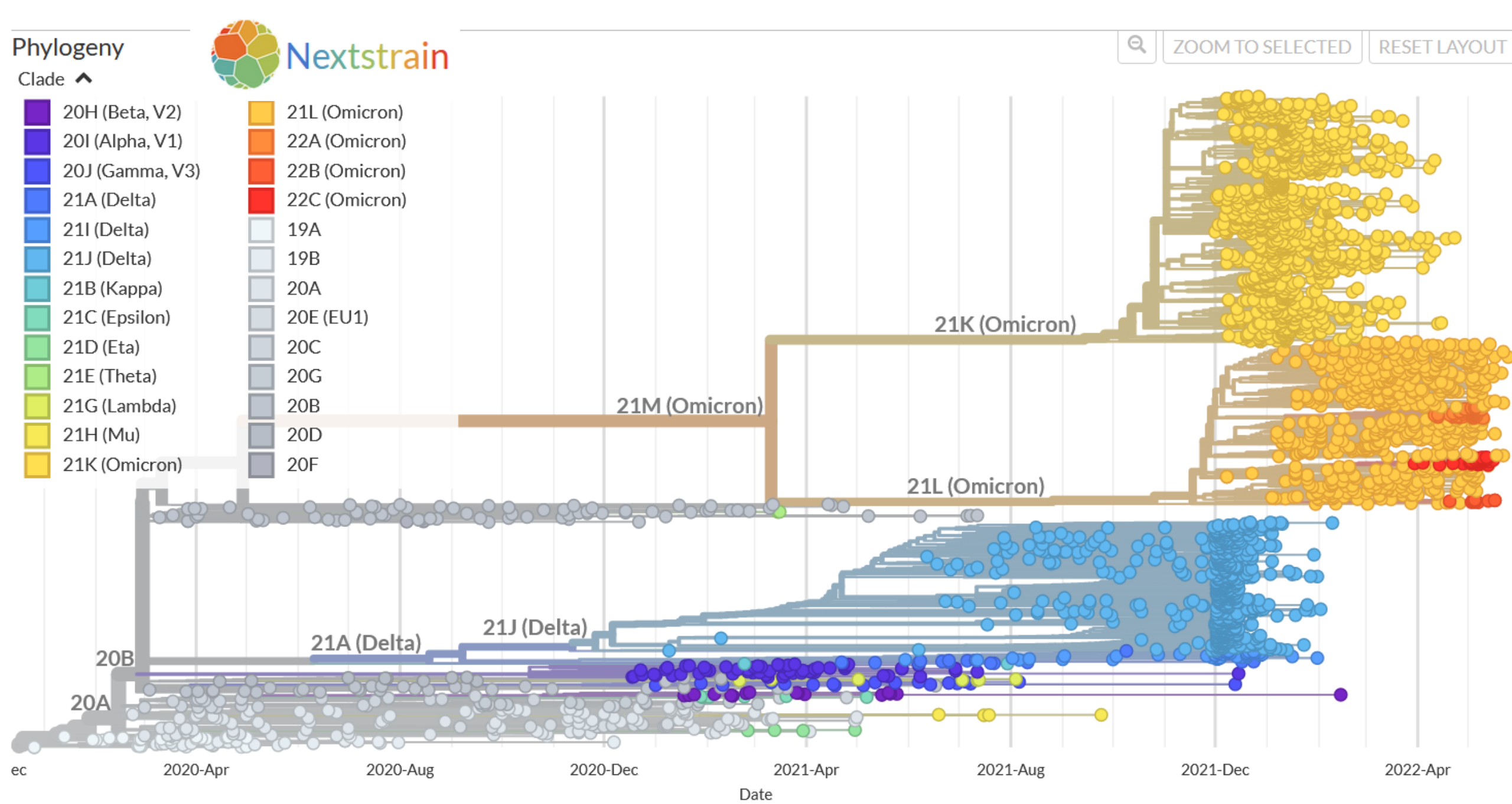
- IgG – anti S, anti trimerizovaný S, anti S1RBD x anti N
- IgM – mohou nastoupit později než IgG
- IgA – setkání s infekcí, post vakcinační vzestup, mohou přetrvávat velmi dlouho

Měření produkce IfFN gama po stimulaci CD4+, CD8+ / quantiferron

PCR diagnostika

- Metody využívají konzervativní úseky – vysoká spolehlivost
- Vhodné sledovat více genů – přetrvávající PCR pozitivita
  - E gen časná infekce
  - Jen N/N2 gen – přetrvávající pozitivita

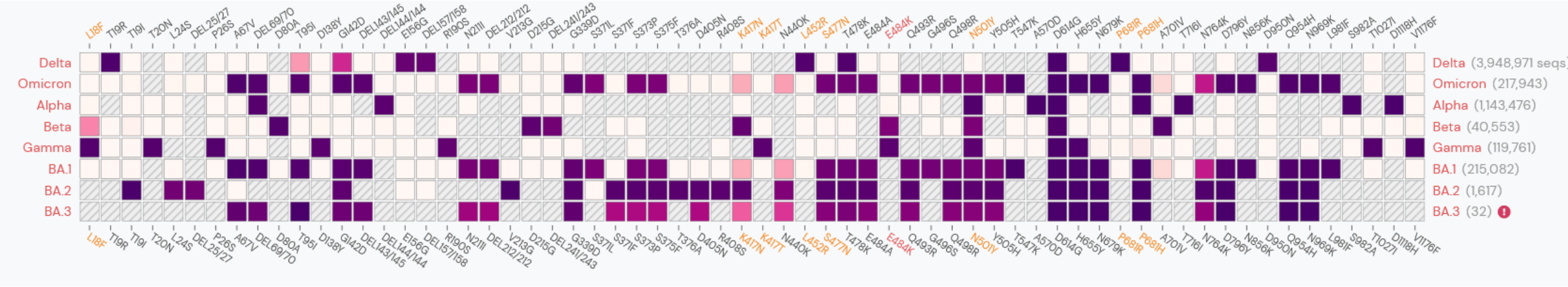
- Diskriminační PCR – umožní detekovat SNP – změna aminokyseliny
- Doporučení sledovat hot spot pozice:
  - RBD 452, 484, 417, 501,
  - NTD del 69-70
  - Furinové štěpné místo 681, 677


Phylogeny
Nextstrain
ZOOM TO SELECTED
RESET LAYOUT
Clade
20H (Beta, V2)
20I (Alpha, V1)
20J (Gamma, V3)
21A (Delta)
21I (Delta)
21J (Delta)
21B (Kappa)
21C (Epsilon)
21D (Eta)
21E (Theta)
21G (Lambda)
21H (Mu)
21K (Omicron)
21L (Omicron)
22A (Omicron)
22B (Omicron)
22C (Omicron)
19A
19B
20A
20E (EU1)
20C
20G
20B
20D
20F
21K (Omicron)
21M (Omicron)
21L (Omicron)
21J (Delta)
21A (Delta)
20B
20A
ec
2020-Apr
2020-Aug
2020-Dec
2021-Apr
2021-Aug
2021-Dec
2022-Apr
Date

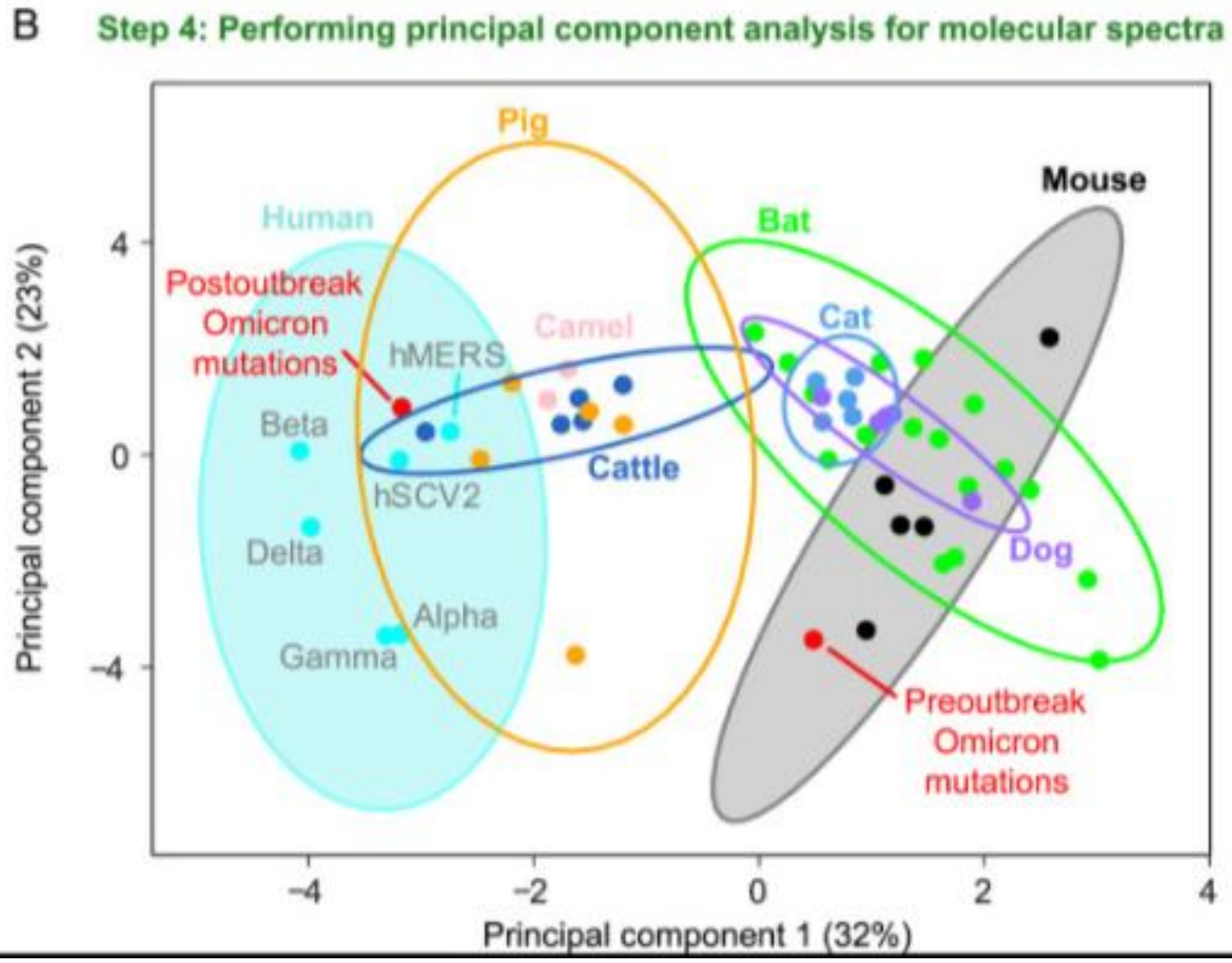
Diskriminační PCR x Mass Array x parciální sekvenace Spike genu

některé mutace ve spike x rozsáhlý souhrn mutací známých x neznámých

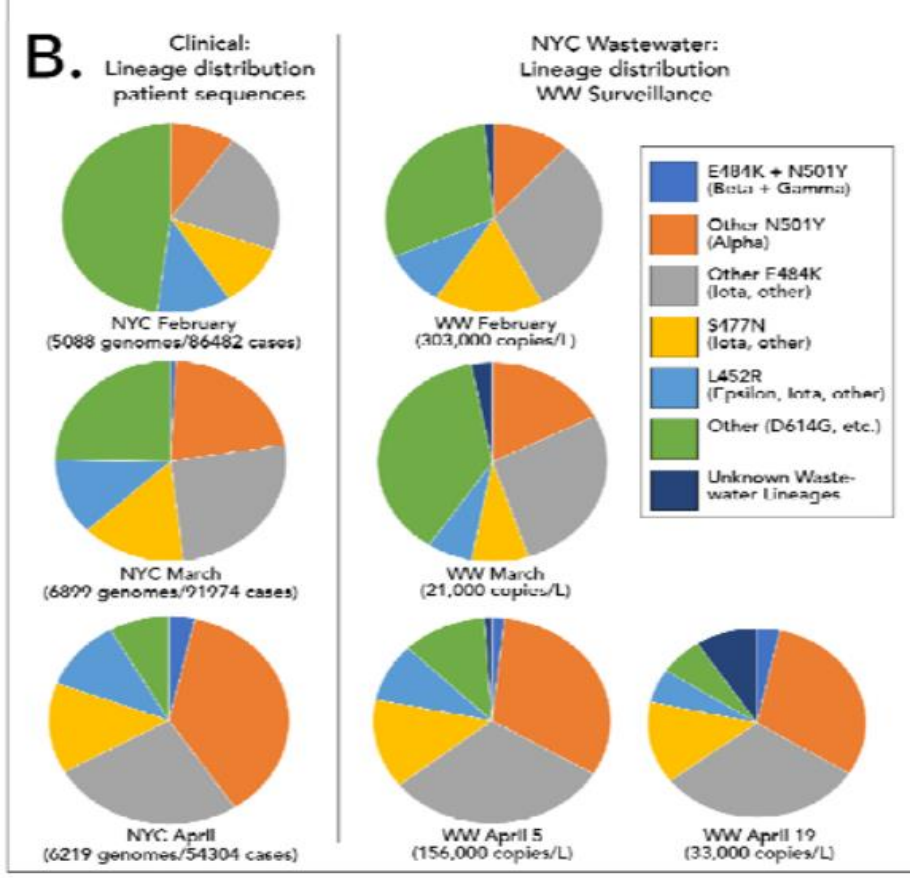
Matice mutací ve spike: jsou zahrnuty i varianty BA.1, BA.2, BA.3
Zdroj: outbreak.info



Omikron – původ – reintrodukce – myš?



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.



NY – monitoring odpadních vod

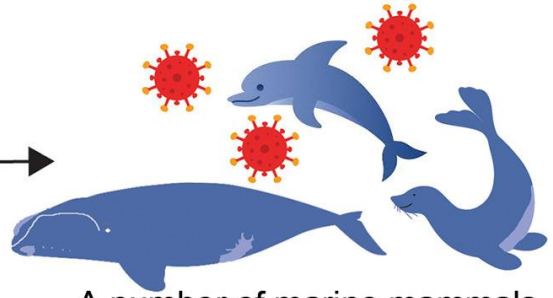
od února atypické mutace: Q493K, Q498Y, H519N and T572N.

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

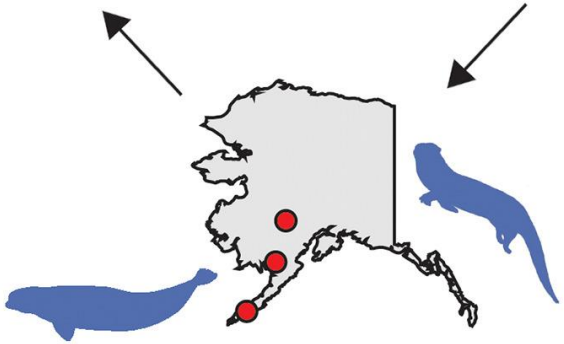
medRxiv preprint doi: https://doi.org/10.1101/2021.07.26.21261142; this version posted July 29, 2021.

Odpadní vody a možnost šíření SARS-CoV-2

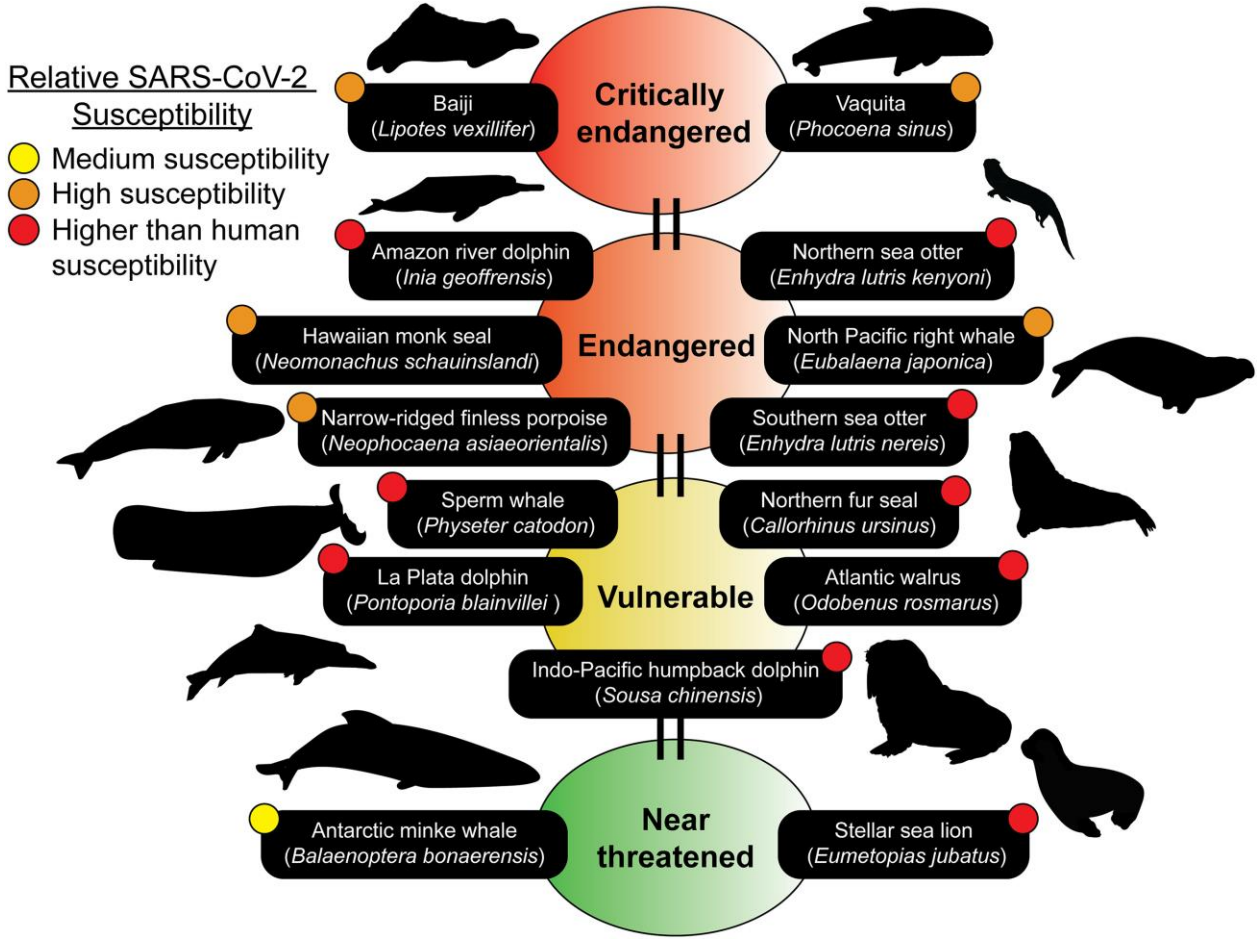
Wastewater transmission of SARS-CoV-2 is an emerging concern



A number of marine mammals are predicted to be highly susceptible to the virus



Wastewater management plants in certain localities are not sufficiently treating sewage, putting threatened and endangered species at-risk such as beluga whales and sea otters.



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

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

Děkuji za pozornost

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.

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.