

Genome evolution of SARS-CoV-2

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SITC, November 13th 2020

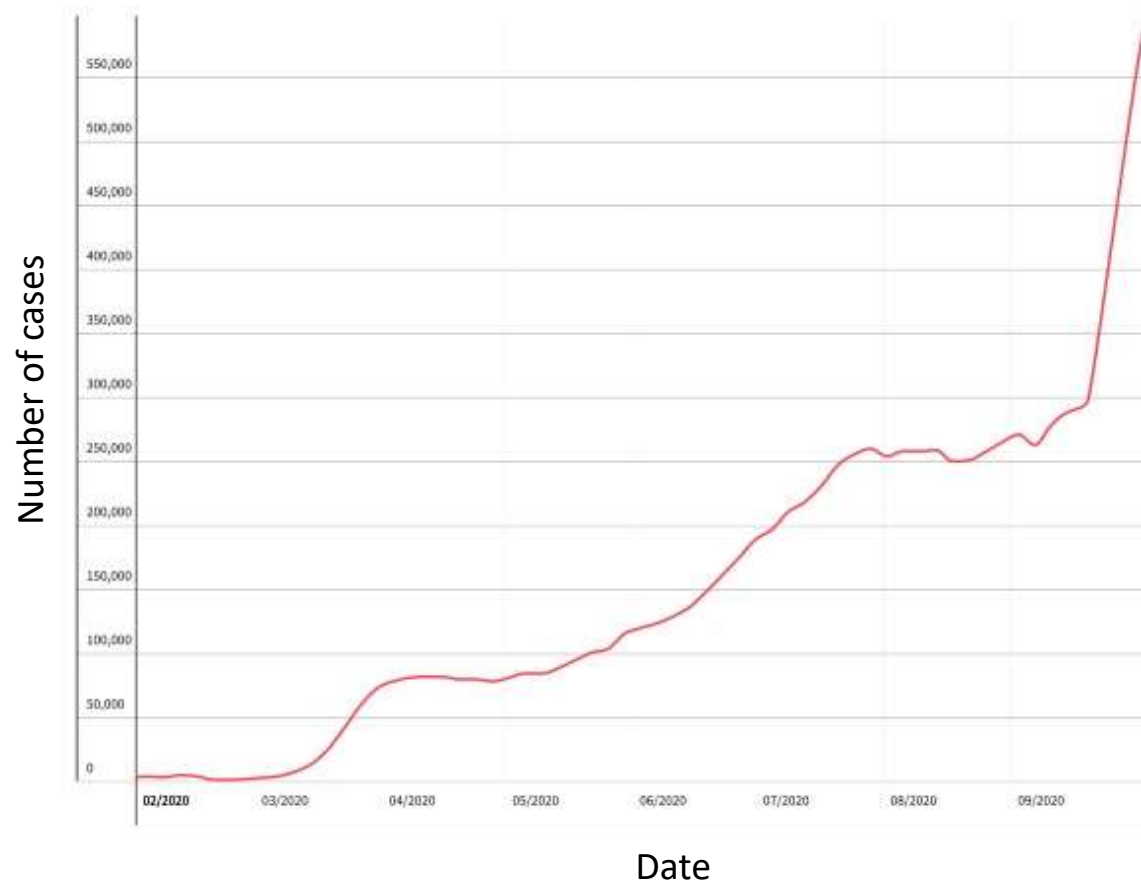
Disclosure

There will not be discussion about the use of products for non-FDA approved indications in this presentation.

Mapping the pandemic

Global case numbers
since February:

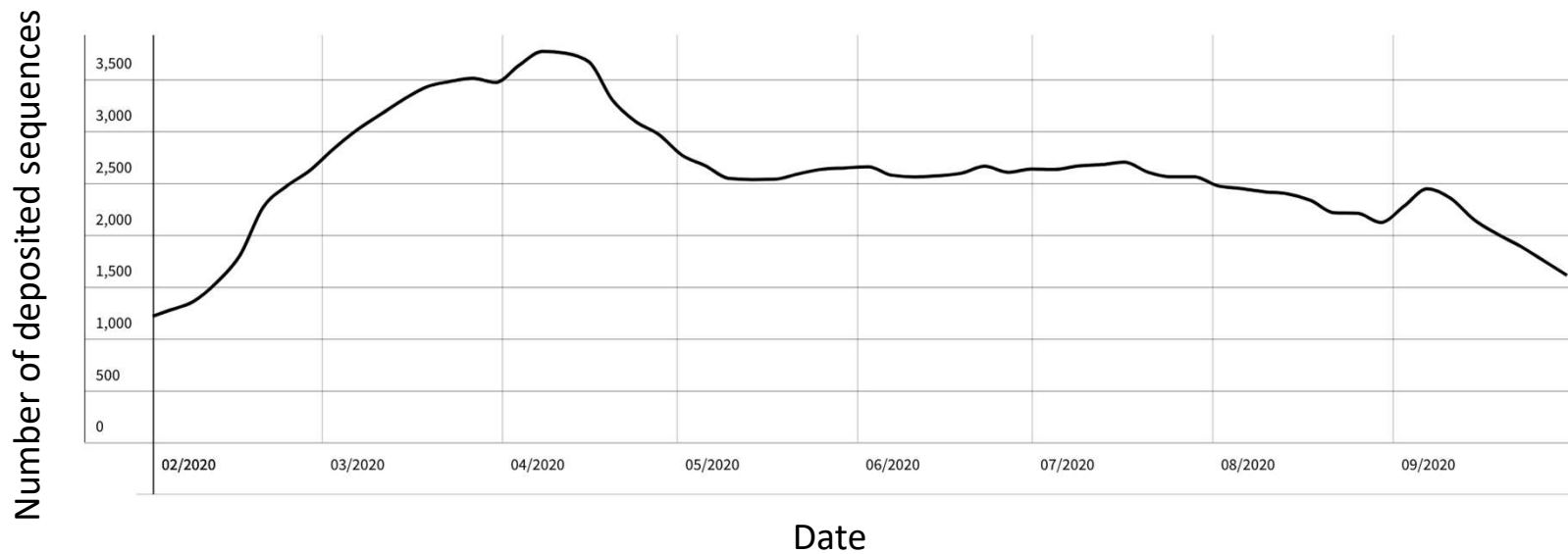
(John Hopkins University, CSSE)



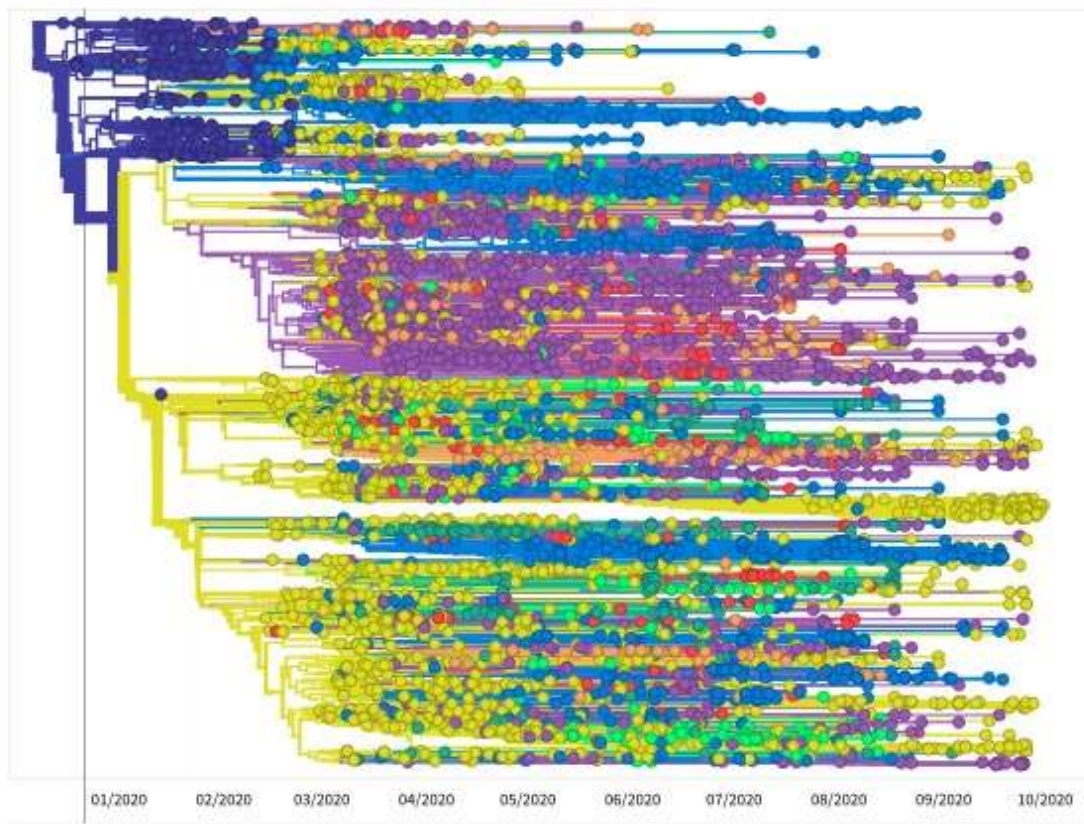
Mapping the evolution

Global sequencing efforts:

- Over 150K genome sequences are currently available



Reconstruction of the evolutionary history



Maximum likelihood inference:

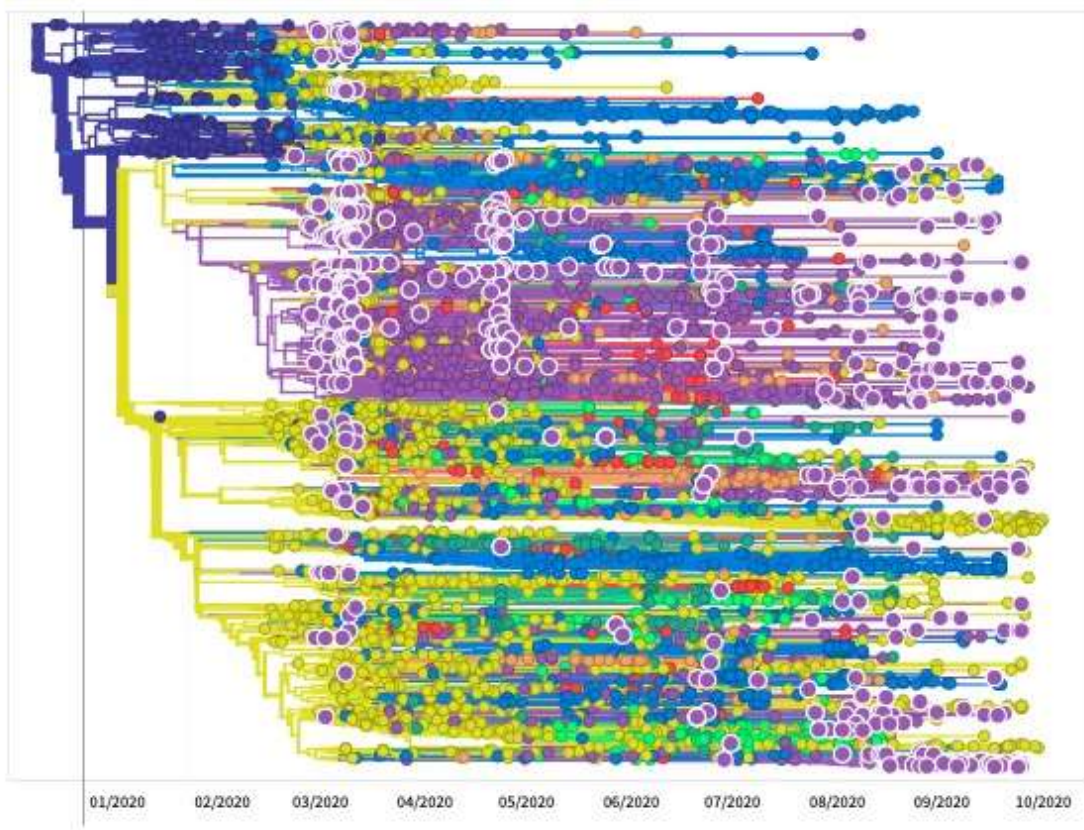
- phylogeny
- timing of mutations
- geographical transmission events
- about 2-3 mutations per month

Color coding:

- Usa East Coast
- Usa West Coast
- North America Remainder
- Europe
- Asia
- China
- South America
- Africa
- Oceania

Flupredict

Example: Mount Sinai sequences from NYC

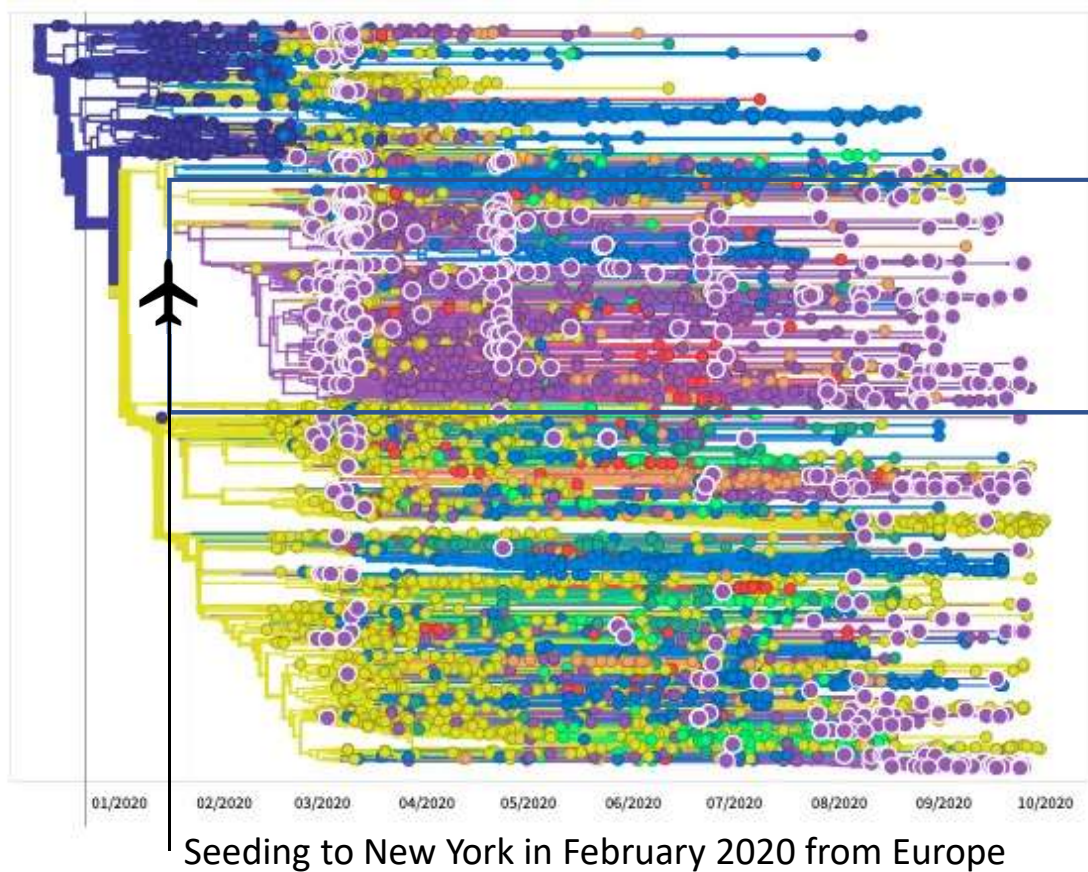


Sequencing efforts at Mount Sinai
(Harm Van Bakel, Viviana Simon)

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Inference of the seeding events in NYC



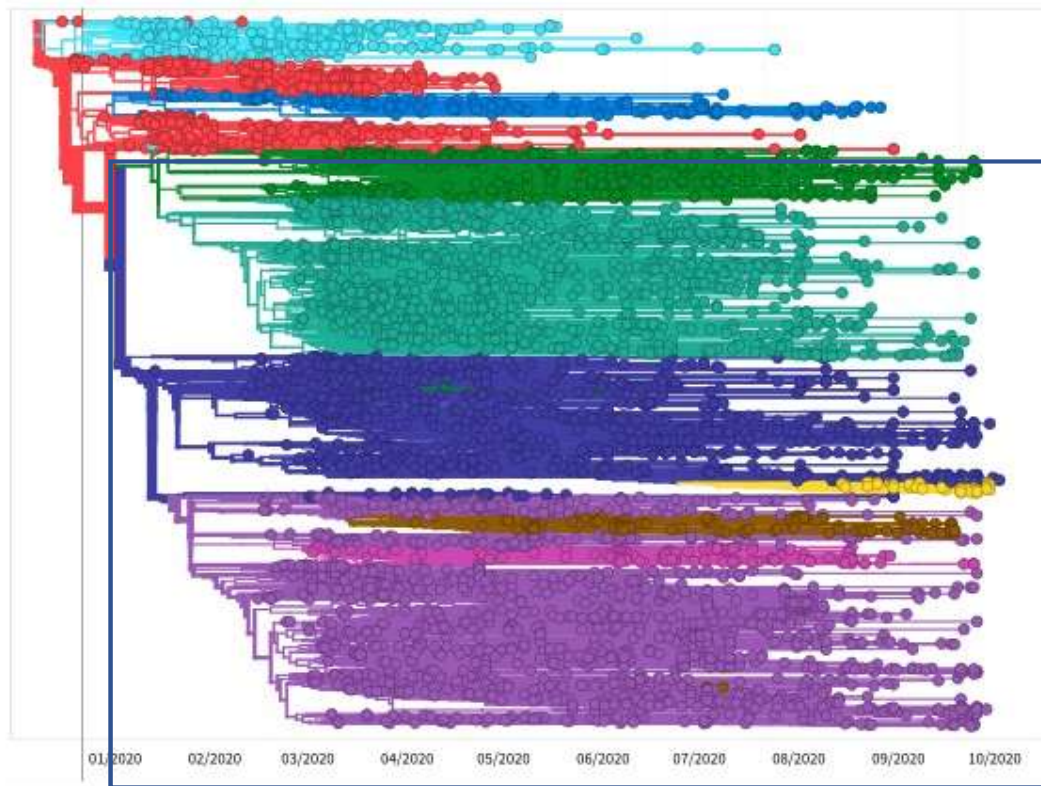
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[Gonzalez-Reiche et al. Science 2020]

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Genetic clade decomposition



Multiple co-circulating clades

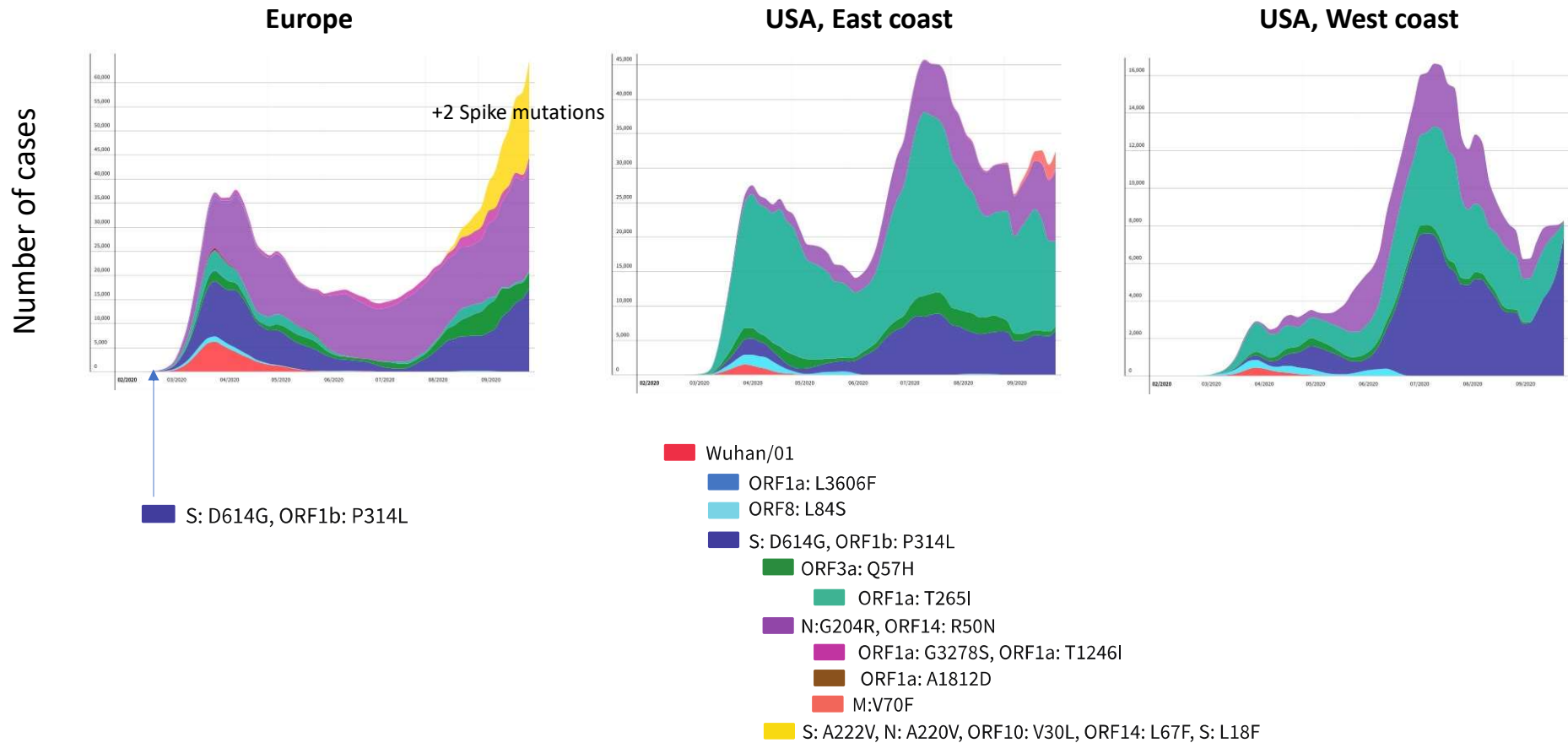
An early **sweep of a spike mutation, S: D614G**

- enhances viral loads in the upper respiratory tract
- no evidence of an antigenic effect

[Plante et al. Nature 2020]

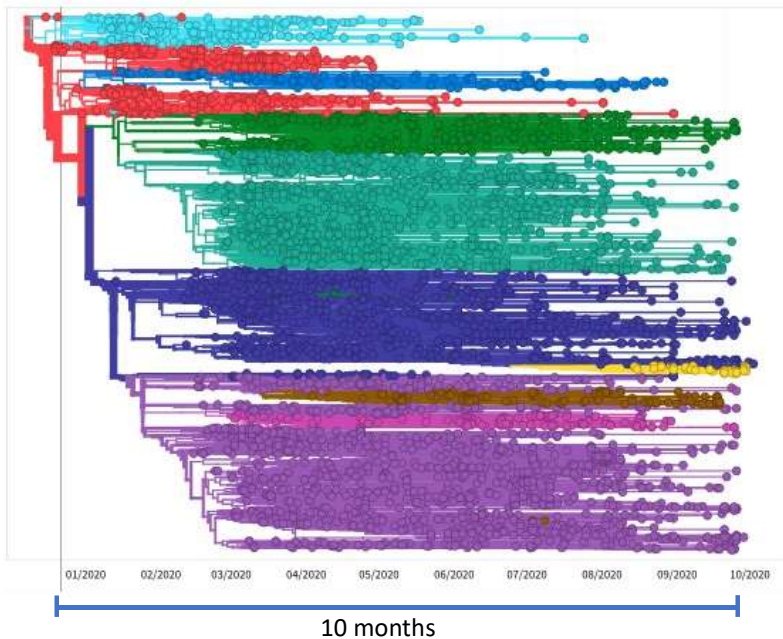
- Wuhan/01
- ORF1a: L3606F
- ORF8: L84S
- S: D614G, ORF1b: P314L
- ORF3a: Q57H
- ORF1a: T265I
- N:G204R, ORF14: R50N
- ORF1a: G3278S, ORF1a: T1246I
- ORF1a: A1812D
- M:V70F
- S: A222V, N: A220V, ORF10: V30L, ORF14: L67F, S: L18F

Regional clade decomposition and dynamics



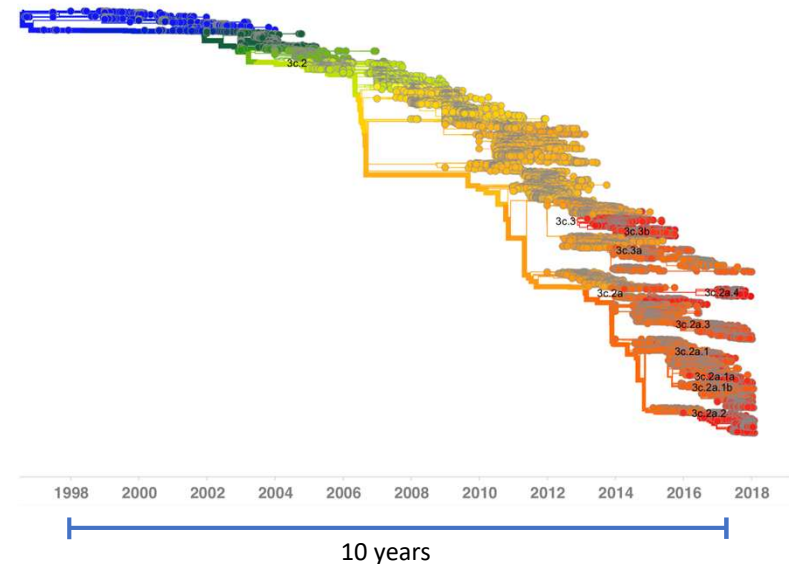
Scenarios of viral evolution

SARS-CoV-2, circulates since late 2019



- Colored by genetic clades

Influenza H3N2, circulates since 1968



- Colored by antigenic advance in the hemagglutinin
- Evolution is driven by
 - **antigenic mutations**
 - **immune interactions**

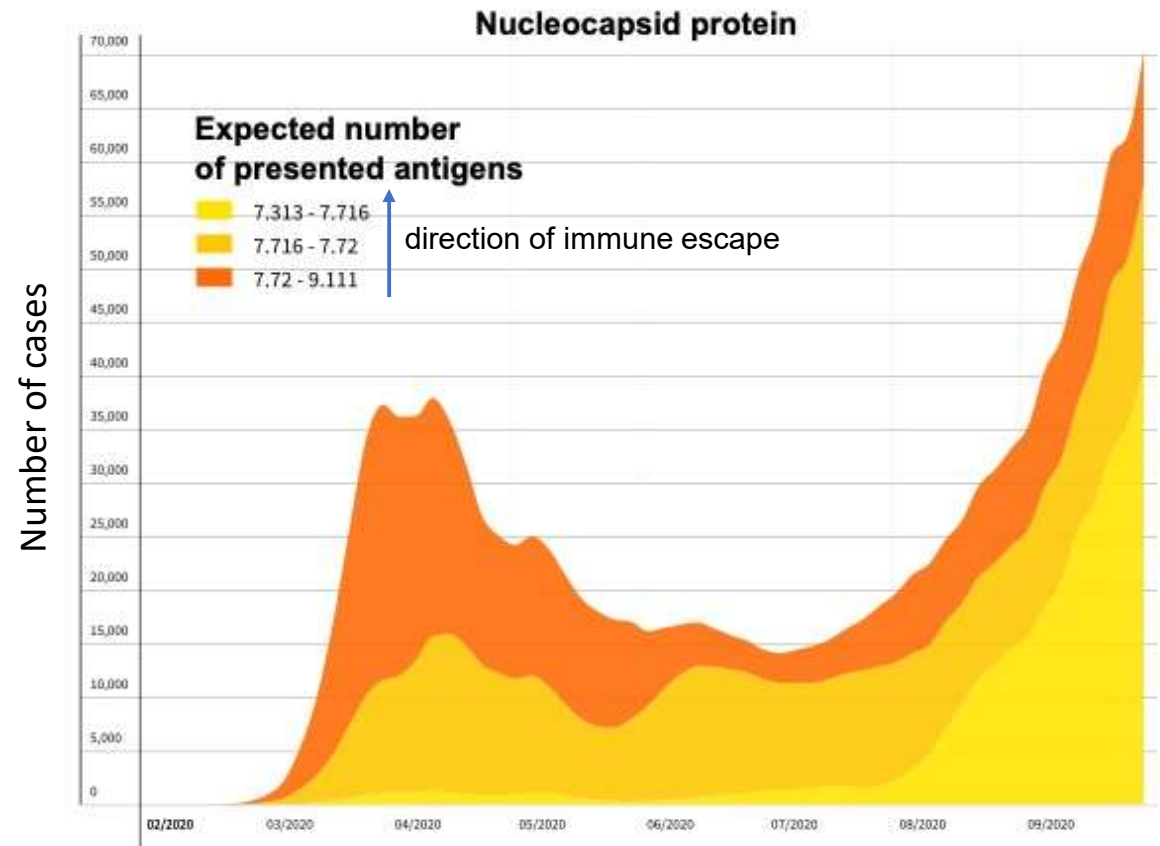
Mapping the immune evolution

Is there an evidence of immune escape?

- Track the **evolutionary dynamics of a quantitative trait**

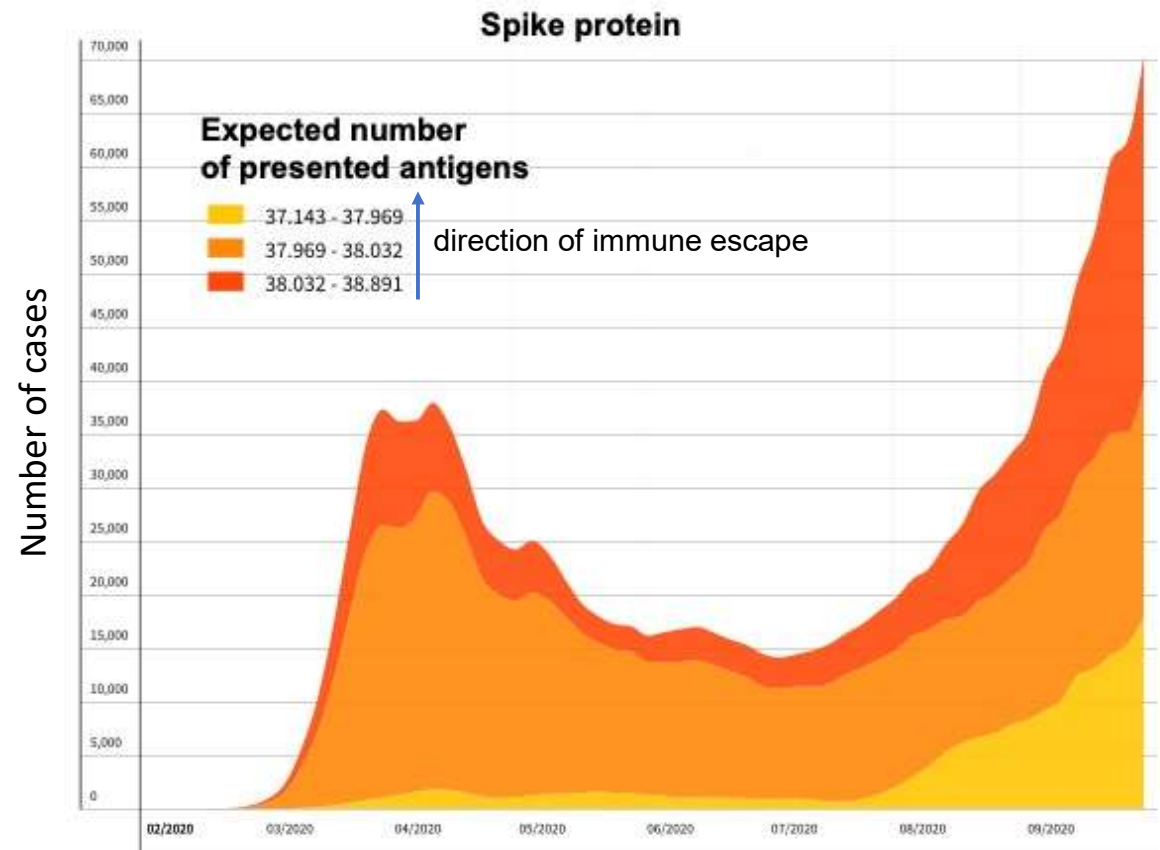
Evolution of adaptive immunity

- Computationally predicted T-cell epitopes (netMHC)
- **Quantitative trait:** the expected number of presented antigens
- evaluated in the European population



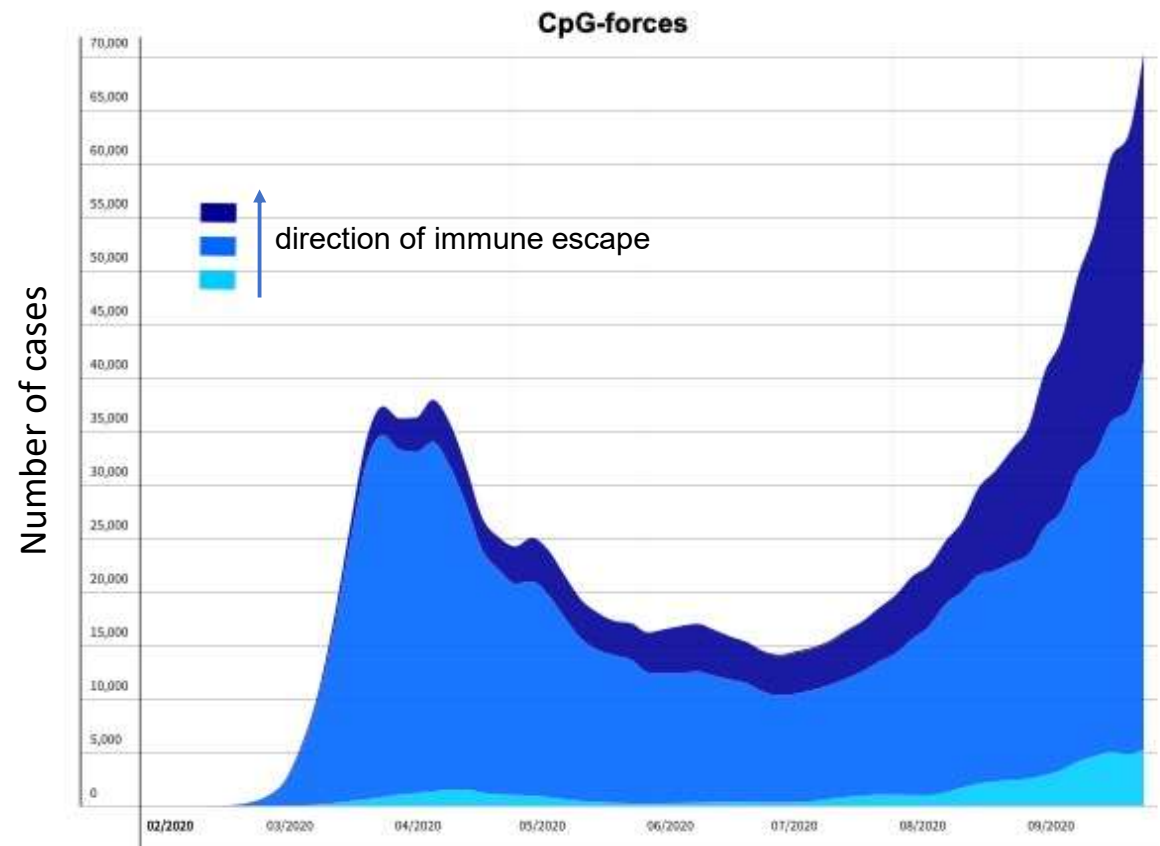
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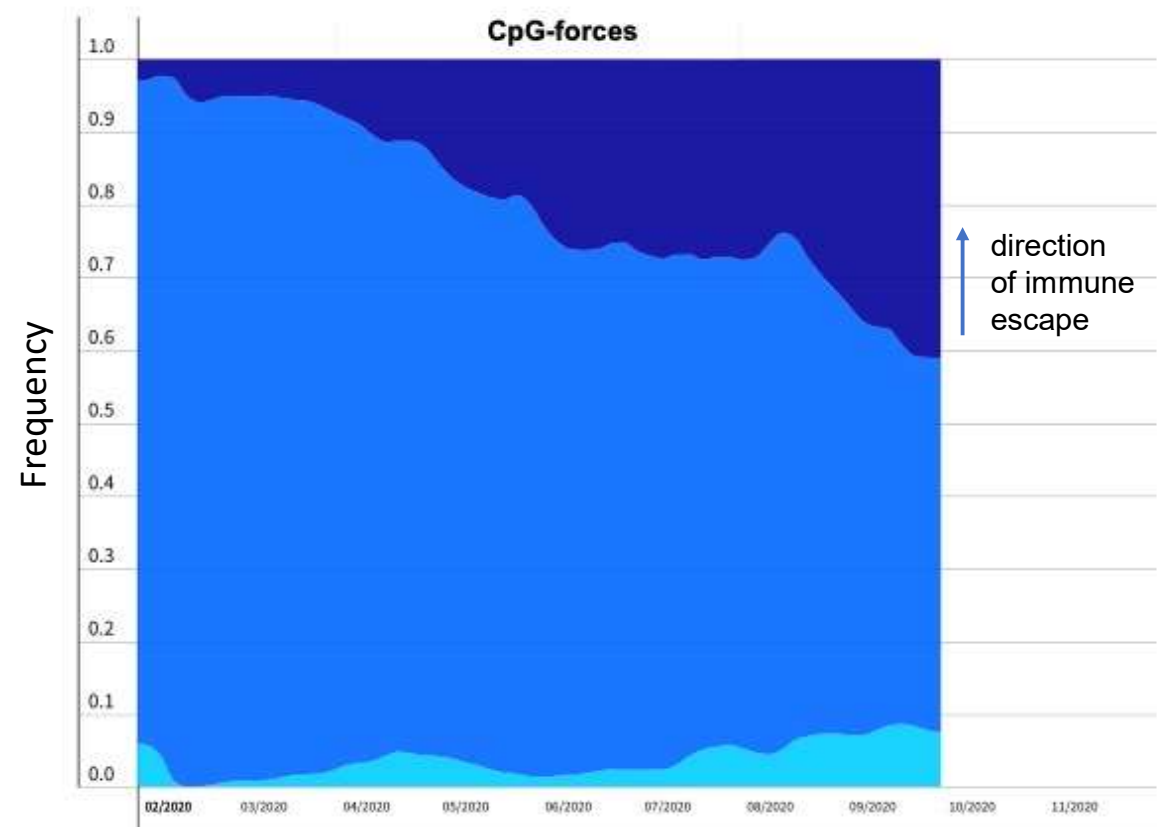
Evolution of innate immunity (with Ben Greenbaum)

- **Innate immunity:**
sequence-based scoring
of di-nucleotide “forces”
- evaluated in the European
population



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Acknowledgments

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The logo for Flupredict, consisting of the word "Flupredict" in white sans-serif font on a dark gray rectangular background.

Flupredict

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Mapping the evolution

