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31 MARCH 2021



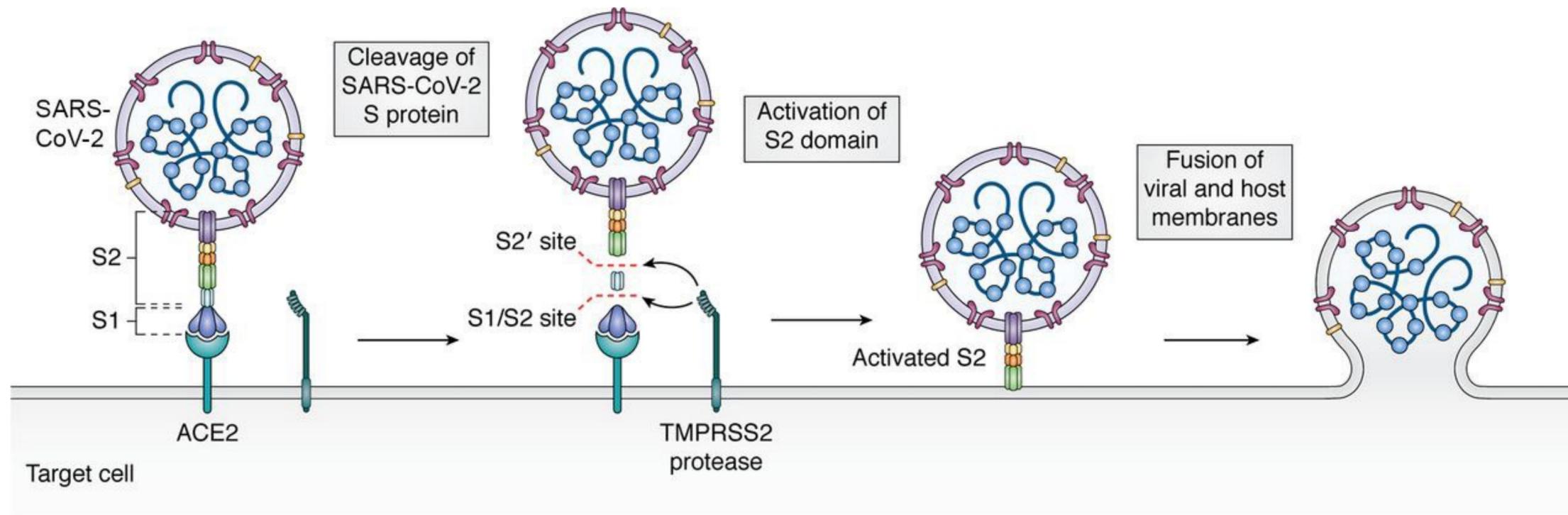
COVID-19 VACCINES AND VARIANTS

Prospects and challenges for controlling COVID-19

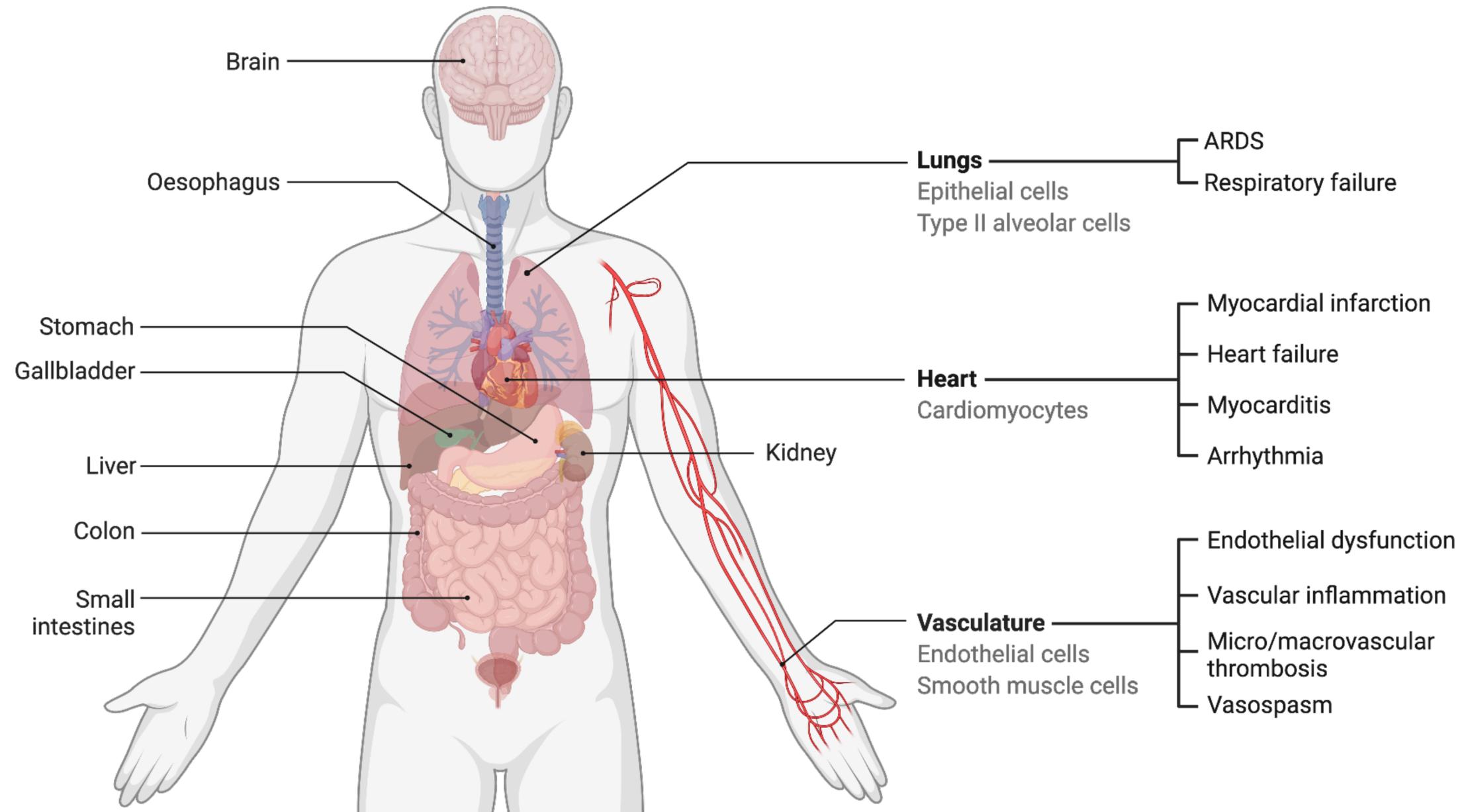
- ▶ How can vaccines protect against SARS-CoV-2? What does “protection” mean?
- ▶ Vaccines approved, in the pipeline, and in the future
 - ▶ Intermission: Q&A
- ▶ Tracking variants to understand SARS-CoV-2 spread in Wisconsin
- ▶ What do emerging variants mean for the future of COVID-19?
 - ▶ Discussion

**WHAT DOES A COVID
VACCINE NEED TO DO?**

SARS-CoV-2 binds ACE2 receptors to enter cells

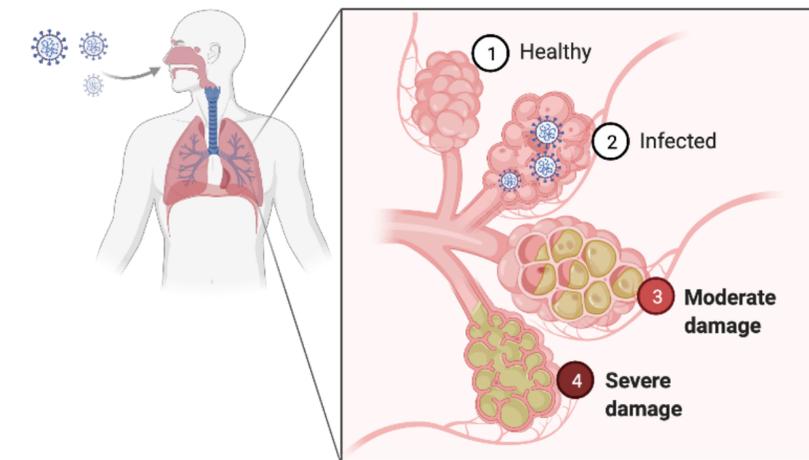


ACE2 is expressed in many tissues of the body

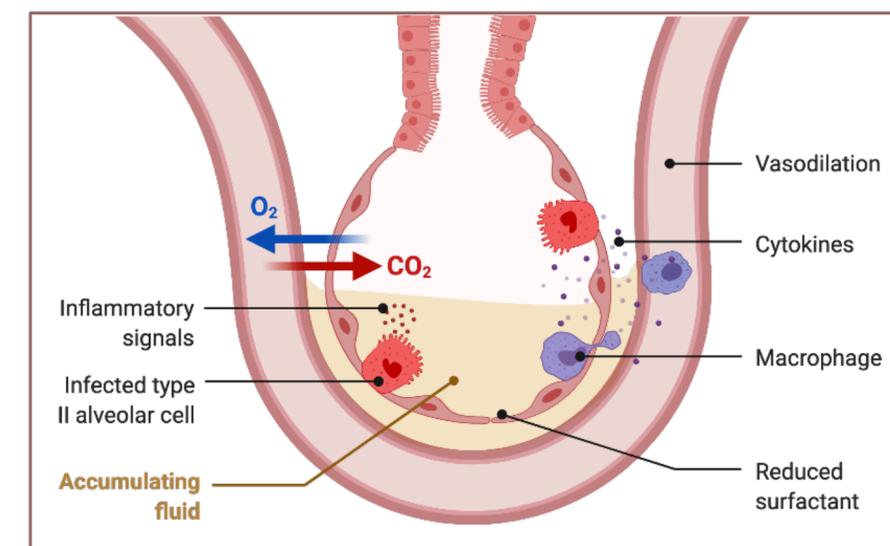


Vaccines must protect the lower respiratory tract

- ▶ Virus is transmitted from upper respiratory tract (URT)
- ▶ Severe disease occurs when virus and the immune response damage the lower respiratory tract (LRT)
- ▶ Protection of LRT prevents severe disease
- ▶ Virus replication in URT may still allow vaccinated person to transmit

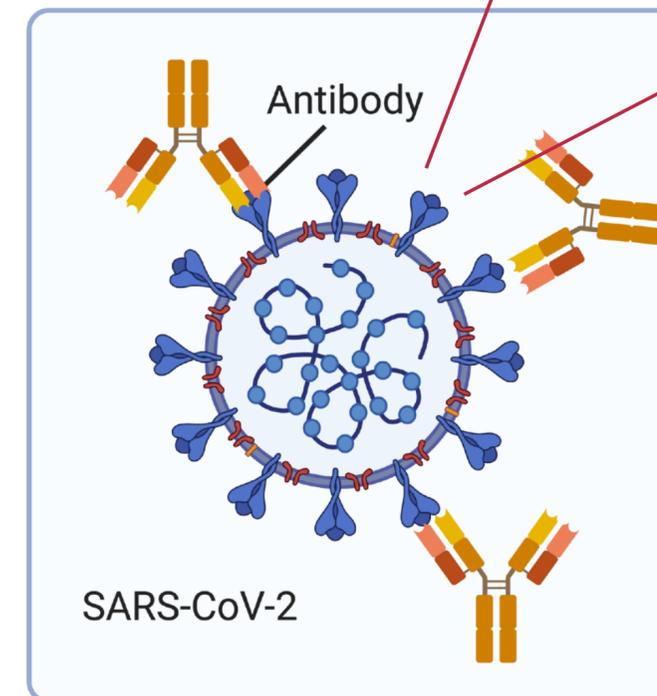
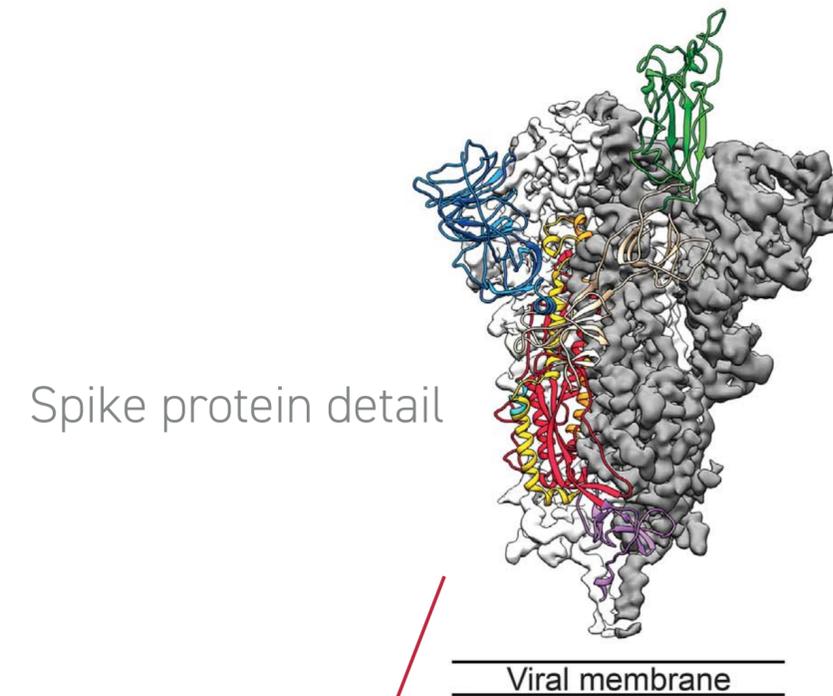


3 Moderate damage: Accumulating fluid, reduced gas exchange



SARS-CoV-2 Spike protein structure

- ▶ Antibodies that bind Spike protein block virus' ability to attach to ACE2
- ▶ Such “neutralizing antibodies” can prevent infection of cells
- ▶ Vaccines present Spike protein to immune system to elicit antibodies



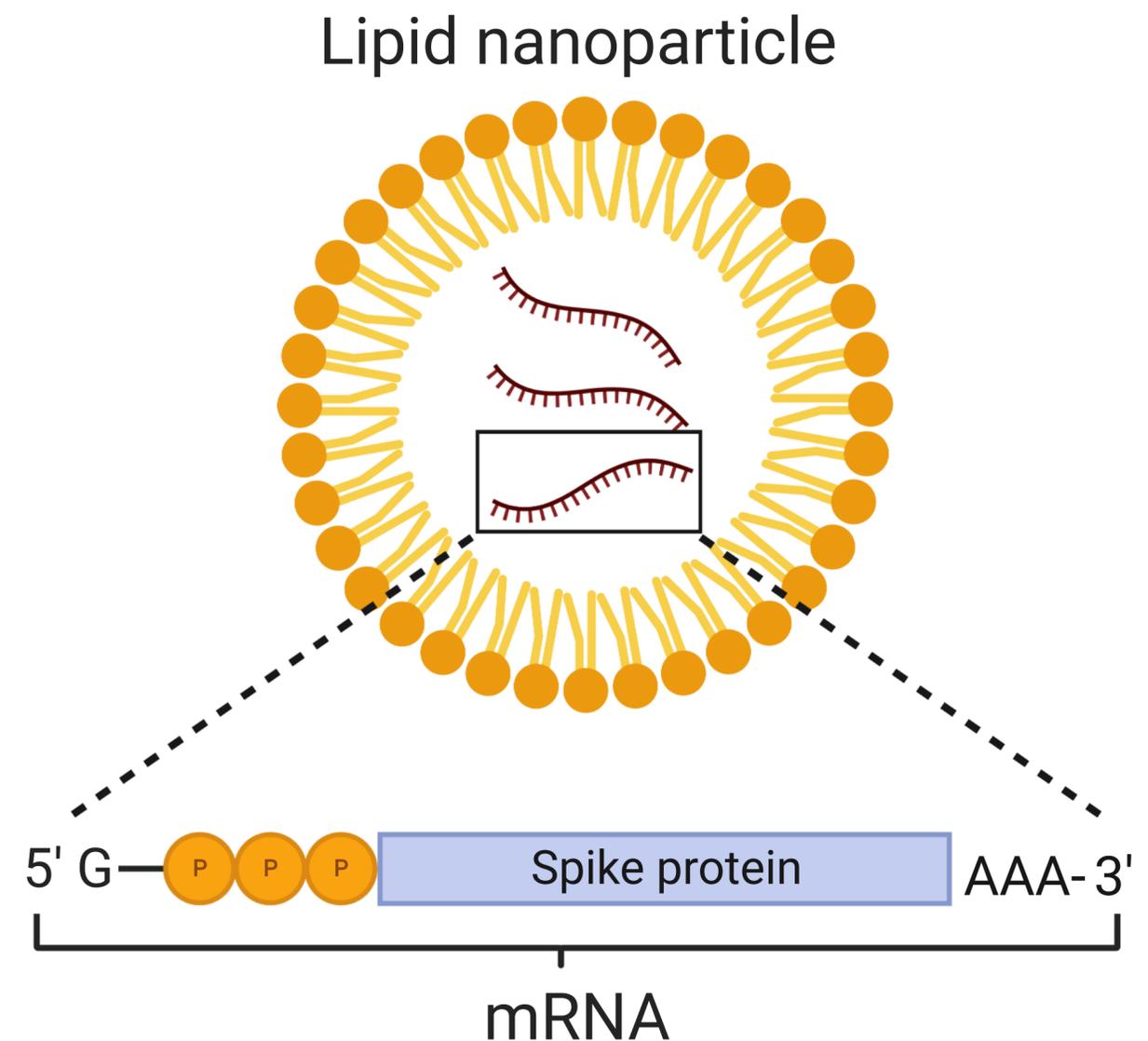
**HOW DO COVID
VACCINES WORK?**

How could COVID vaccines be made so quickly?

- ▶ Technology for next-generation vaccines has been in **development for decades**. Candidates for Zika, Ebola have not advanced because outbreaks were controlled.
- ▶ Understanding of SARS-CoV-2 builds on nearly **20 years' experience** thinking about emerging coronaviruses: "SARS Classic" and MERS-CoV
- ▶ Vaccine development using new approaches could begin as soon as gene sequences were published, **before labs had actual samples of SARS-CoV-2**
- ▶ Very large trial populations and high levels of SARS-CoV-2 transmission sped up clinical trial processes

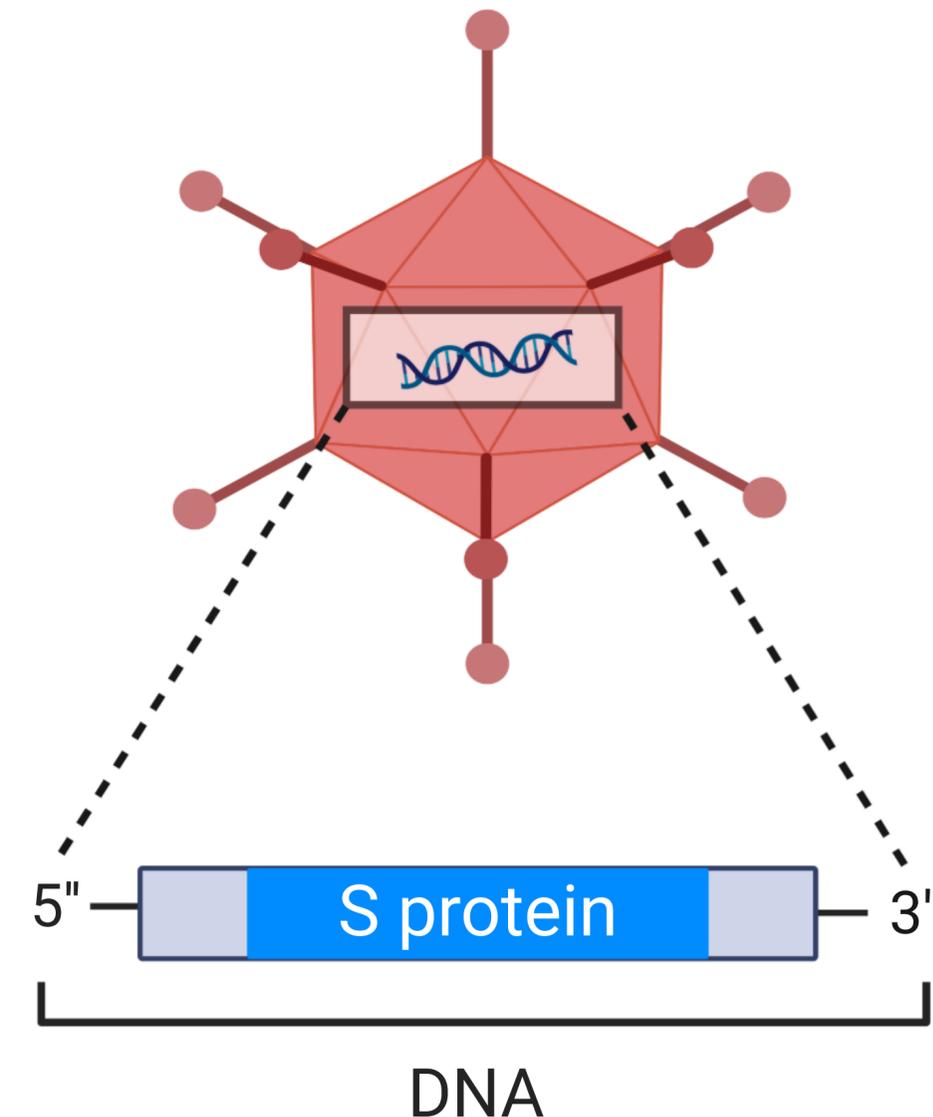
Pfizer/BioNTech and Moderna vaccines use mRNA

- ▶ Genetically engineered messenger RNA encodes the Spike protein
- ▶ RNA introduced into cells using a lipid particle that fuses with cell membranes
- ▶ Once inside the cell, mRNA is decoded (translated) into Spike proteins
- ▶ Spike proteins decorate the cell surface, where they can be bound by antibodies



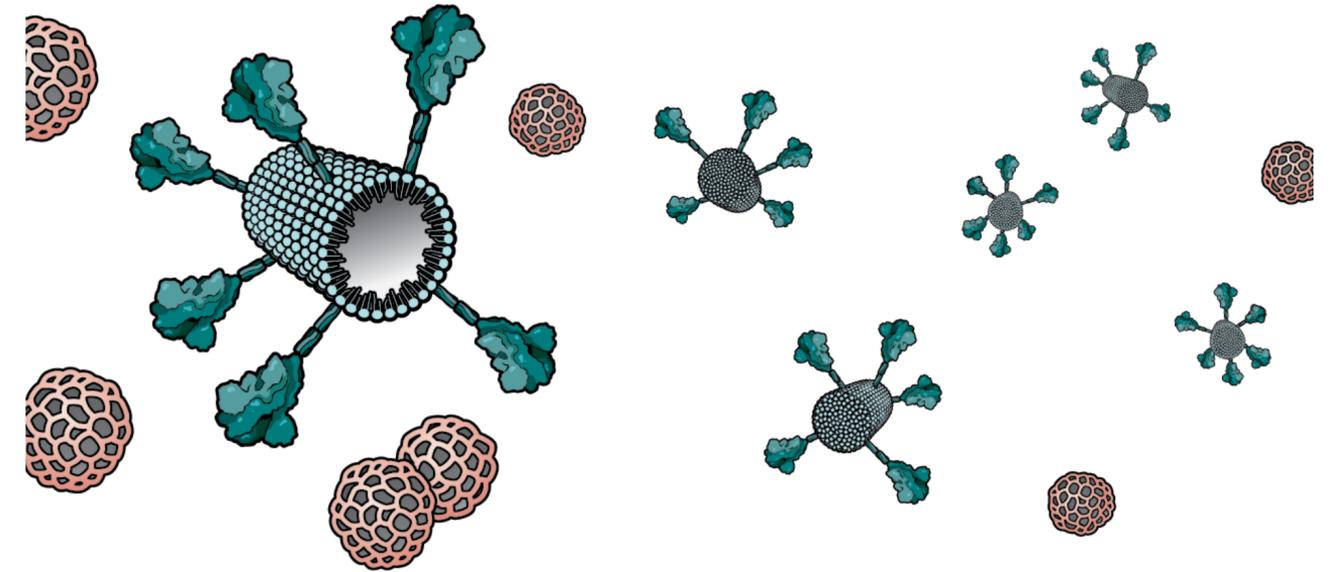
Johnson & Johnson and AstraZeneca vaccines use viral vectors

- ▶ Spike protein gene introduced into DNA of an attenuated adenovirus
- ▶ Adenovirus can infect cells near injection site, but cannot replicate further
- ▶ Spike proteins are made along with adenovirus proteins
- ▶ Spike proteins decorate the cell surface, where they can be bound by antibodies



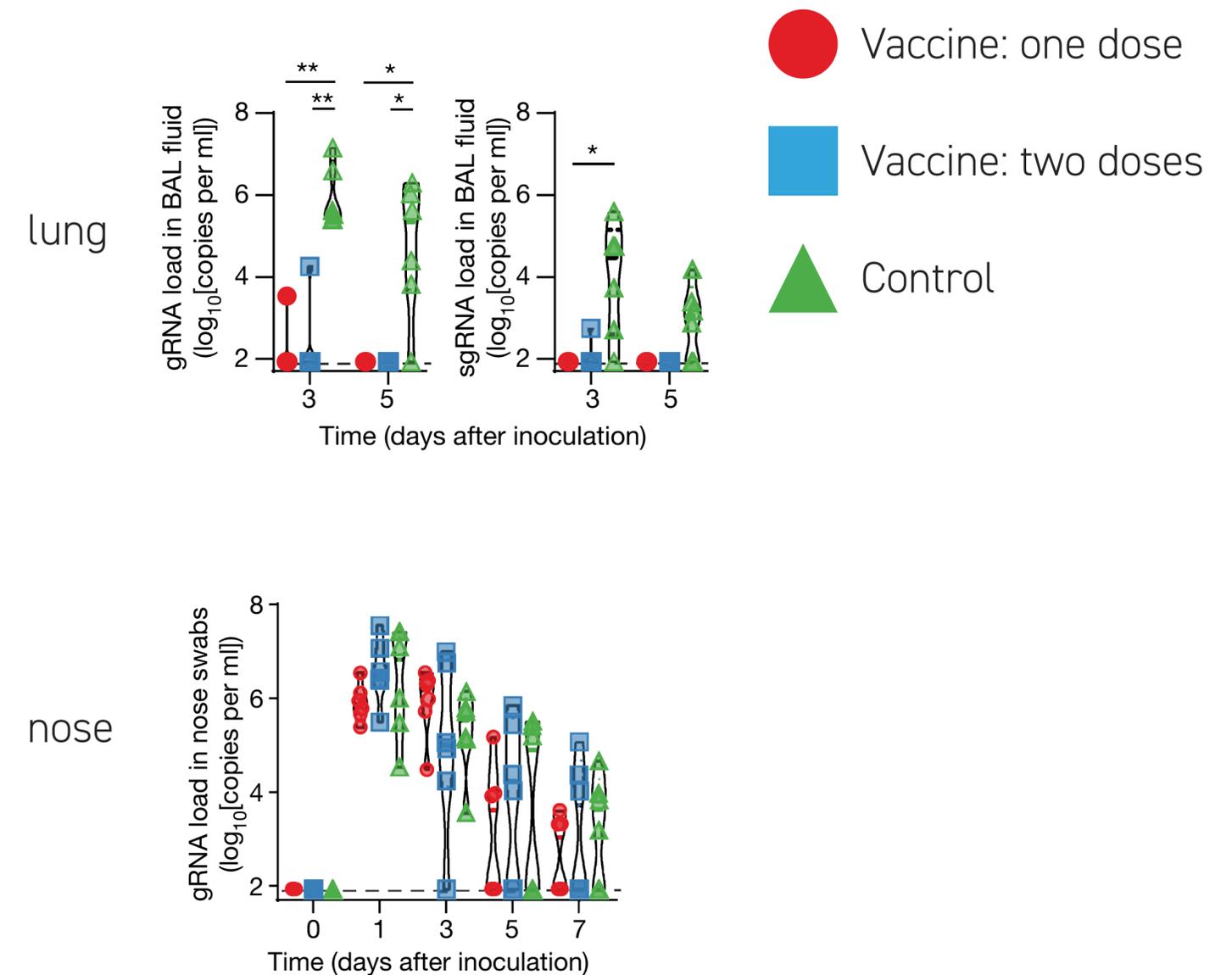
Novavax uses a nanoparticle decorated with Spike proteins

- ▶ Spike proteins produced in insect cells and assembled onto a synthetic scaffold
- ▶ Scaffolds display Spike to immune system and elicit antibodies
- ▶ Novavax not yet approved



Vaccines may protect LRT, but not URT

- ▶ Vaccines given intramuscularly are not expected to induce potent URT immunity
- ▶ In a preclinical trial, the AstraZeneca vaccine gave robust protection to LRT
- ▶ But there was no difference in virus in URT vs. controls
- ▶ This is why we are concerned about transmission in vaccinated people



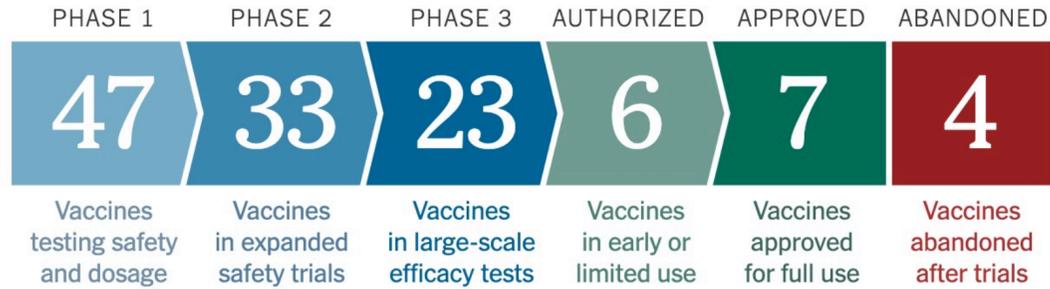
**WHAT IS THE NEAR-TERM
OUTLOOK FOR VACCINES?**

Current leading vaccine candidates

vaccine	type	adult efficacy	notes
Pfizer/BioNTech	mRNA	~95%	currently needs ultra-cold freezers
Moderna	mRNA	~95%	6 weeks to achieve full immunity
Johnson & Johnson	adenovirus	72%	single dose; easier storage than mRNA
AstraZeneca	adenovirus	79% (?)	not yet approved in US
Novavax	protein	96%; 49% against B.1.1.351	currently in Phase 3; data in April

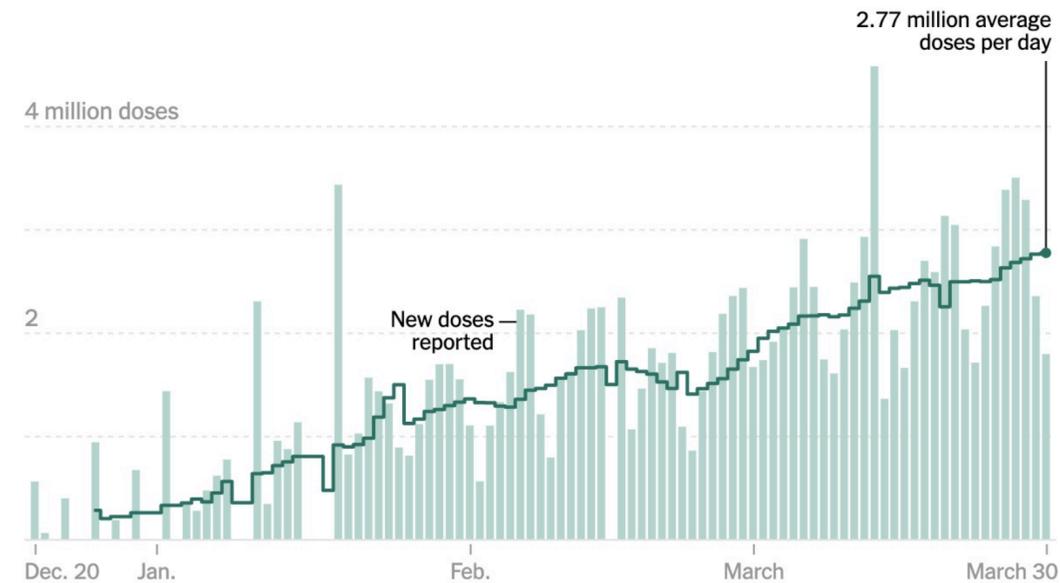
Coronavirus Vaccine Tracker

By Carl Zimmer, Jonathan Corum and Sui-Lee Wee Updated March 30, 2021

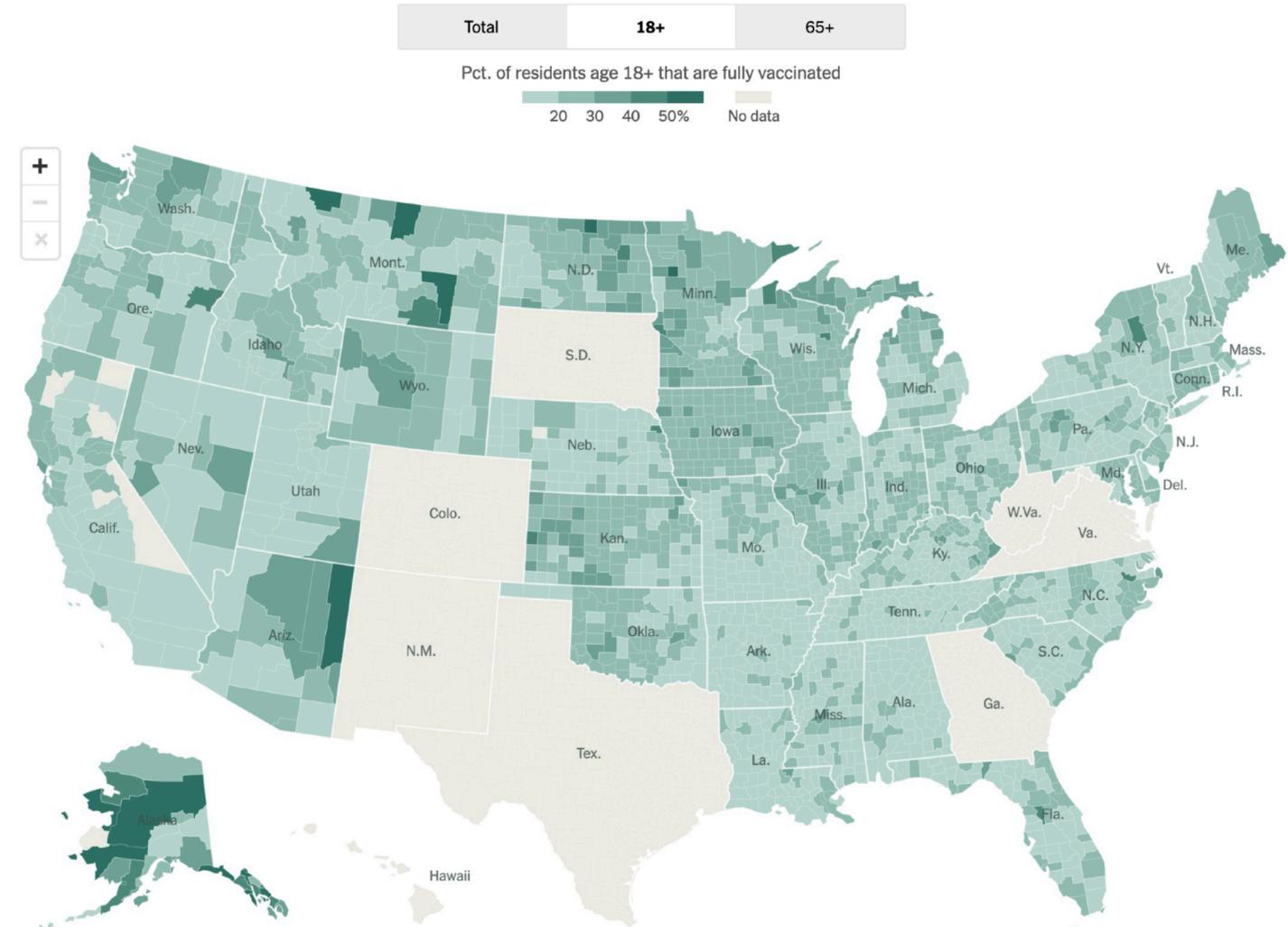


116 vaccines in development tracked by New York Times

New reported doses administered by day



Updated March 30, 2021



Source: [Centers for Disease Control and Prevention](https://www.cdc.gov/) | Note: No data available for Hawaii, New Mexico, Texas and some counties. Five other states were excluded because more than a quarter of data is missing.

<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>
<https://www.nytimes.com/interactive/2020/us/covid-19-vaccine-doses.html>

The Pfizer-BioNTech vaccine is highly effective in adolescents 12 to 15 years old, a clinical trial suggests.



Taking part in the Pfizer vaccine trial at Cincinnati Children's Hospital. Cincinnati Children's Hospital

The Pfizer-BioNTech Covid vaccine is extremely effective in adolescents 12 to 15 years old, perhaps even more so than in adults, the companies reported on Wednesday. No infections were found among children who received the vaccine in a recent clinical trial; they produced strong antibody responses and experienced no serious side effects.

Vaccine prognostication

- ▶ Success of new vaccine approaches opens possibilities for developing future vaccines
- ▶ Collaborative efforts on development show what science can do to respond to a crisis
- ▶ Vaccine equity is a major issue for this and future pandemics
- ▶ We are now in a race between vaccines and variants. Updates will be needed.

**QUESTIONS ON
VACCINES?**

PART 2

SARS-COV-2 VARIANTS

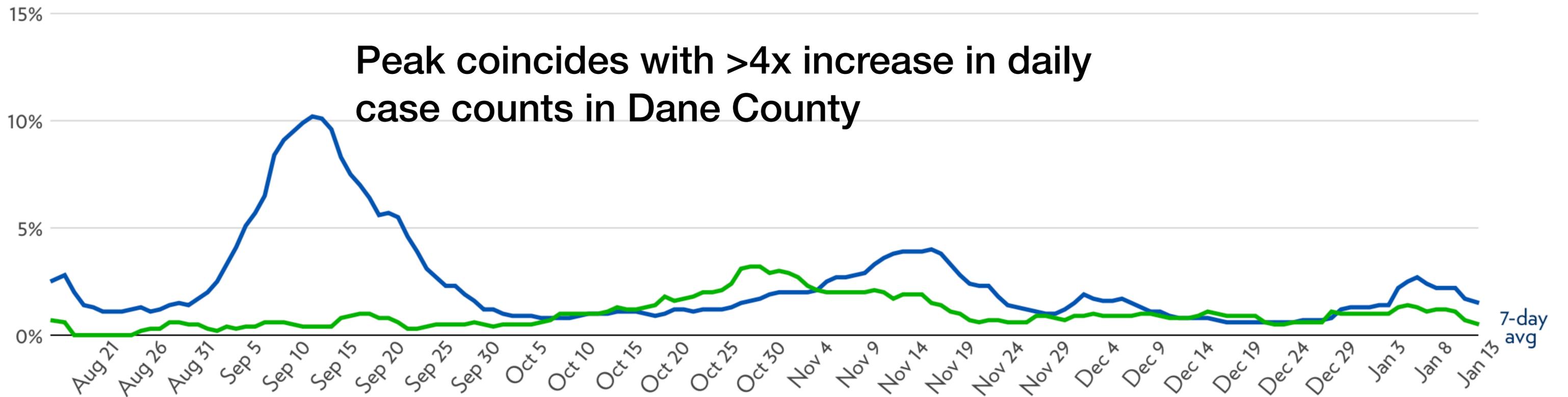
SARS-CoV-2 genomic epidemiology

- ▶ Mutations accumulate as viruses spread, giving rise to many different genetic lineages
- ▶ We can use these lineages like fingerprints to track the spread of specific viruses through space and time
- ▶ Molecular epidemiology questions:
 - ▶ How big is this outbreak? How many outbreaks are happening concurrently?
 - ▶ Is this outbreak growing or shrinking? How quickly? Impact of interventions?
 - ▶ Could person A have become infected from person B?
 - ▶ Is this virus evading immune detection?

**CASE STUDY:
UW CAMPUS OUTBREAK,
FALL 2020**

UW-Madison outbreak timeline

Percent Positive 7-Day Average

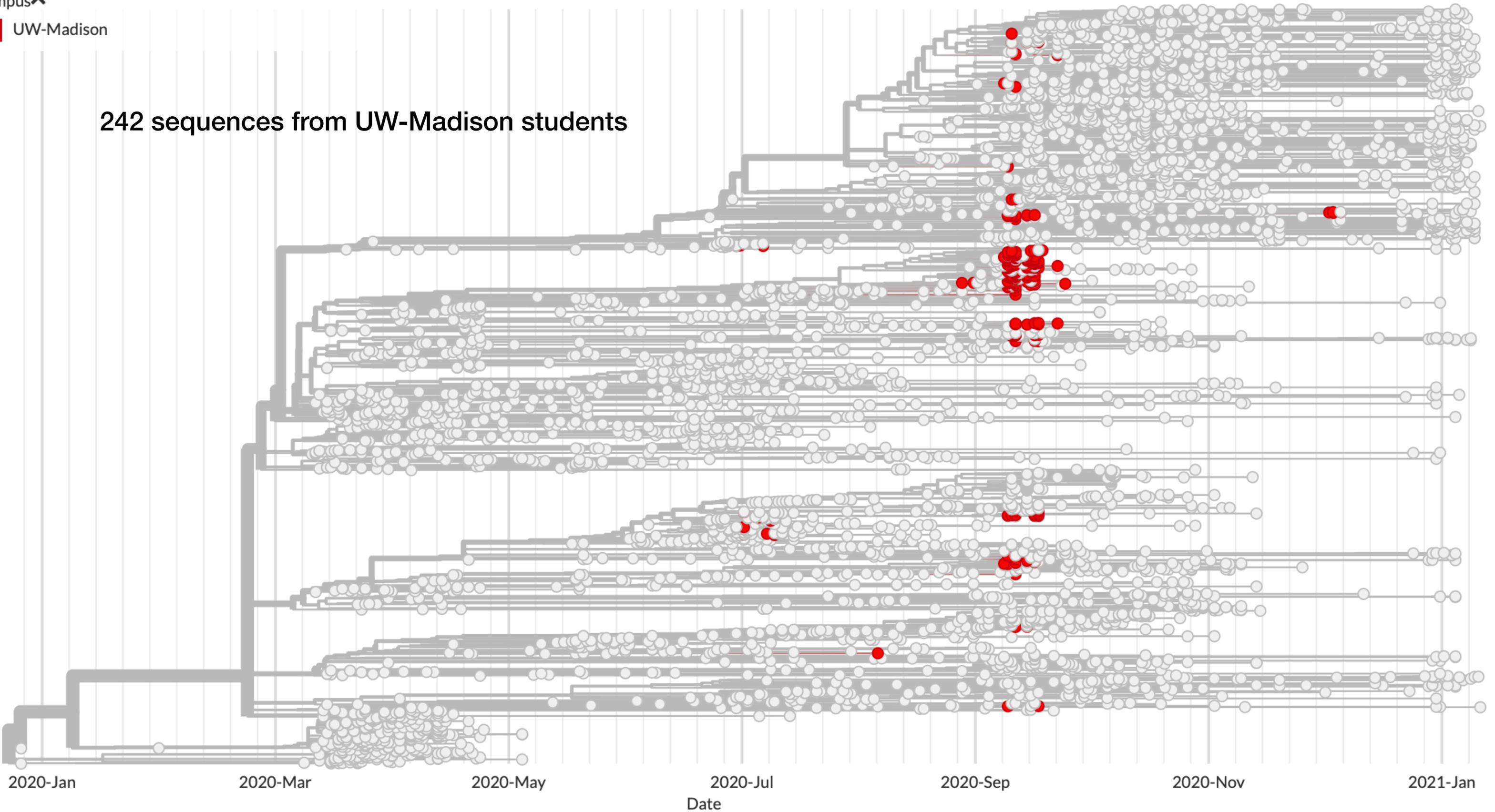


data: UW-Madison, Public Health Madison Dane County

Campus ^

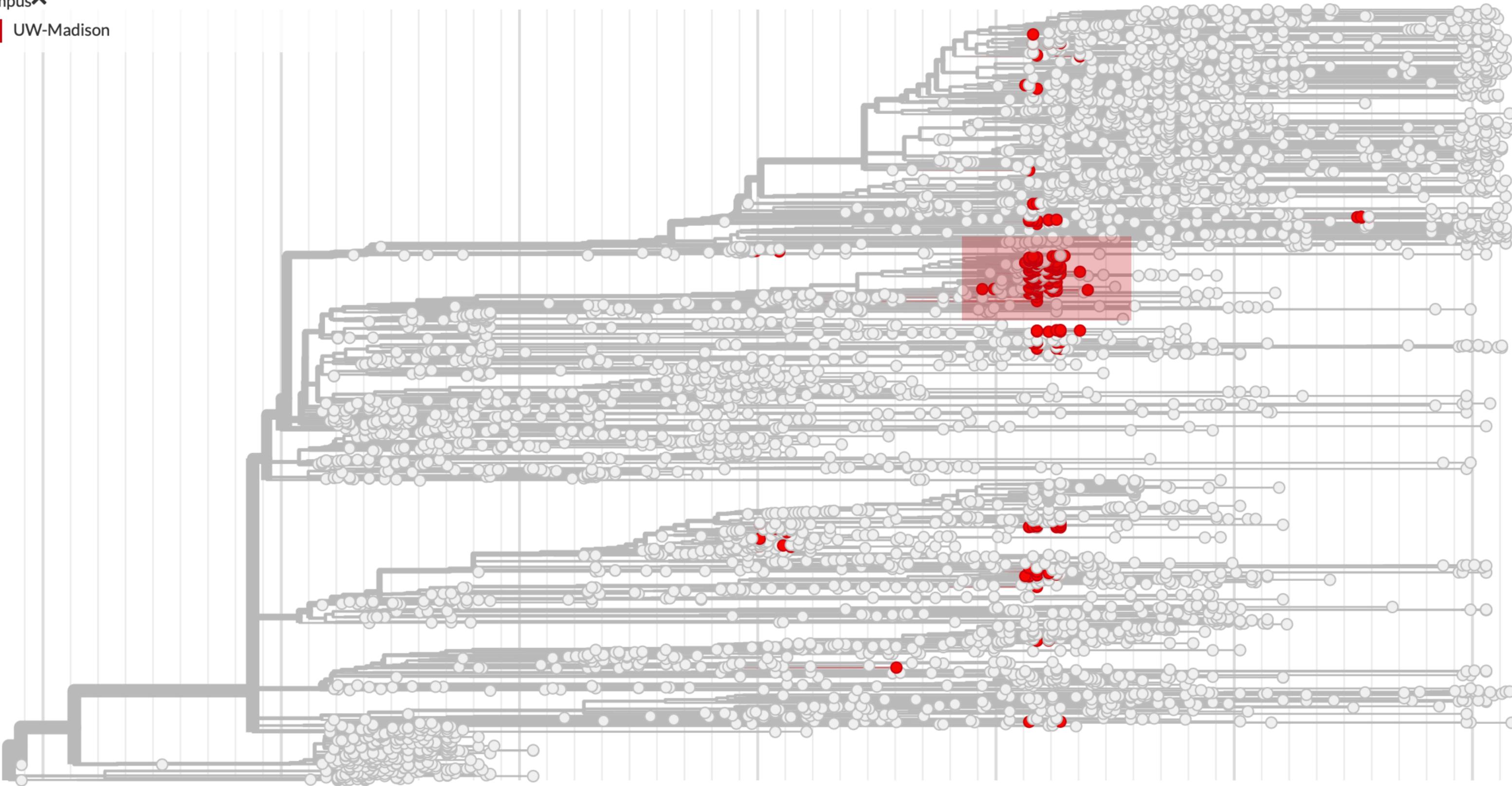
■ UW-Madison

242 sequences from UW-Madison students



Campus

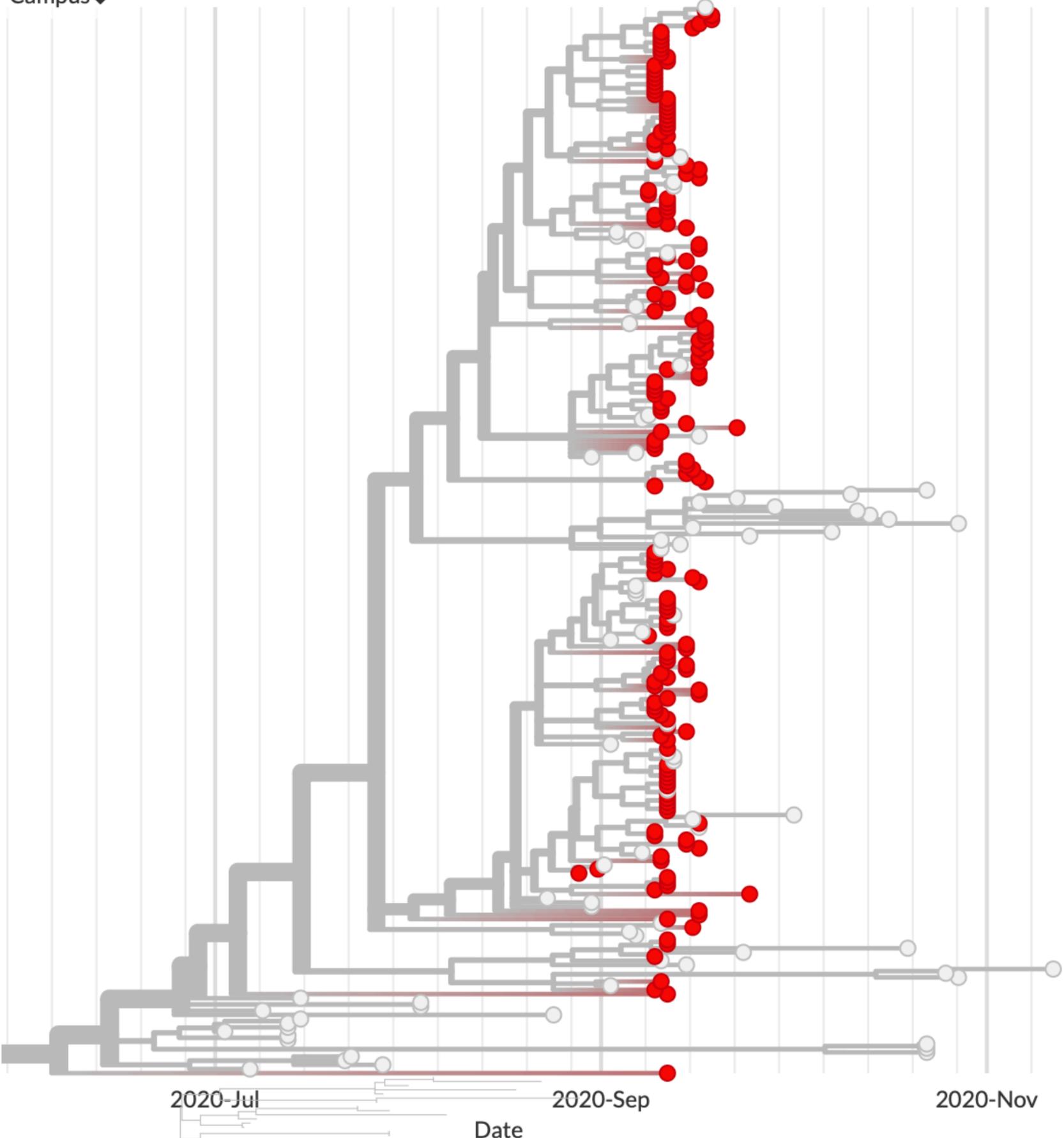
■ UW-Madison



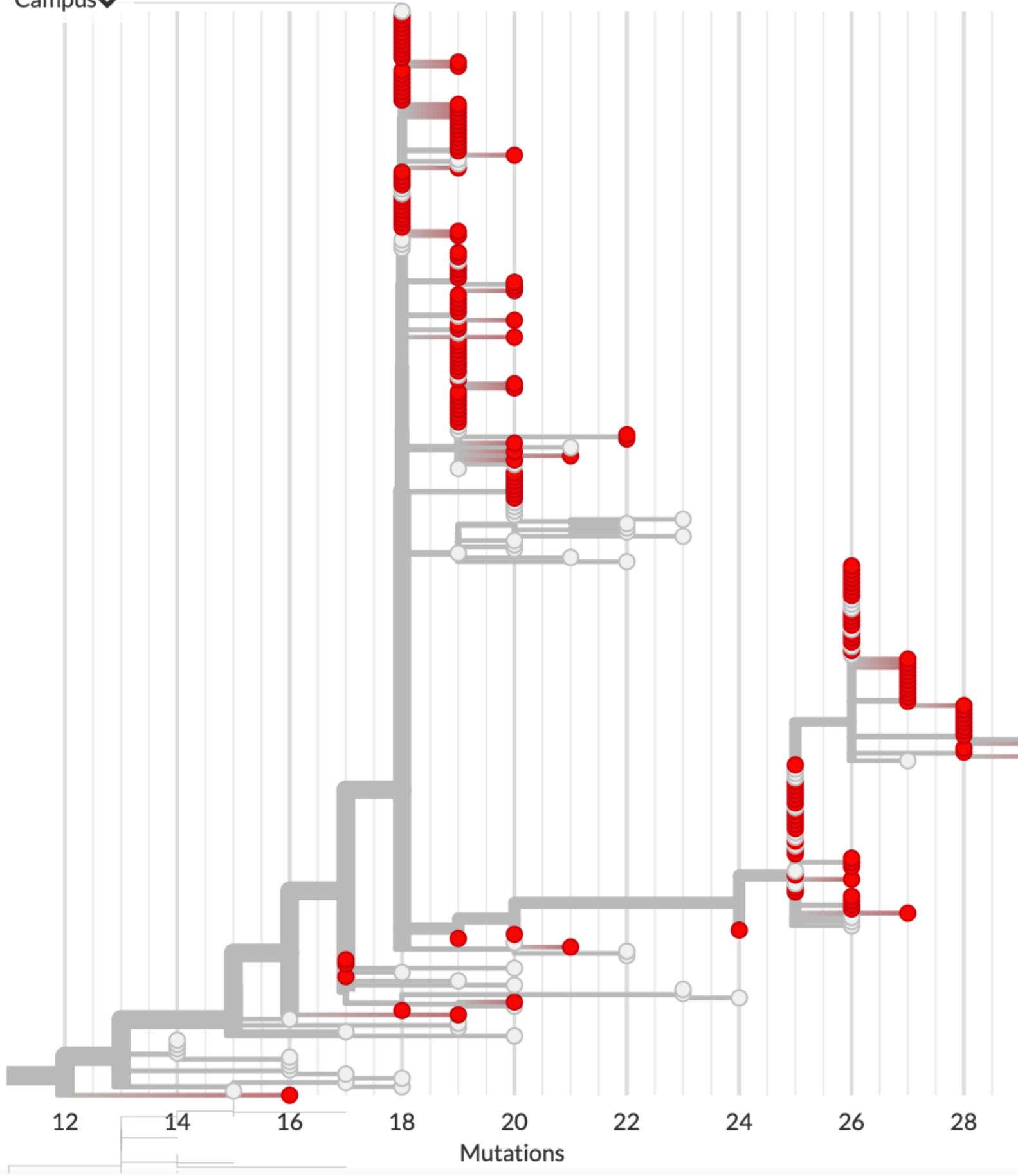
2020-Jan 2020-Mar 2020-May 2020-Jul 2020-Sep 2020-Nov 2021-Jan

Date

Campus ▾



Campus ▾



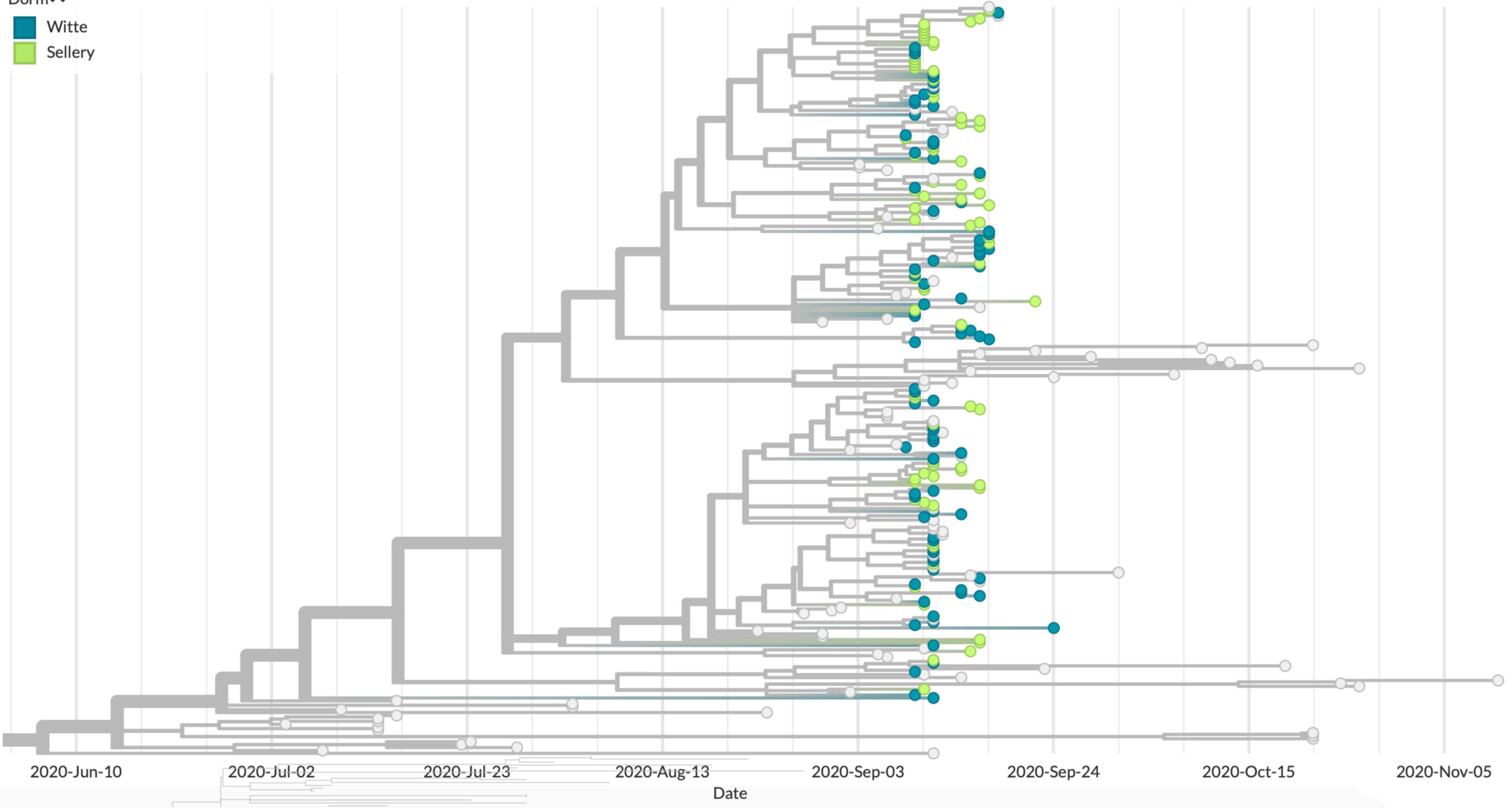
Extensive mixing of lineages

- Two high-rise dormitories (census ~1,100 residents each) quarantined for 2 weeks
- Share a common green space and dining hall
- Attack rates ~30%



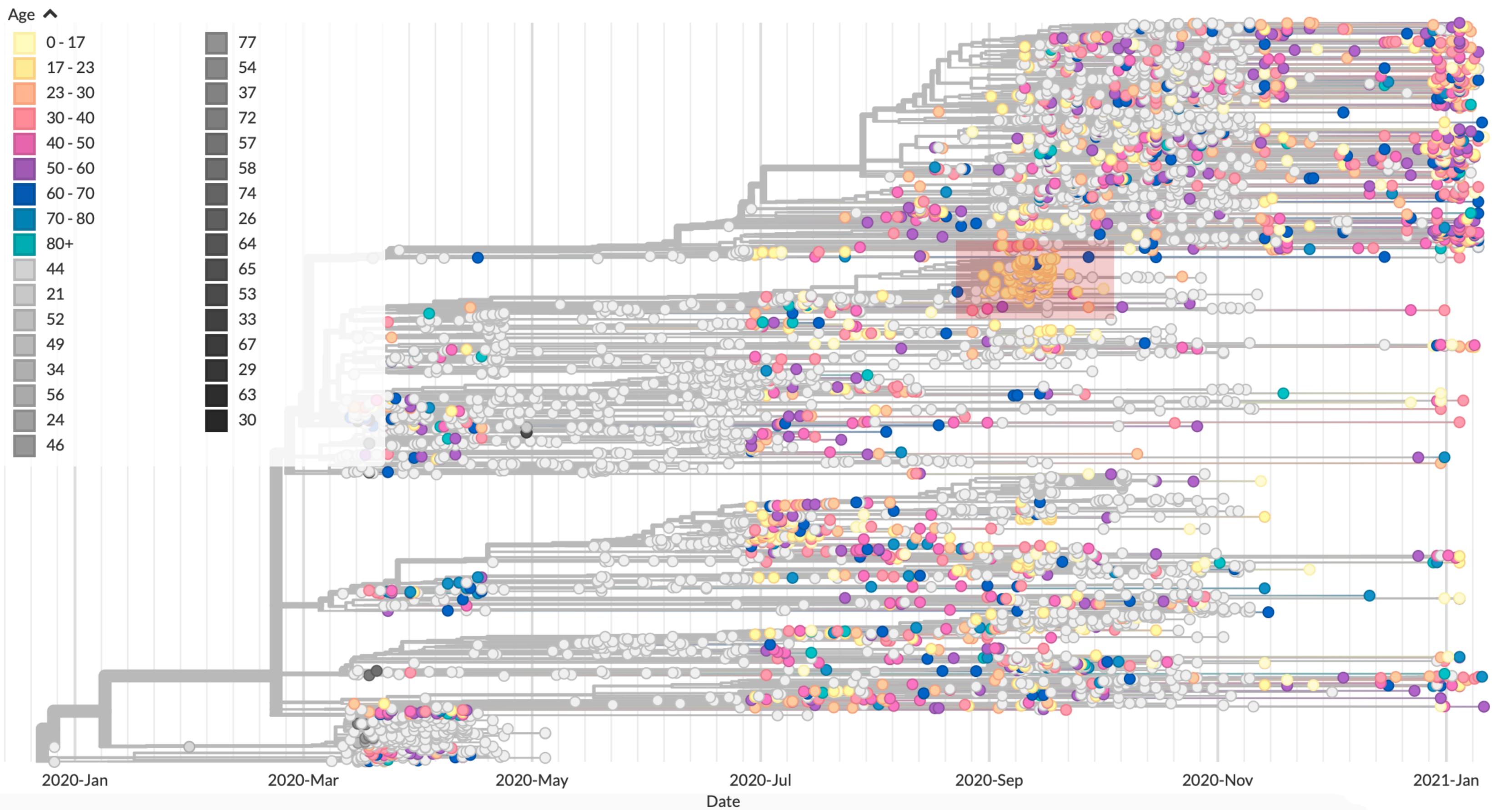
Dorm ^

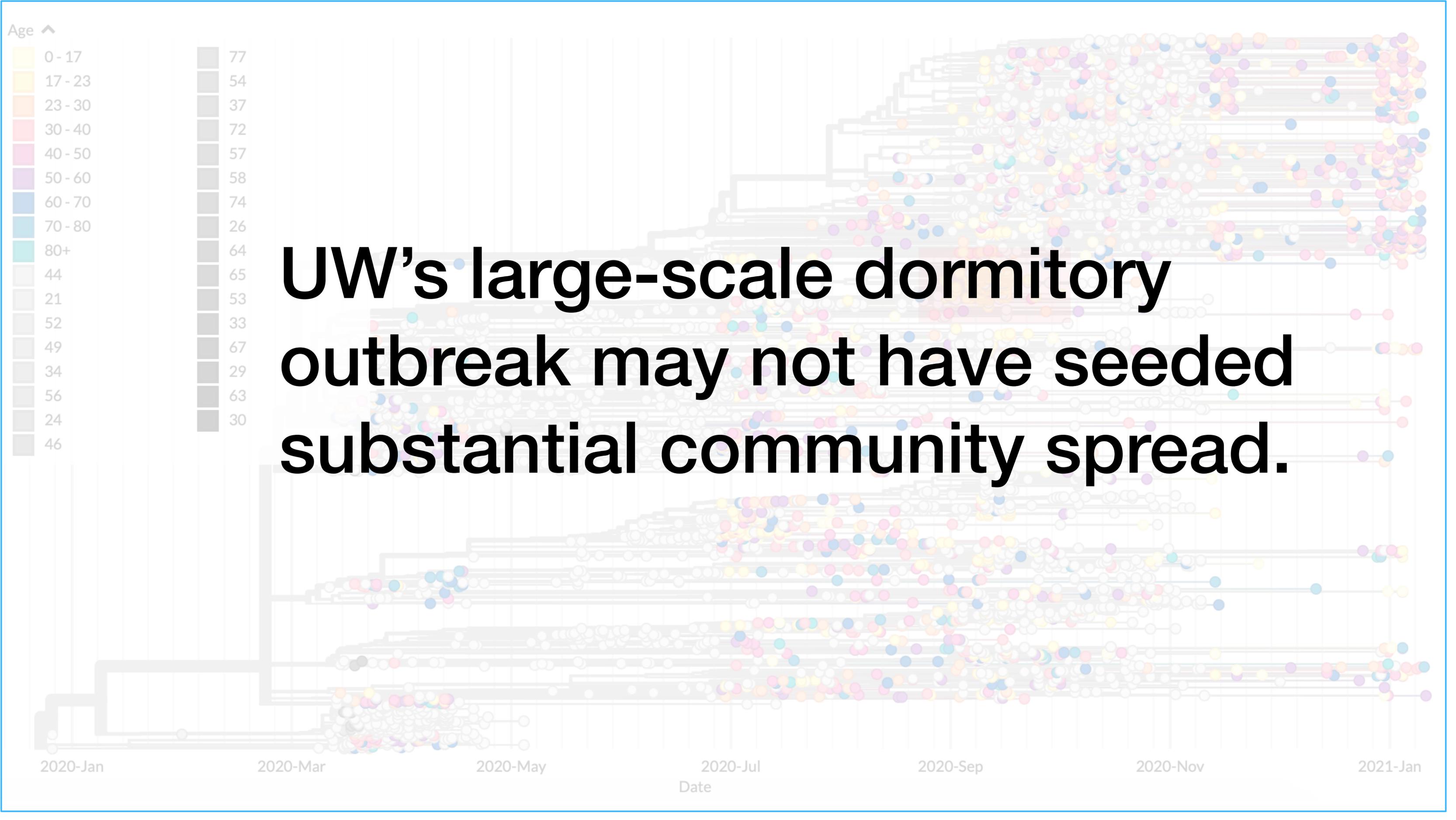
- Witte
- Sellery



Has this outbreak spilled over into the community?

- Concerns that college outbreaks may intensify community outbreaks; there is some evidence for this
- UW students mix with the broader community at bars, restaurants, and other congregate settings
- Cell phone mobility data suggests that students in heavily affected dorms may have been more likely than others to visit nearby bars in the weeks prior to the outbreak





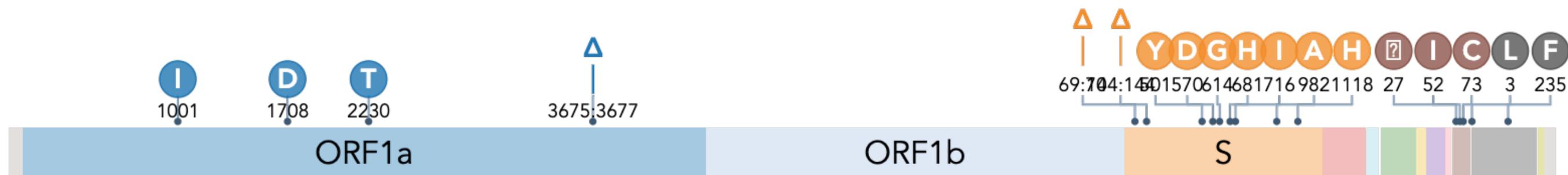
VARIANTS OF CONCERN

Variants of concern

- ▶ “Variant” = virus with characteristic combination of mutations
- ▶ Most variants do not have clear biological differences
- ▶ Reasons for potential concern:
 - ▶ Infection of people who have pre-existing immunity
 - ▶ Spread in a region thought to have high levels of population immunity
 - ▶ Continued or accelerating spread despite ongoing interventions
 - ▶ Association with more severe disease

Current variants of concern

B.1.1.7 characteristic mutations



B.1.351 characteristic mutations



P.1 characteristic mutations



Pfizer vaccine induces antibodies against multiple VOCs

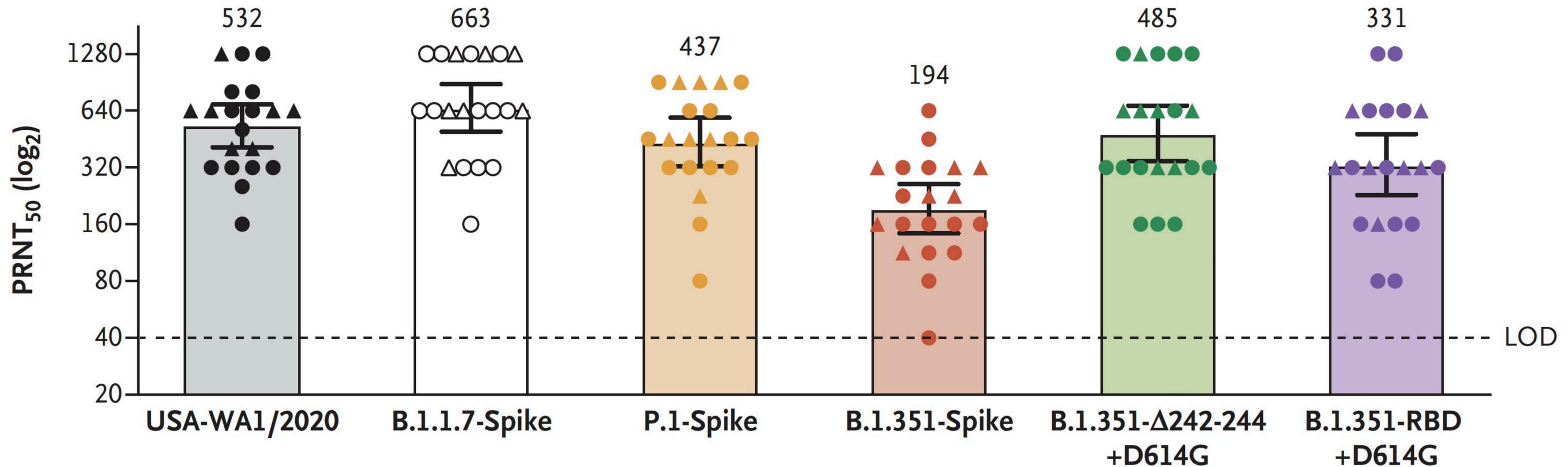
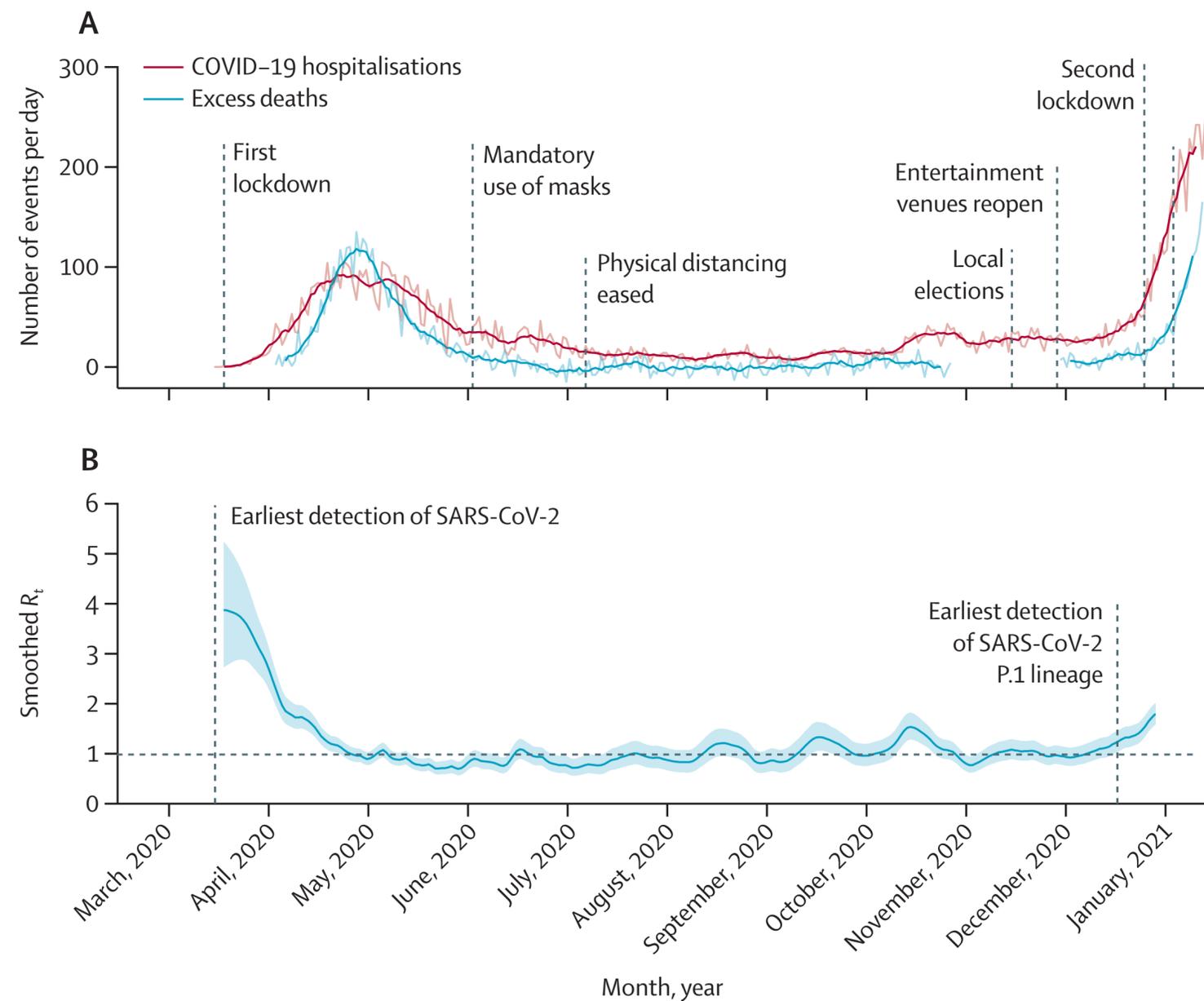


Figure 1. Serum Neutralization of Variant Strains of SARS-CoV-2 after the Second Dose of BNT162b2 Vaccine.

Resurgence of COVID-19 in Manaus, Brazil



QUESTIONS?