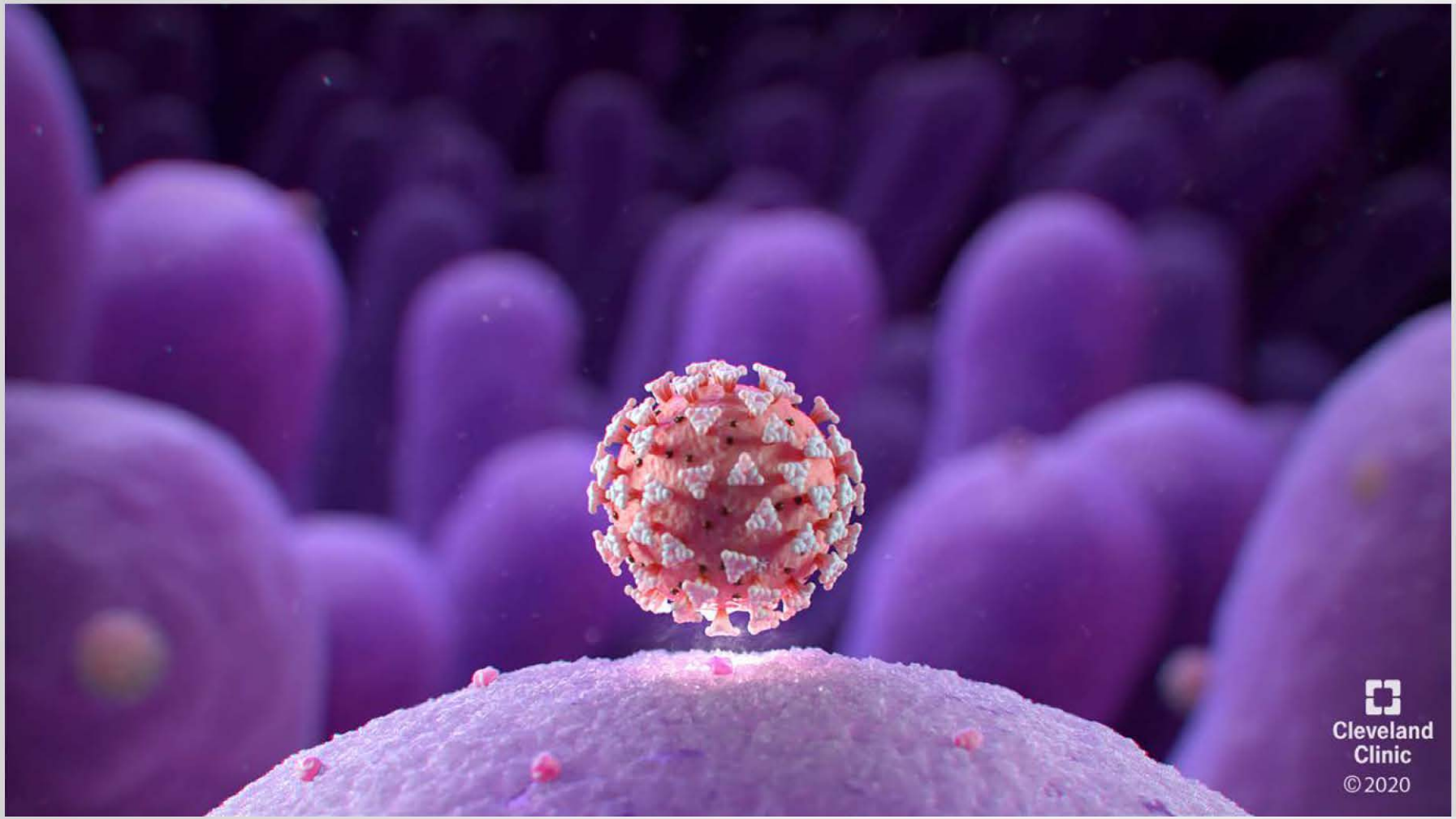
SARS-CoV-2

Biology, Testing, Genetics, & Evolution



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Instagram: surfing_scientist

I am a developmental evolutionary Biologist.

- I mostly use butterflies wing color pattern to study study the evolution of biological diversity.
- I use an array of molecular tools to determine genetic changes that underlie the development of distinct morphologies

I AM INTERESTED IN THE CELLULAR, MOLECULAR AND DEVELOPMENTAL MECHANISMS UNDERLYING BIODIVERSITY




WHAT MAKES US UNIQUE?

INTRODUCTION OF THE CORONAVIRUSES

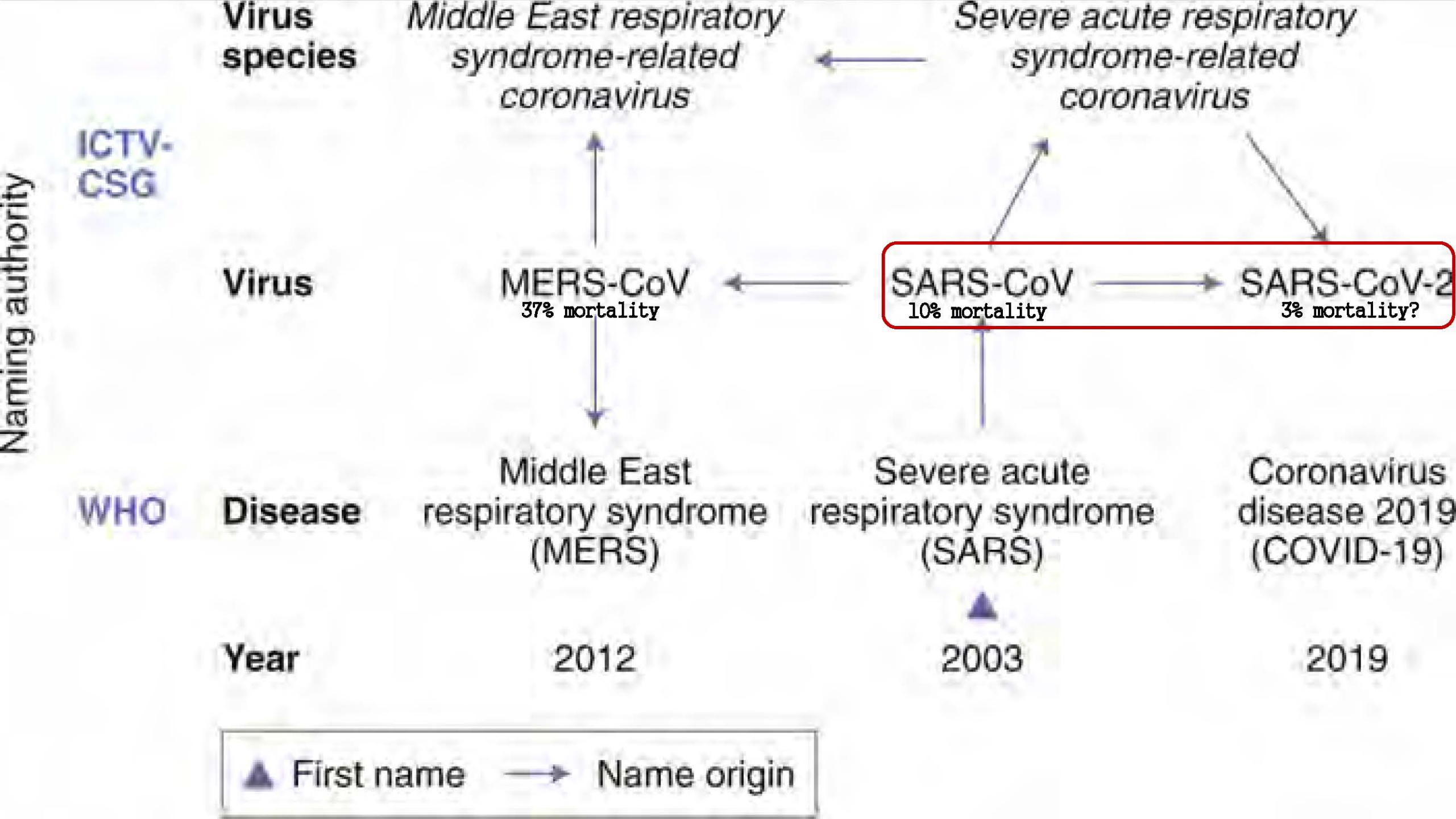
Coronaviruses, named for the crown-like spikes on their surface (Latin: corona = crown), are positive-sense RNA viruses that belong to the Coronvirinae subfamily, in the Coronaviridae family.

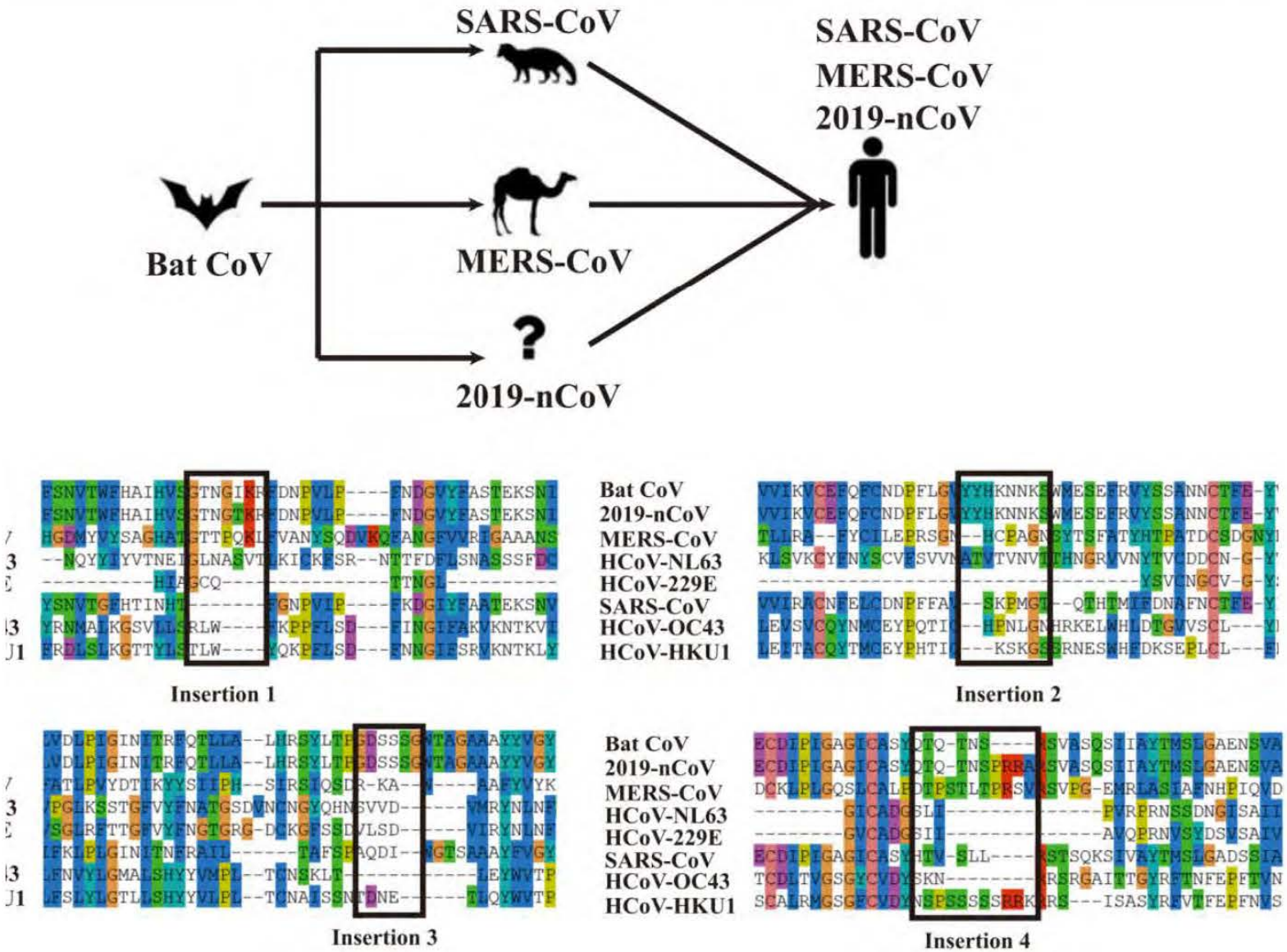
<u>The name of the virus and the disease</u>

- **Diseases and the viruses or bacteria that cause them often have different names. For instance, the "human immunodeficiency virus", HIV, causes "acquired immunodeficiency syndrome", AIDS.**
- **The virus causing the current outbreak is called *severe acute respiratory syndrome coronavirus 2*, shortened to SARS-CoV-2. The disease is called *coronavirus disease*, shortened to COVID-19.**

<u>What is a coronavirus?</u>

- **Although people often refer to the virus causing COVID-19 as "the coronavirus", there are many different coronaviruses.**
- **Including the SARS-CoV-2 seven different coronaviruses are now known to infect humans.**
- **Coronaviruses are the cause for around 30% of cases of the common cold. Corona is Latin for "crown" – this group of viruses is given its name due to the fact that its surface looks like a crown under an electron microscope.**
- **Two outbreaks of new diseases in recent history were also caused by coronaviruses – SARS in 2003 that resulted in around 1,000 deaths (10% mortality) and MERS in 2012 that resulted in 862 deaths (37% mortality).**


Naming authority
Virus species
Middle East respiratory syndrome-related coronavirus
Severe acute respiratory syndrome-related coronavirus
ICTV-CSG
Virus
MERS-CoV
37% mortality
SARS-CoV
10% mortality
SARS-CoV-2
3% mortality?
WHO
Disease
Middle East respiratory syndrome (MERS)
Severe acute respiratory syndrome (SARS)
Coronavirus disease 2019 (COVID-19)
Year
2012
2003
2019
First name
Name origin



COMPARISON BETWEEN AMINO ACIDIC SEQUENCES OF THE DIFFERENT CORONAVIRUSES

Zhang C. et al. (2020). Protein structure and sequence re-analysis of 2019-nCoV genome does not indicate snakes as its intermediate host or the unique similarity between its spike protein insertions and HIV-1. doi: https://doi.org/10.1101/2020.02.04.933135

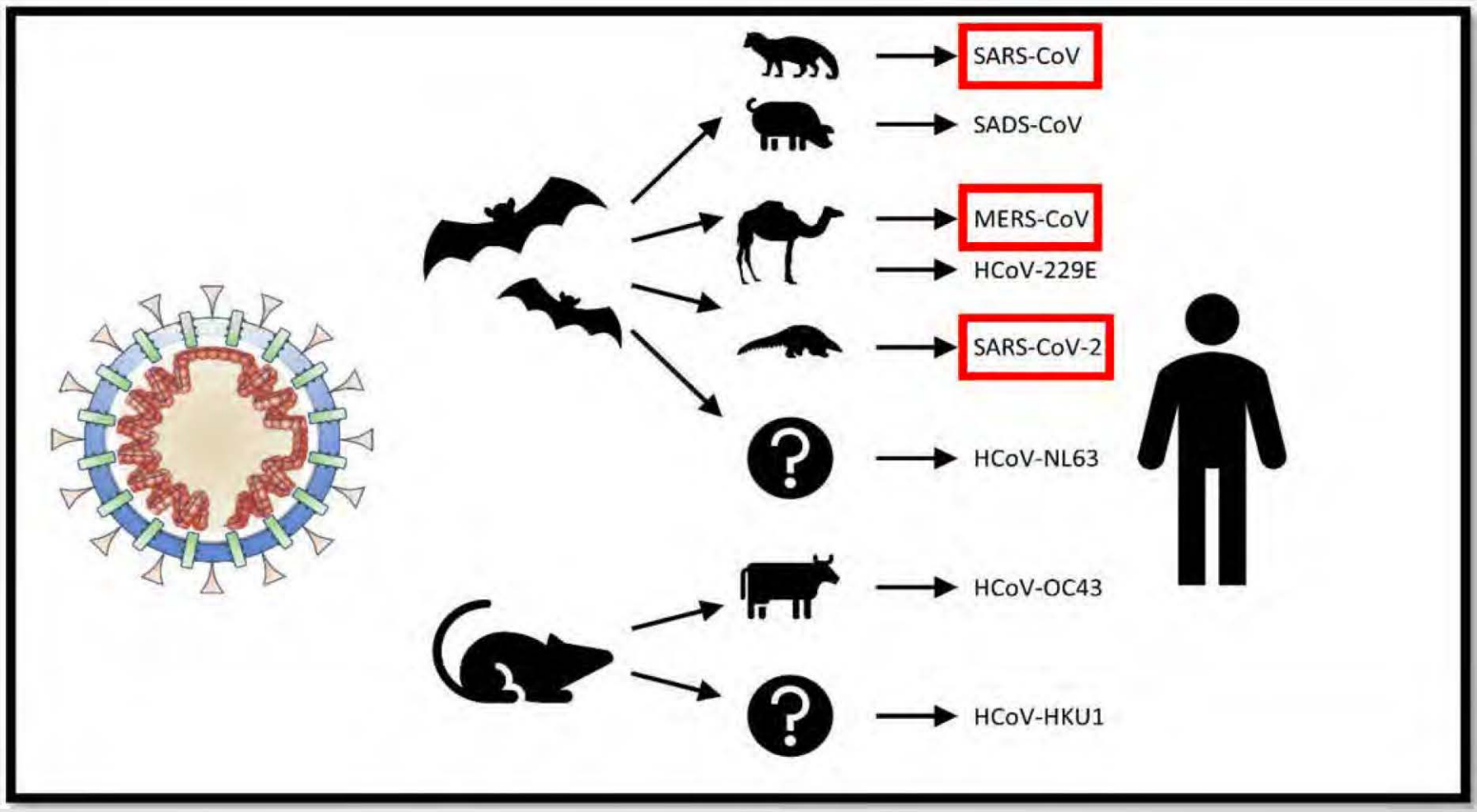
ORIGIN OF CORONAVIRUSES

All coronaviruses that have caused diseases to humans have had animal origins generally either in bats or rodents.

In the case of SARS-CoV and MERS-CoV, they were transmitted directly to humans from civet cats and dromedary camels respectively.

The 2019 SARS-CoV-2 was likely transmitted to humans through pangolins.

There was some early speculation that SARS-CoV-2 emerged from a manmade manipulation of an existing coronavirus, but there is no evidence to support such a theory.



Under certain conditions, some pathogens can jump across species to humans; this is known as zoonotic transmission

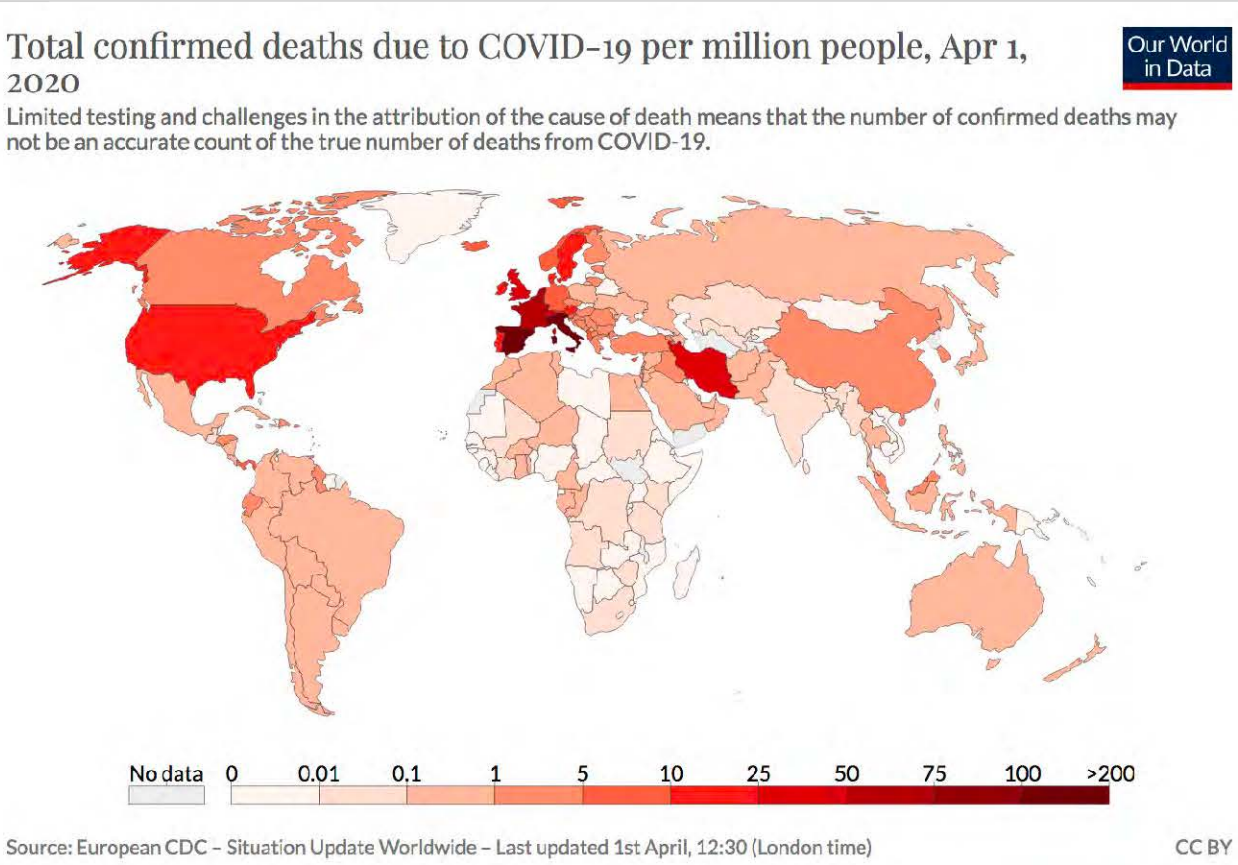
SARS-COV-2

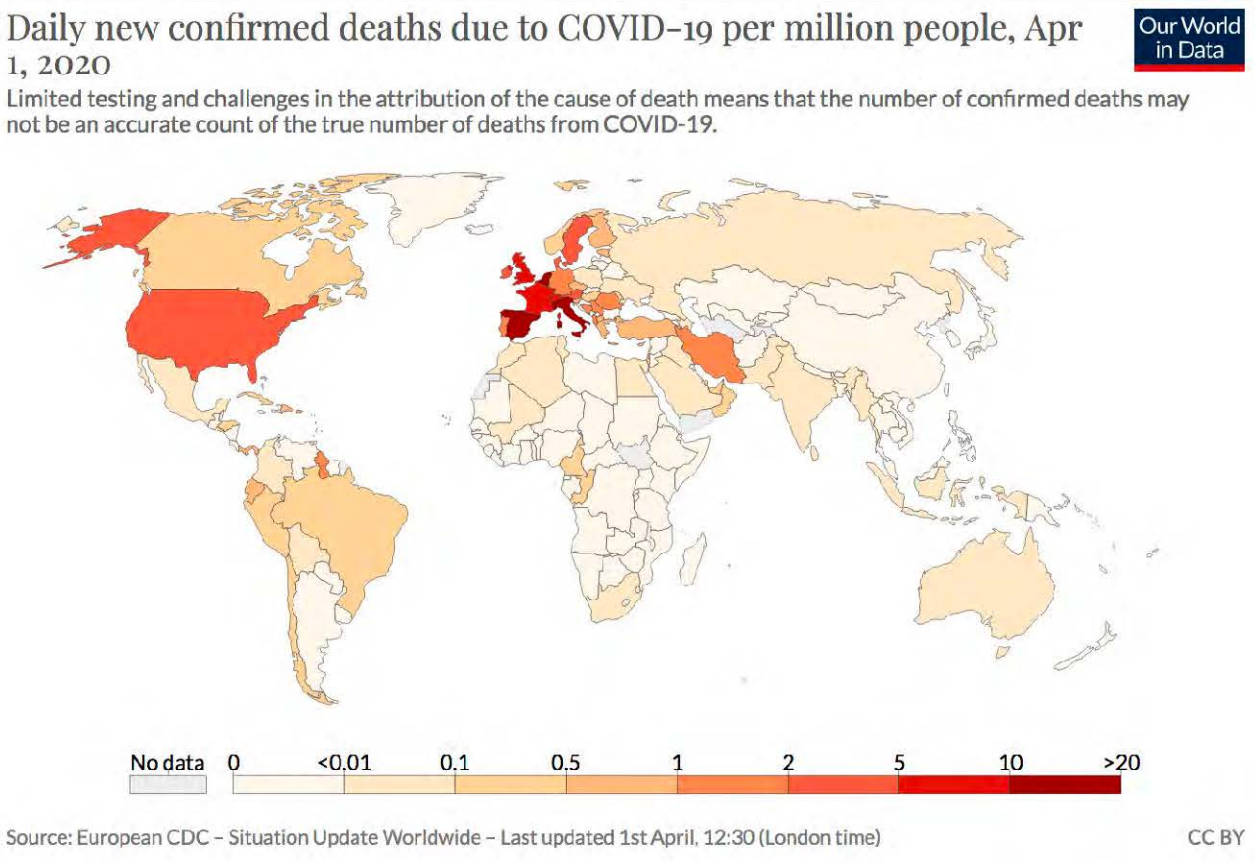
- Is a positive RNA, which make it similar to our mRNA
- The size of the virus genome is around 30,000 nucleotides that code for about 20 structural and non-structural proteins that are needed for its replication
- The RNA sequence of the virus is new, not seen before in other viruses that infect humans
- It uses our cellular machinery to replicate and make multiple copies of itself
- The immune system has never encountered this virus and therefore we have no antibodies (proteins responsible for protecting us from pathogens) available to fight it rapidly.

THE IMPACT OF COVID-19

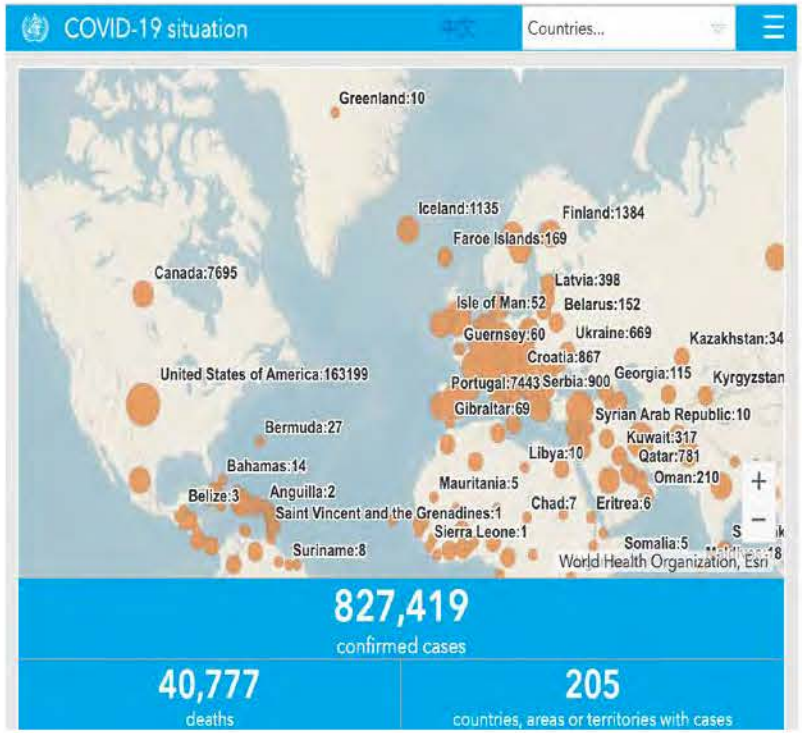
- **Even the best existing research and data is preliminary and do not represent the complete impact and progress of the current pandemic**
- **The total number of COVID-19 cases is not known. It is certain that the total number of infected individuals is higher than the number of known confirmed cases. This is mainly due to limited testing.**
- **Without widespread testing for COVID-19 we are incapable to know how the pandemic is spreading and therefore appropriately respond to it.**
- **Reported cases on any given day does not necessarily represent the actual number of new cases on that day**

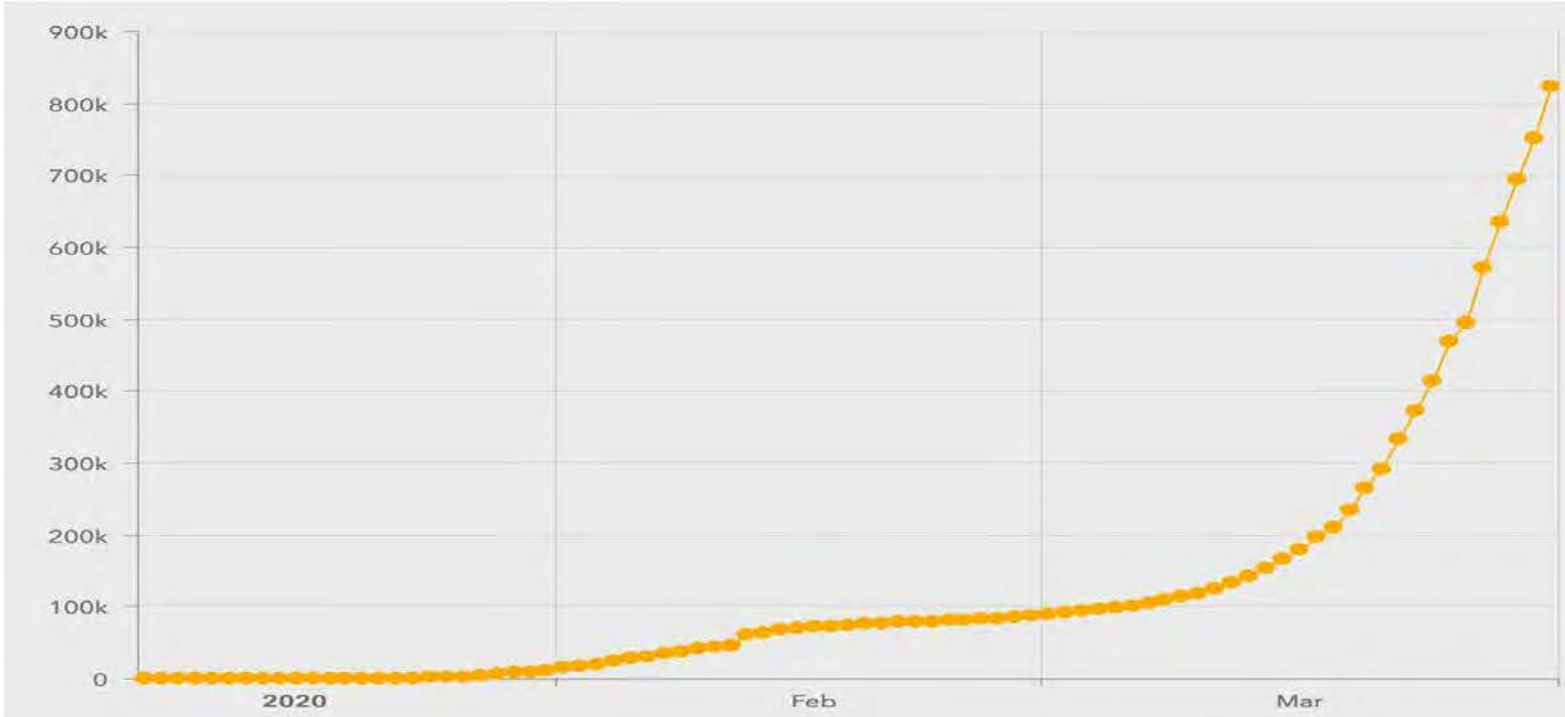
DISTRIBUTION OF DEATHS AROUND THE WORLD





To understand how infectious the disease is, and how dangerous, we need to test people to see if they have it. For instance, if you know that 100 people have died from it, it makes a difference whether that's out of 1,000 people who have had the disease, or 100,000. The best way to fight against a disease that spreads very easily but doesn't kill many of those infected is very different to the best way to fight against a disease that spreads more slowly but is more deadly.





CORONAVIRUS IN NUMBER

Case fatality rates: COVID-19 vs. US Seasonal Flu

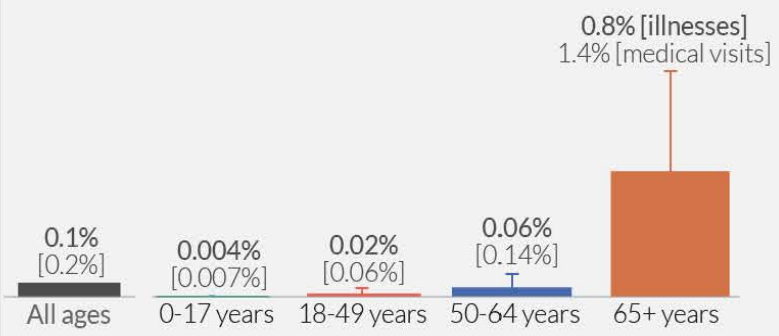
Case fatality rate (CFR) is specific to a location and time. It is calculated by dividing the total number of deaths from a disease by the number of confirmed cases.

Our World in Data

Seasonal Flu

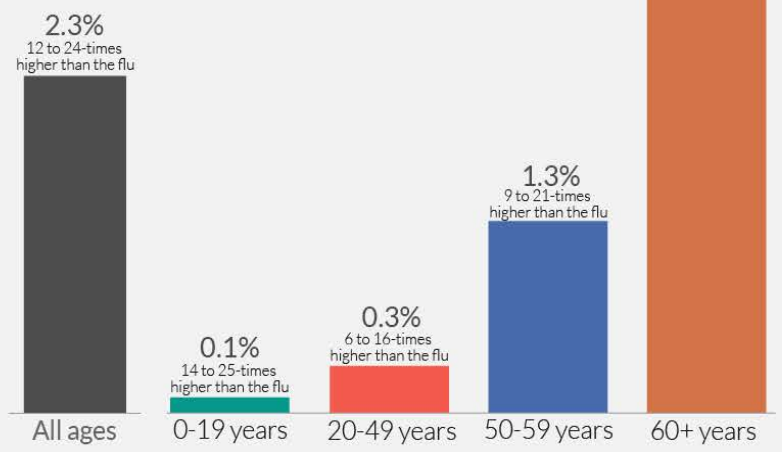
Case fatality rates for the influenza season 2018-19 in the USA.

Symptomatic cases are calculated based on models which aim to account for underreporting – figures based on medical visits are therefore also shown in square brackets, which may be a closer comparison to COVID-19 case fatality rates.



COVID-19

Case fatality rates for the COVID-19 outbreak in China, for the period up to February 11, 2020.

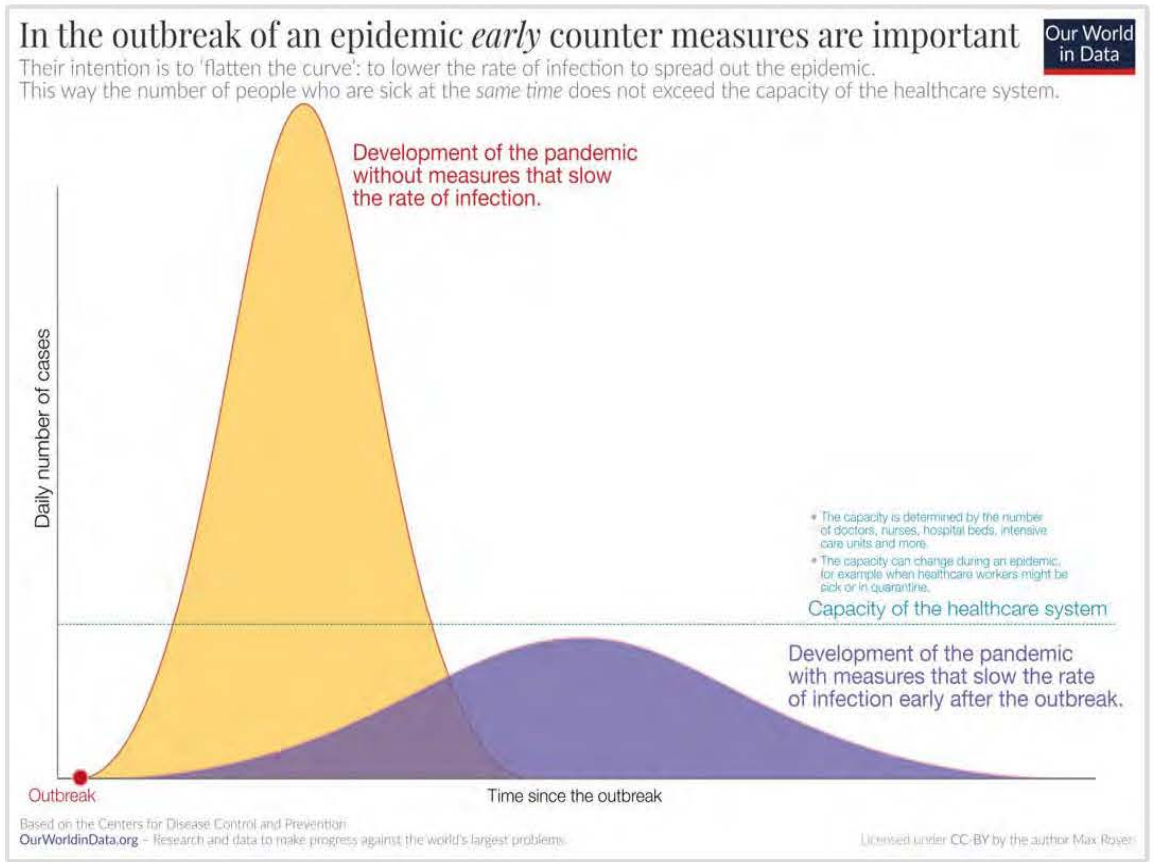


Data: Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. *Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020.* China CDC Weekly.
US Influenza data is sourced from the US Centers for Disease Control and Prevention (CDC).

OurWorldinData.org – Research and data to make progress against the world's largest problems.

COMPARISON BETWEEN INFLUENZA AND COVID-19

THE VALUE OF EARLY CONTAINMENT



Because this is a new virus for which no one is protected, and it spreads fast, we are facing a pandemic of the disease. The most dangerous problem (to be avoided) is the collapse of the healthcare system. There are only a limited number of hospitals, beds, doctors, nurses and intensive care units. If many people get sick all at once the capacity of the healthcare system is compromised. This is extremely important for a place like Puerto Rico given the natural disasters and other problems recently encountered.

TESTING FOR COVID-19

One of the most important things that countries are doing to help understand and stop the spread of COVID-19 is testing.

Why is testing important?

Testing allows infected people to *know* that they are infected. This can help them receive the care they need; and it can help them take measures to reduce the probability of infecting others. People who don't know they are infected might not stay at home and thereby risk infecting others. Every health worker should be tested every two weeks.

What is the capacity for COVID 19 testing?

Unfortunately, the capacity for COVID-19 testing is still low in many countries around the world. For this reason we still do not have a good understanding of the spread of the pandemic.

Why few COVID 19 testing?

- Shortage of materials (swabs, kits…) demand/offer
- Regulations that impose strict standards and controls
- Bureaucracy

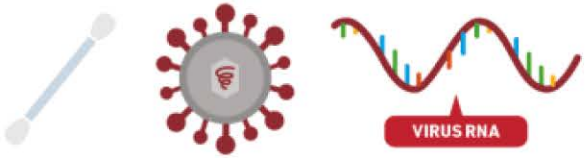
How are COVID-19 tests done?

The most common tests for COVID-19 involve taking a swab from a patient's nose and throat and checking them for the genetic footprint of the virus. They are called "PCR tests".

HOW DO THE TESTS FOR CORONAVIRUS WORK?

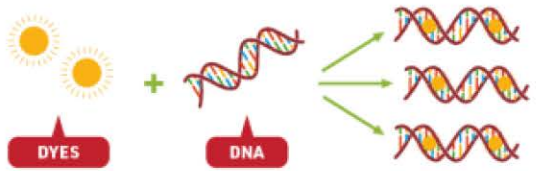
HOW CURRENT TESTS WORK

1. A swab is taken of the inside of a patient's nose or the back of their throat. This sample is then sent to a lab to test.

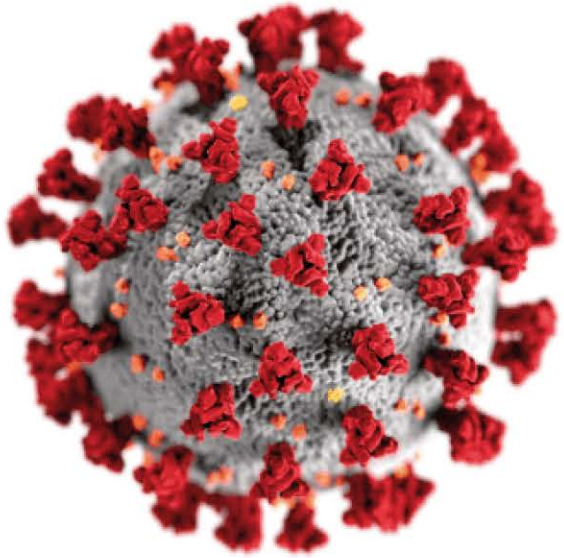


2. The RNA of the virus is extracted and purified. An enzyme, reverse transcriptase, converts the RNA to DNA.

3. The DNA is mixed with primers, sections of DNA designed to bind to characteristic parts of the virus DNA. Repeatedly heating then cooling DNA with these primers and a DNA-building enzyme makes millions of copies of virus DNA.



4. Fluorescent dye molecules bind to the virus DNA as it is copied. Binding makes them give off more light, which is used to confirm the presence of the virus in the sample.



ISSUES WITH TESTING

REAGENT ISSUES

High demand and issues with reagents have delayed testing in some countries.

TIME-CONSUMING

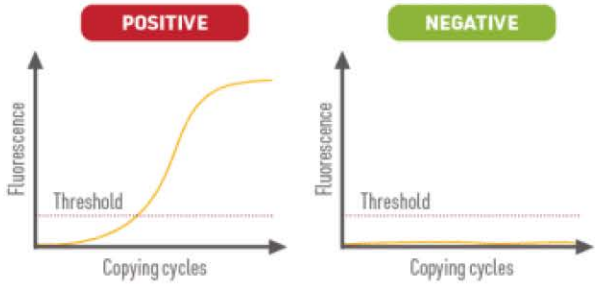
It takes a few hours to get results from the test, limiting how many tests can be done.

FALSE POSITIVES AND NEGATIVES

In some cases sample degradation or contamination can affect the results.

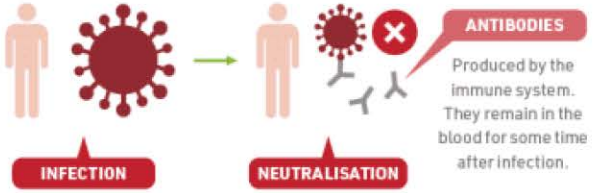
POSITIVE AND NEGATIVE TESTS

The fluorescence increases as more copies of the virus DNA are produced. If it crosses a certain threshold, the test is positive. If the virus isn't present, no DNA copies are made and the threshold isn't reached. In this case, the test is negative.

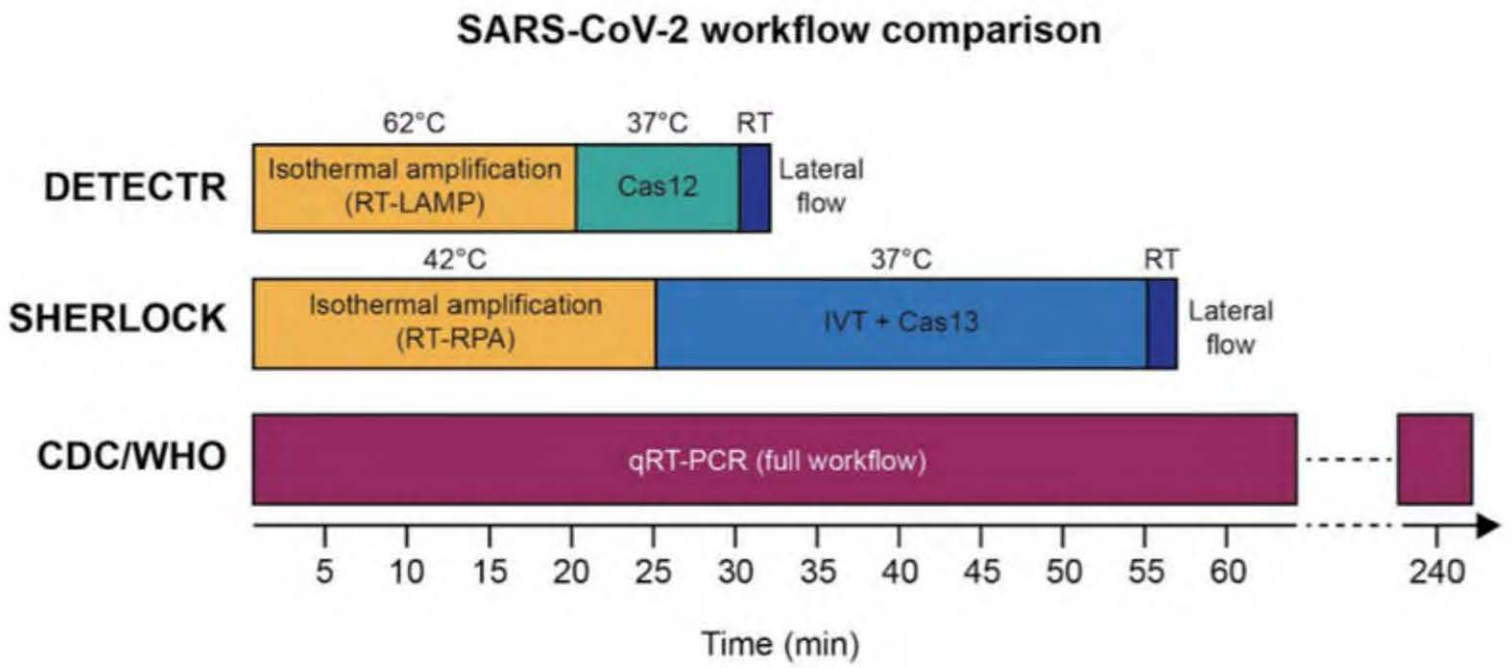


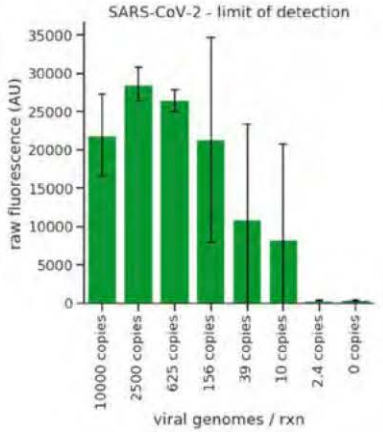
FUTURE TESTS

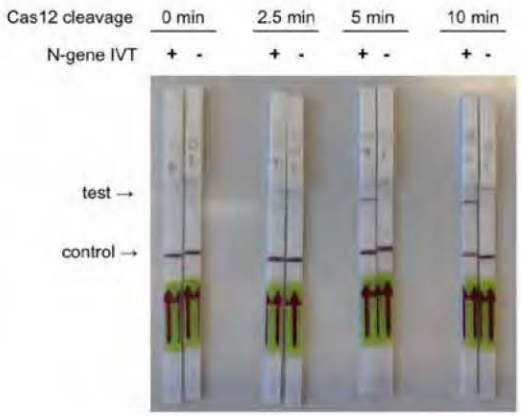
The current tests are good for diagnosing an infection – but they can't tell us if someone has had it and then recovered. Tests that look for antibodies against the virus can do this.



Tests that look for proteins on the surface of the virus are also in development. These tests are faster, but less accurate.



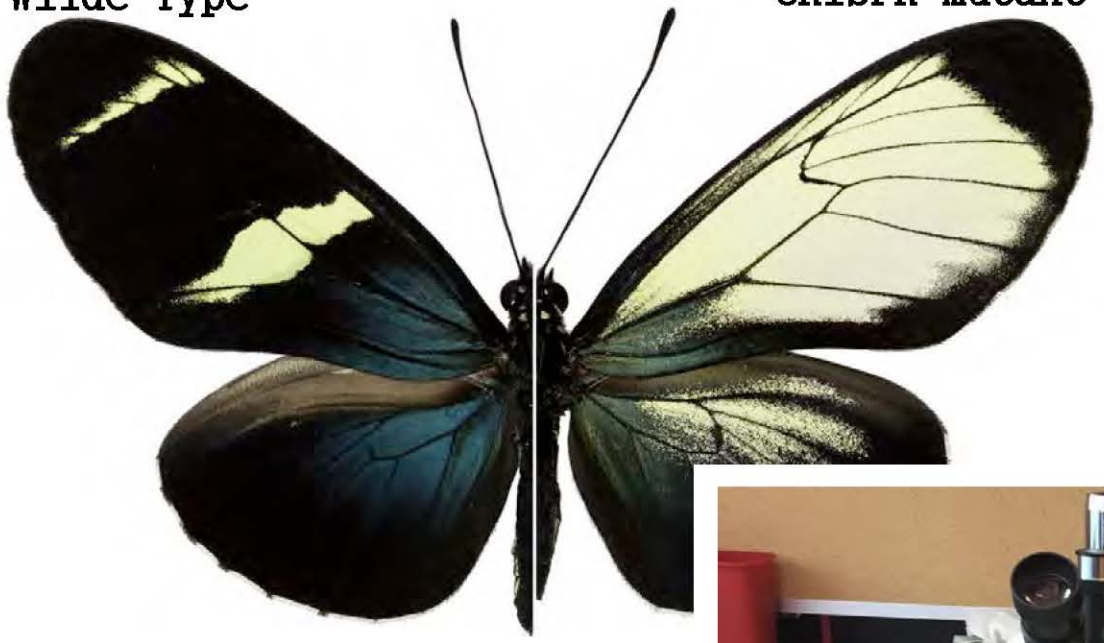


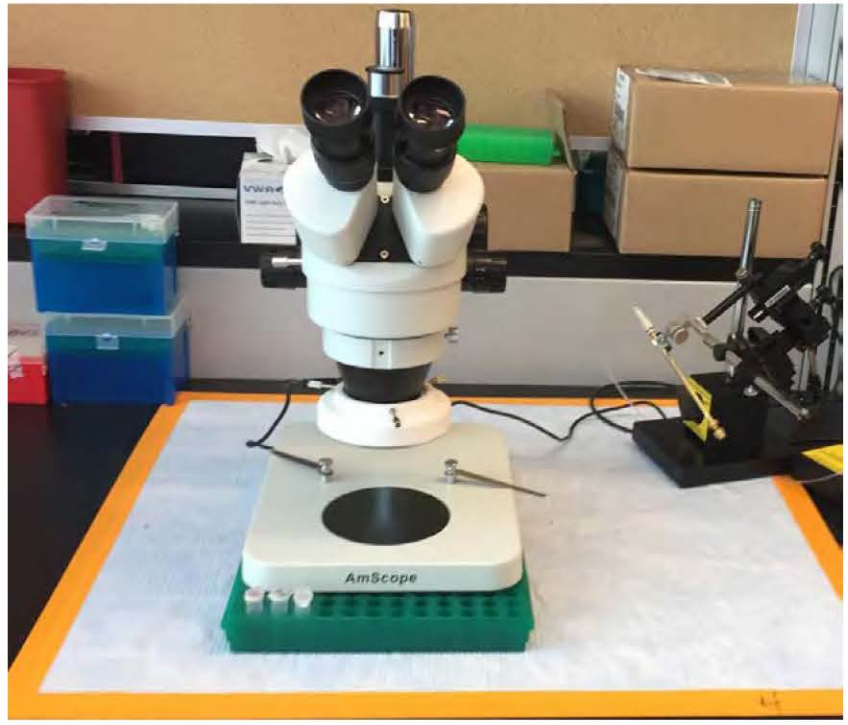


ALTERNATIVE TESTING CRISPR/CAS APPROACH

Wilde Type

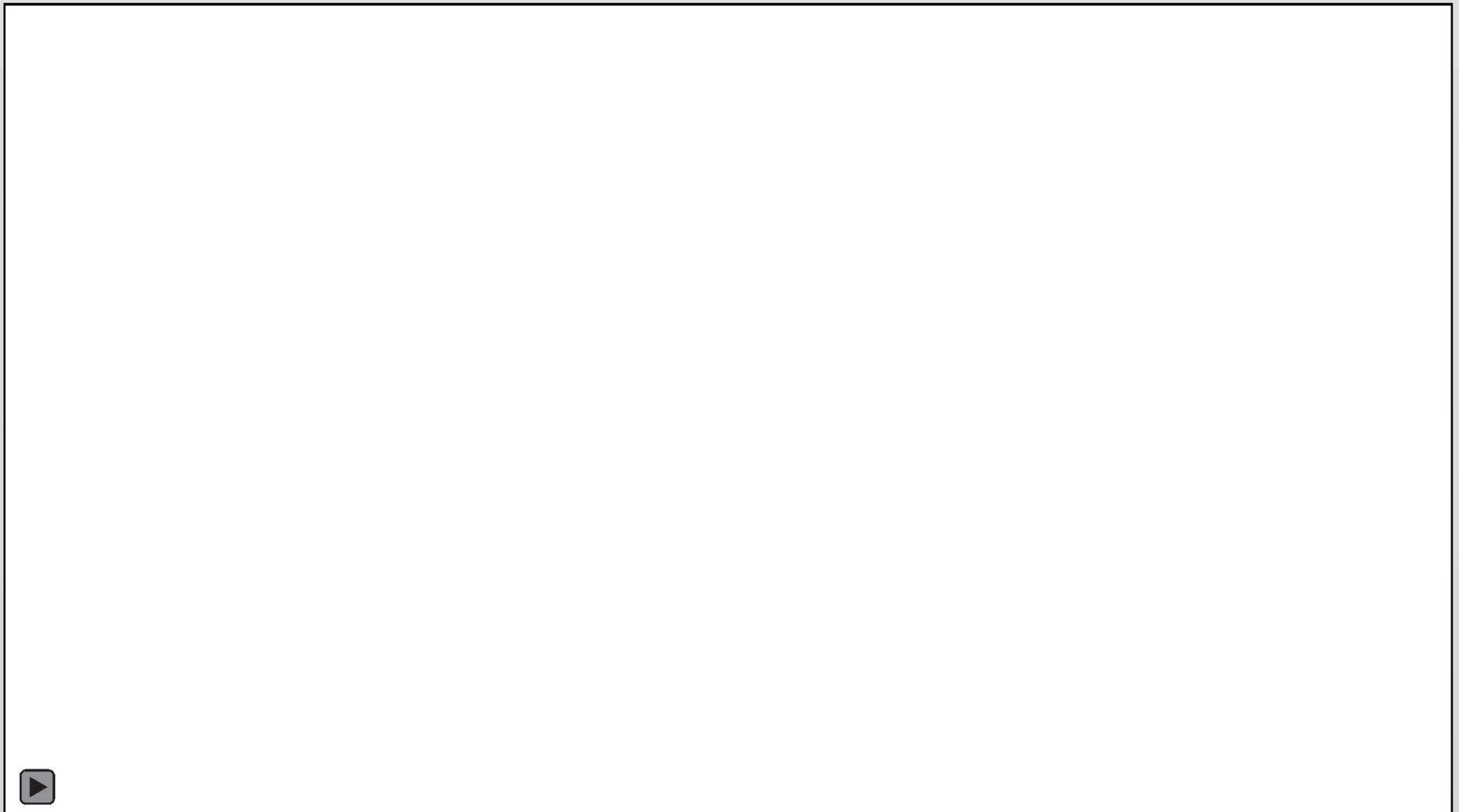
CRISPR mutant





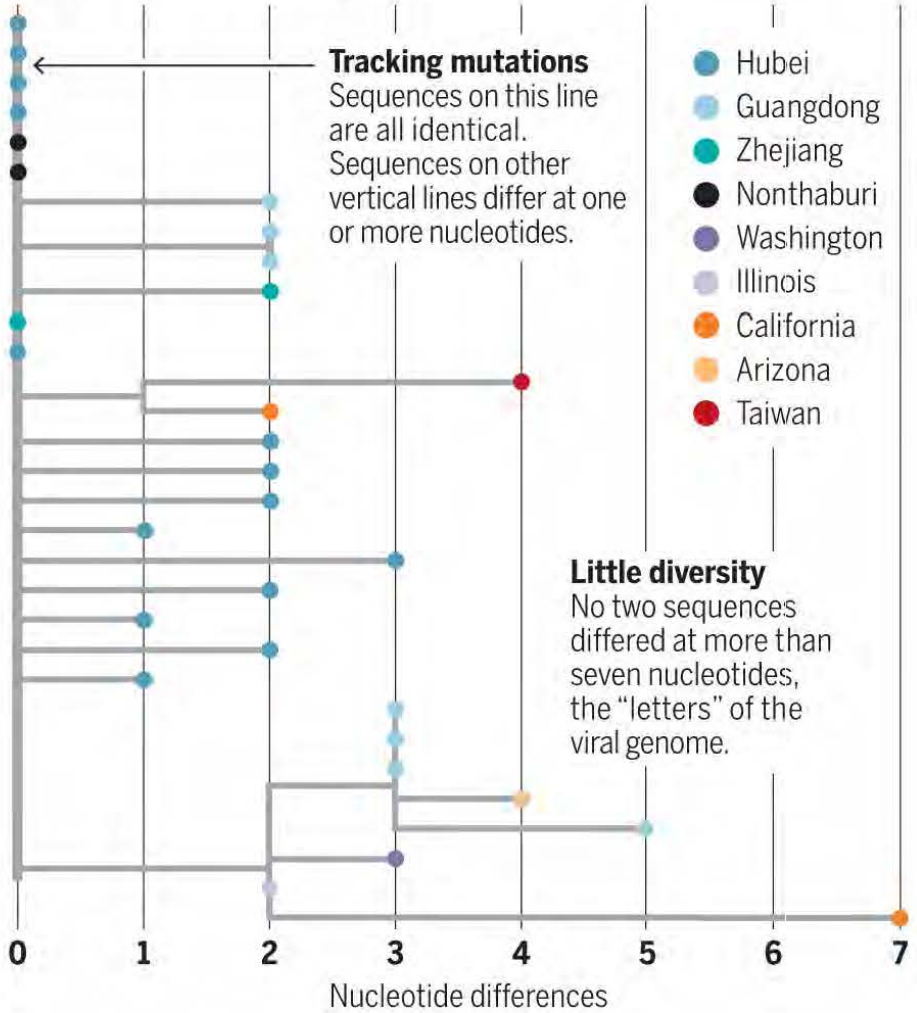
GENOME EDITING (CRISPR/CAS9)

A CRISPR/CAS PROTEIN TO DETECT SARS-COV-2



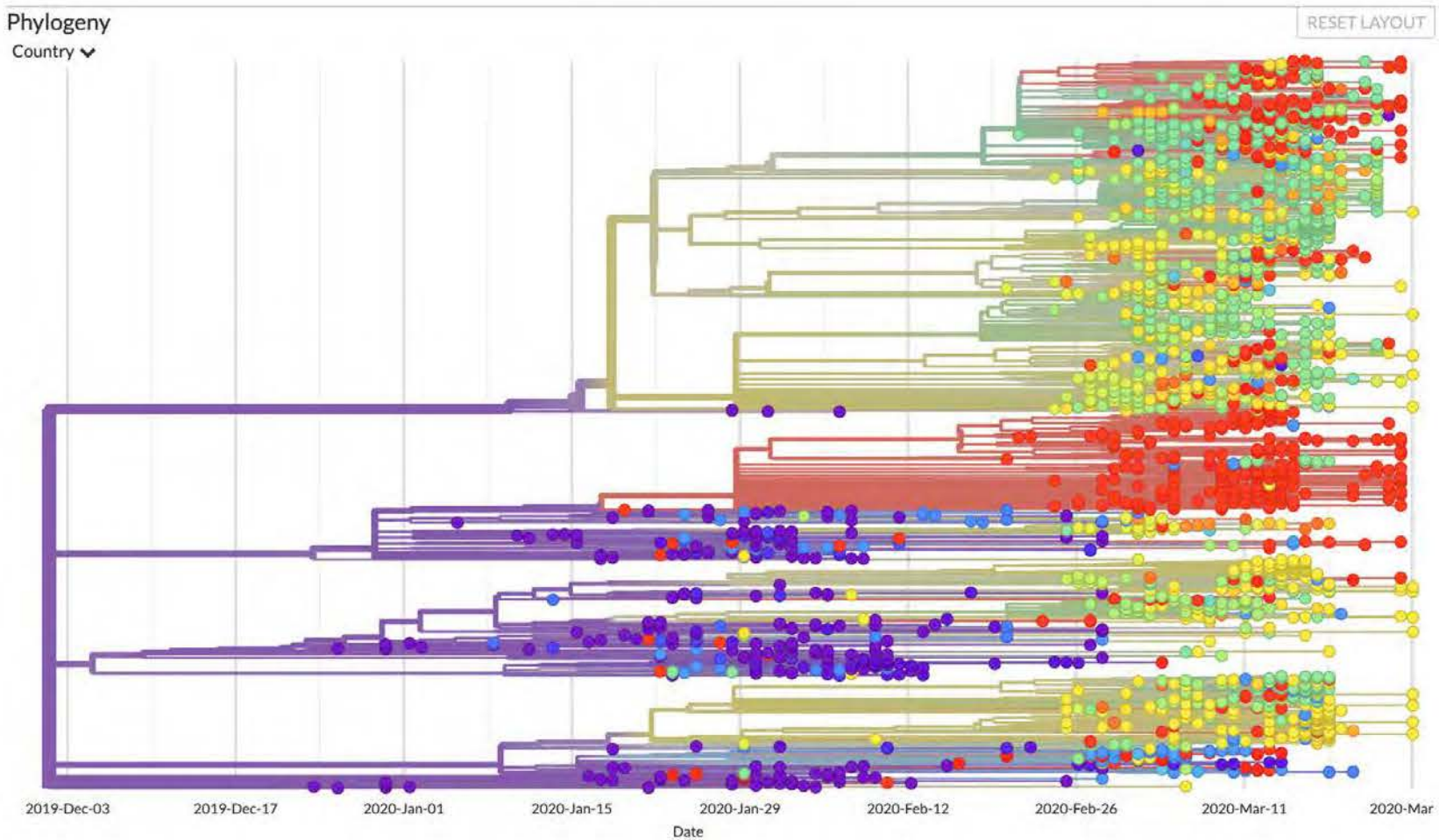
Genomes offer clues about virus's past

A phylogenetic tree of viral sequences from dozens of patients shows very few differences between them, indicating the new virus began to spread in humans recently.



GENOMIC EPIDEMIOLOGY

Jon Cohen (2020). New coronavirus threat galvanizes scientists. *Science* 31 Jan 2020: Vol. 367, Issue 6477, pp. 492-493. DOI: 10.1126/science.367.6477.492

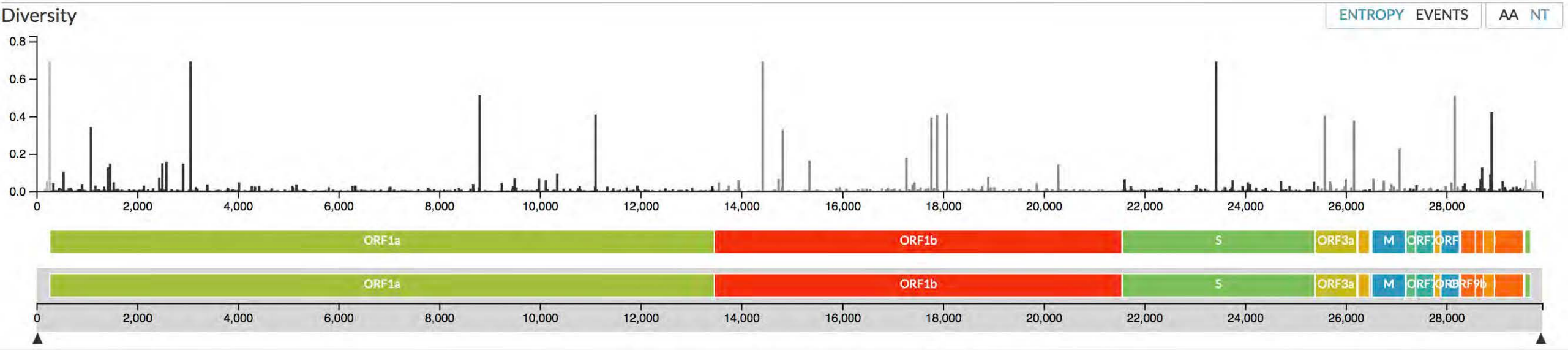


2544 genome sequences

https://nextstrain.org/

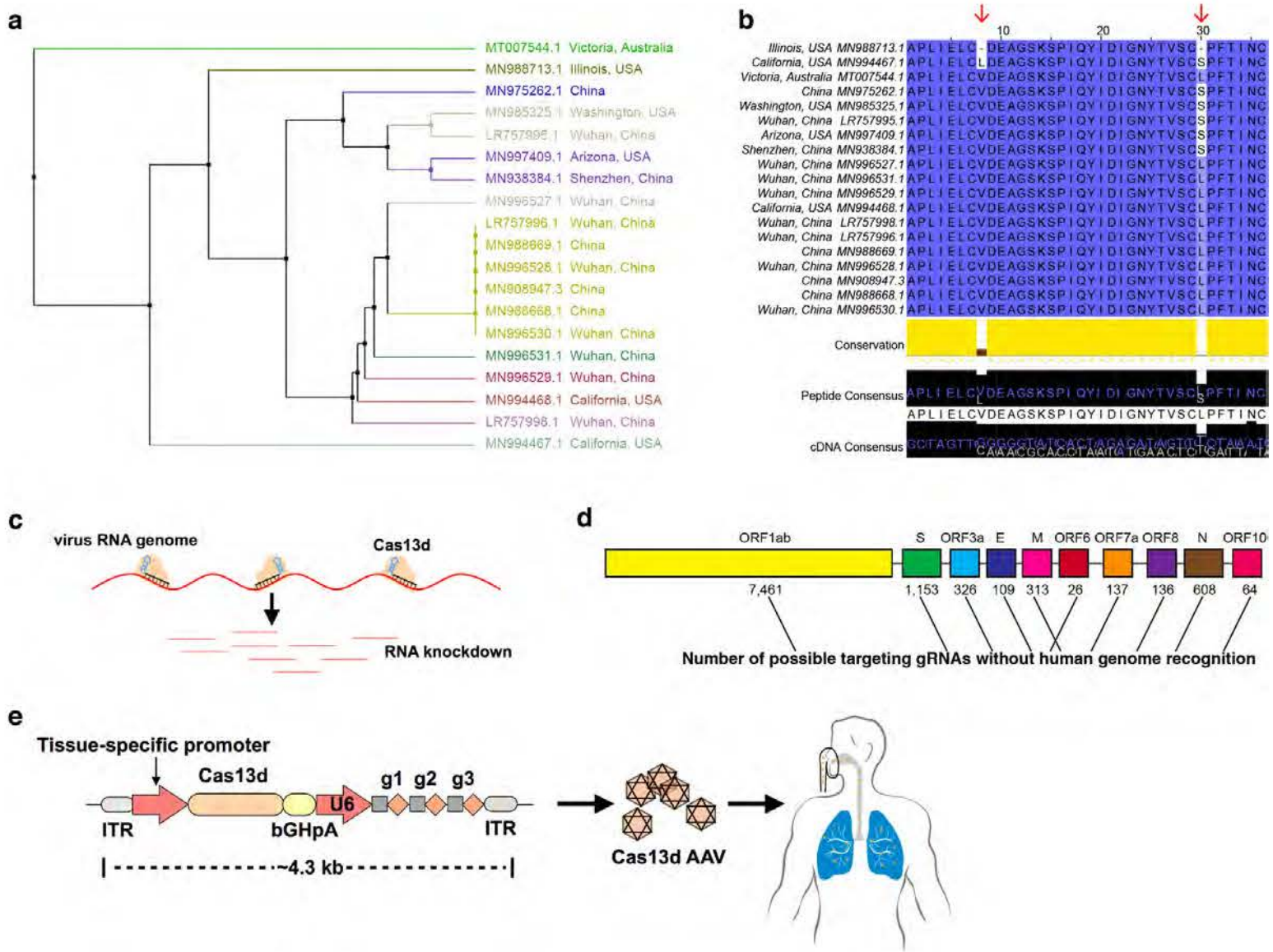
GENOMIC EPIDEMIOLOGY

MUTATIONS



https://nextstrain.org/

ABOUT 8 DIFFERENT SARS-COV-2 VARIANTS



SCIENTIFIC KNOWLEDGE AND POTENTIAL TREATMENT

Nguyen, T.M., Zhang, Y. & Pandolfi, P.P. Virus against virus: a potential treatment for 2019-nCov (SARS-CoV-2) and other RNA viruses. *Cell Res* **30,** 189–190 (2020). https://doi.org/10.1038/s41422-020-0290-0