Lessons learned from the global COVID-19 pandemic

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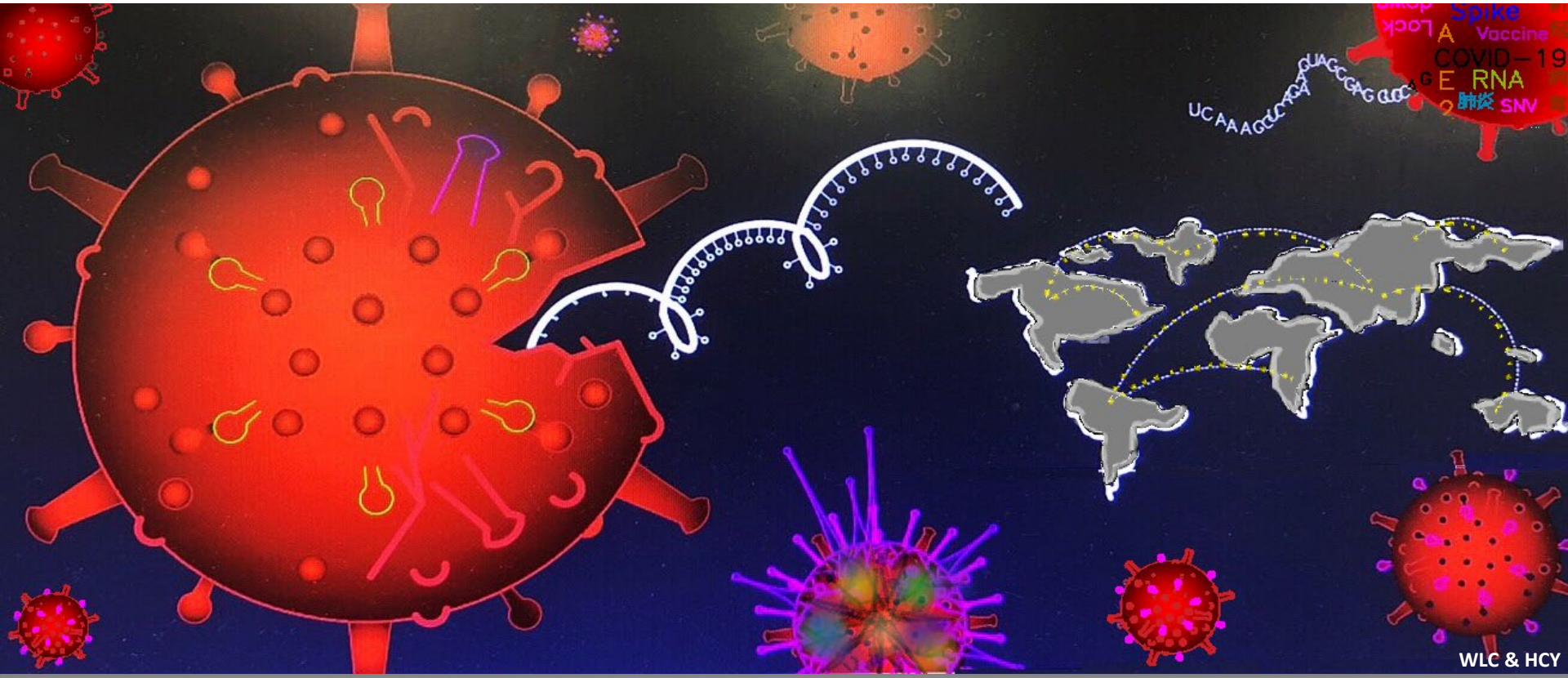


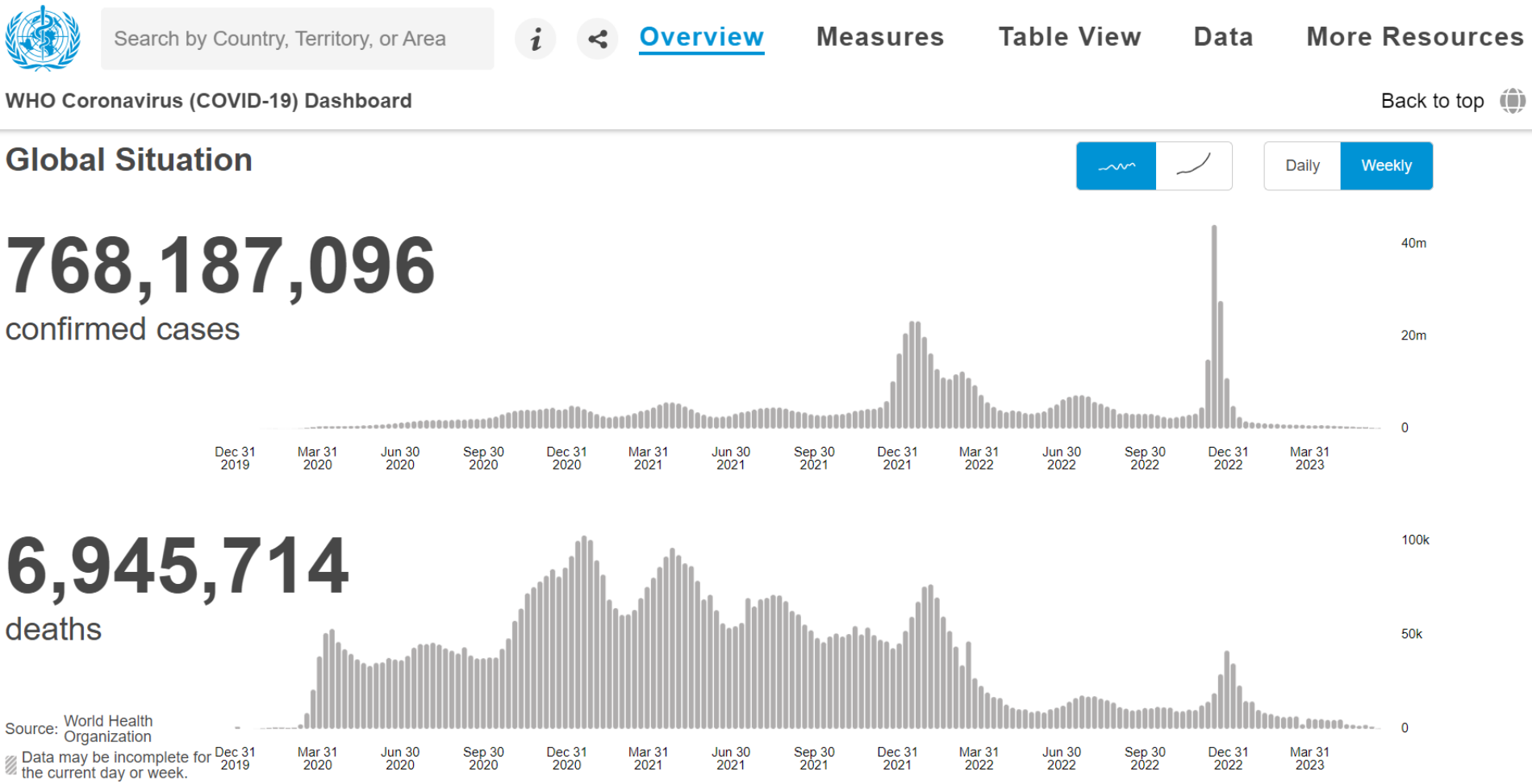
COVID-19: Coronavirus disease 2019

- Dec 2019: the first case of the human-to-human transmission of a novel coronavirus was reported in Wuhan, China.
- Feb 2020: World Health Organization (WHO) gave the disease a name, "Coronavirus disease 2019" (i.e., COVID-19).
- Feb 2020, the International Committee on Taxonomy of Viruses (ICTV) named the causal agent for COVID-19, "Severe Acute Respiratory Syndrome Coronavirus 2" (i.e., SARS-CoV-2).
- SARS-CoV-2 (Beta genera) as the 7th human coronavirus: Other six are: OC43 (Beta, 1960-1970), 229E (Alpha, 1960-1970), SARS-CoV (Beta, 2003), NL63 (Alpha, 2004), HKU1 (Beta, 2005), and MERS-CoV (Beta, 2012, 2015, 2018). Green color: common colds.

Symptoms of COVID-19

- **Incubation period: 2 to 14 days after exposure**
- **Pre-symptomatic transmission ("before symptoms")**
- **Common symptoms are similar to other colds and flu:**
  - ✓ **Fever**
  - ✓ **Cough**
  - ✓ **Tiredness**
  - ✓ **Loss of taste or smell**
  - ✓ **Headache**
  - ✓ **Sore throat**
  - ✓ **Shortness of breath**

Statistics of COVID-19 Infection and Deaths

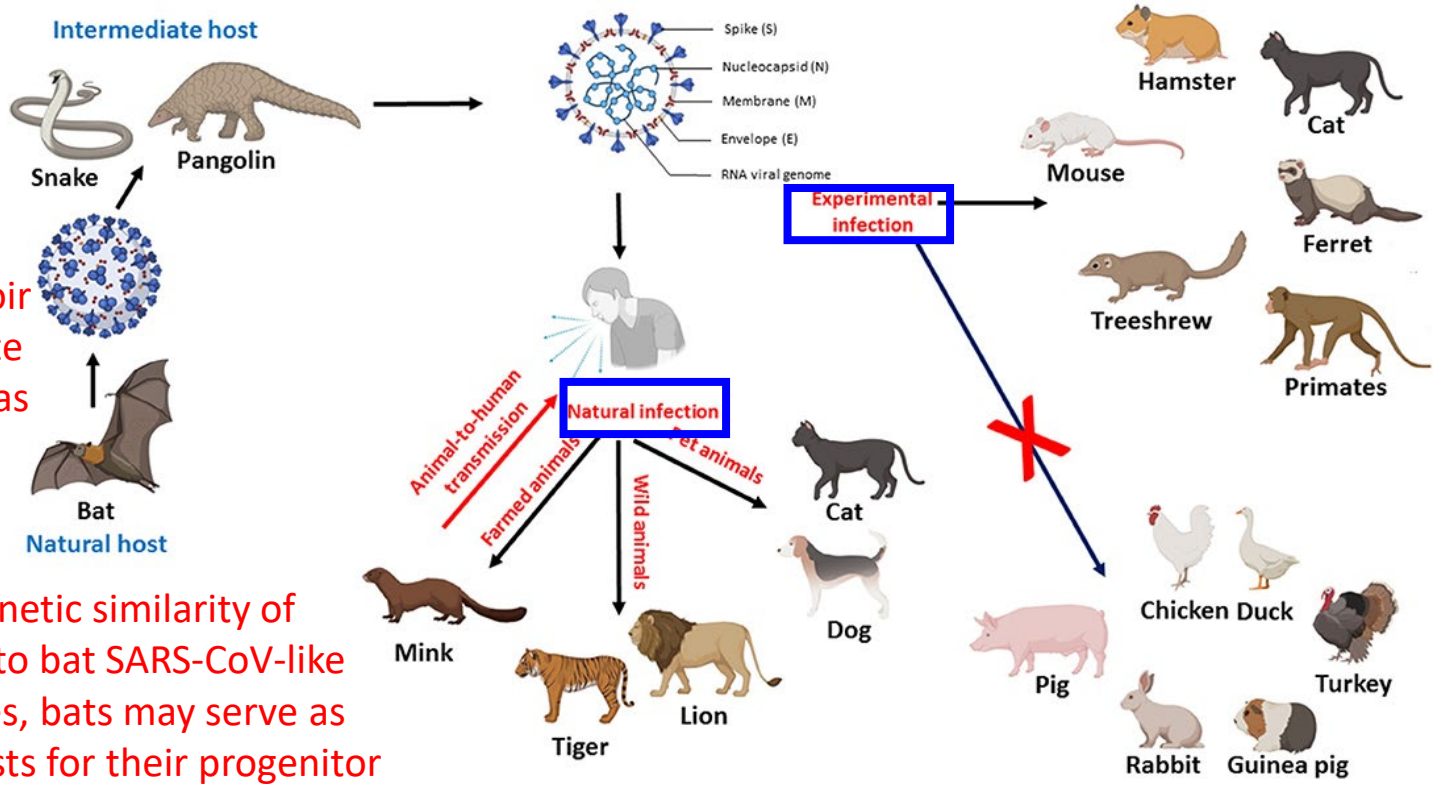


Globally, as of **12:15pm CEST, 21 June 2023**, there have been **768,187,096 confirmed cases** of COVID-19, including **6,945,714 deaths**, reported to WHO. As of **19 June 2023**, a total of **13,461,344,203 vaccine doses** have been administered.

Source: WHO Coronavirus (COVID-19) Dashboard

Origin of SARS-CoV-2

There are two competing ideas: a "zoonotic emergence" and a "laboratory escape" scenario.

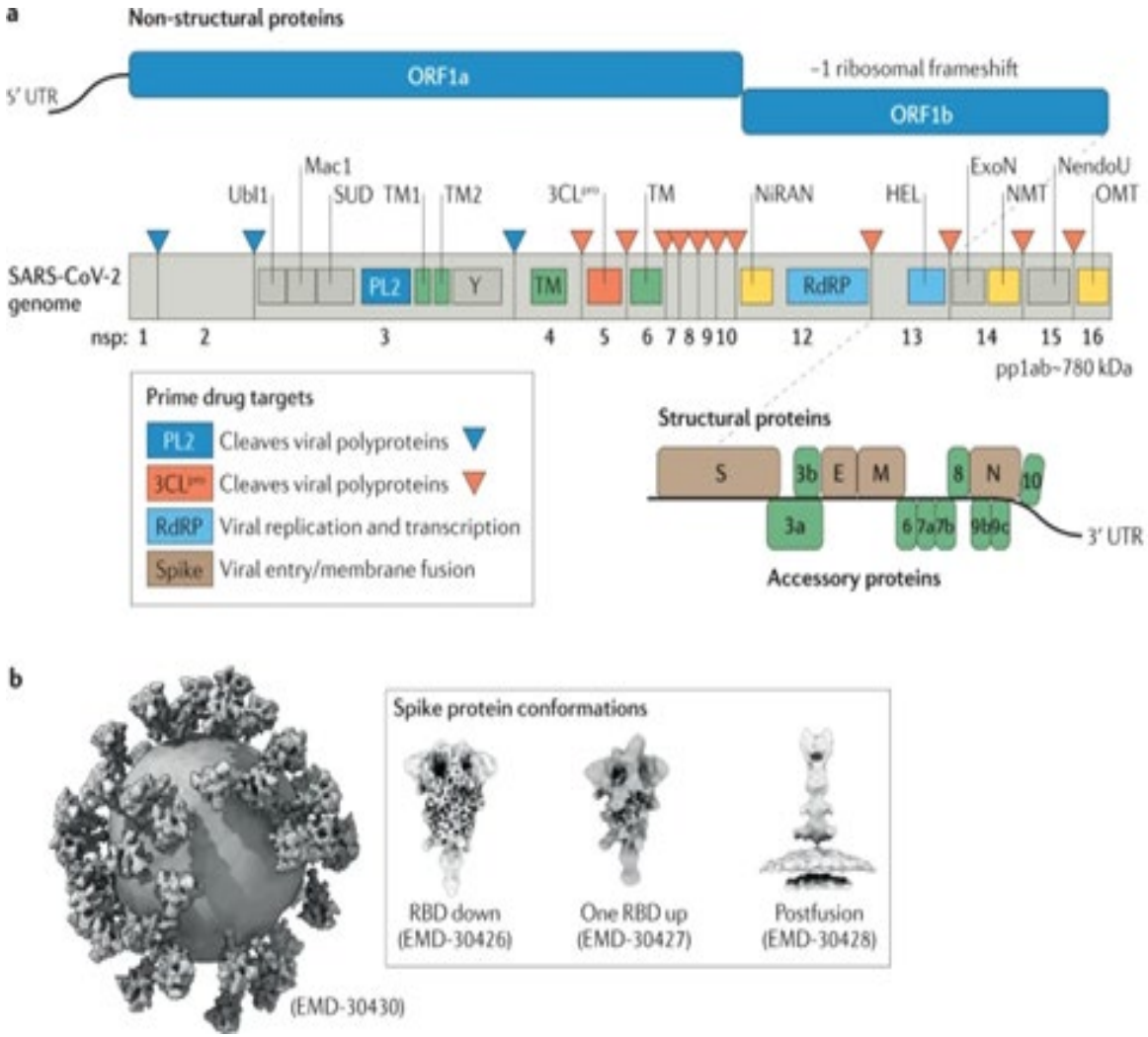


No bat reservoir or intermediate animal host was confirmed.

Given the genetic similarity of SARS-CoV-2 to bat SARS-CoV-like coronaviruses, bats may serve as reservoir hosts for their progenitor

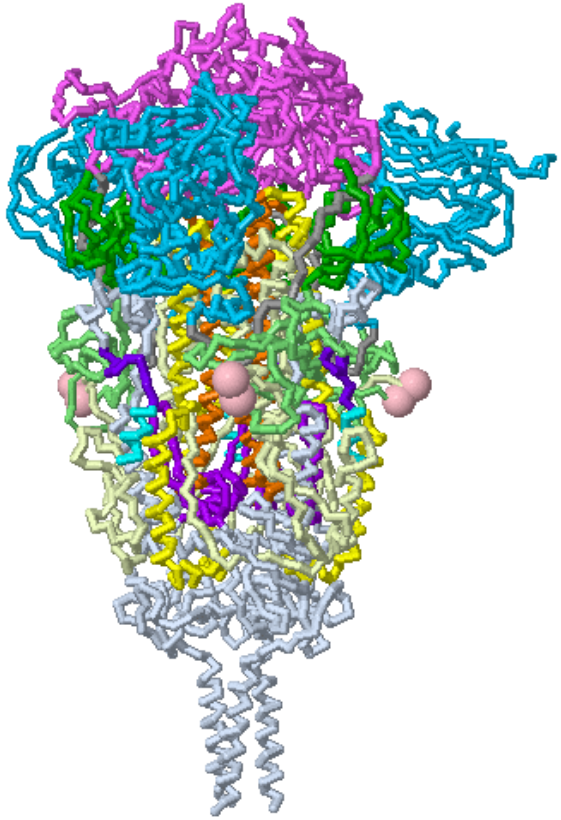
Andersen et al (2020, Nature Medicine), Holmes et al (2021, Cell), and Mahdy et al (2020, Front. Vet. Sci.)

Structure and Mechanisms of SARS-CoV-2



Haitao Yang & Zihe Rao (2021, Nature Reviews Microbiology)

Spike protein of SARS-CoV-2



Jmol

S protein is responsible for the following:

(1) Attachment at the host cell surface

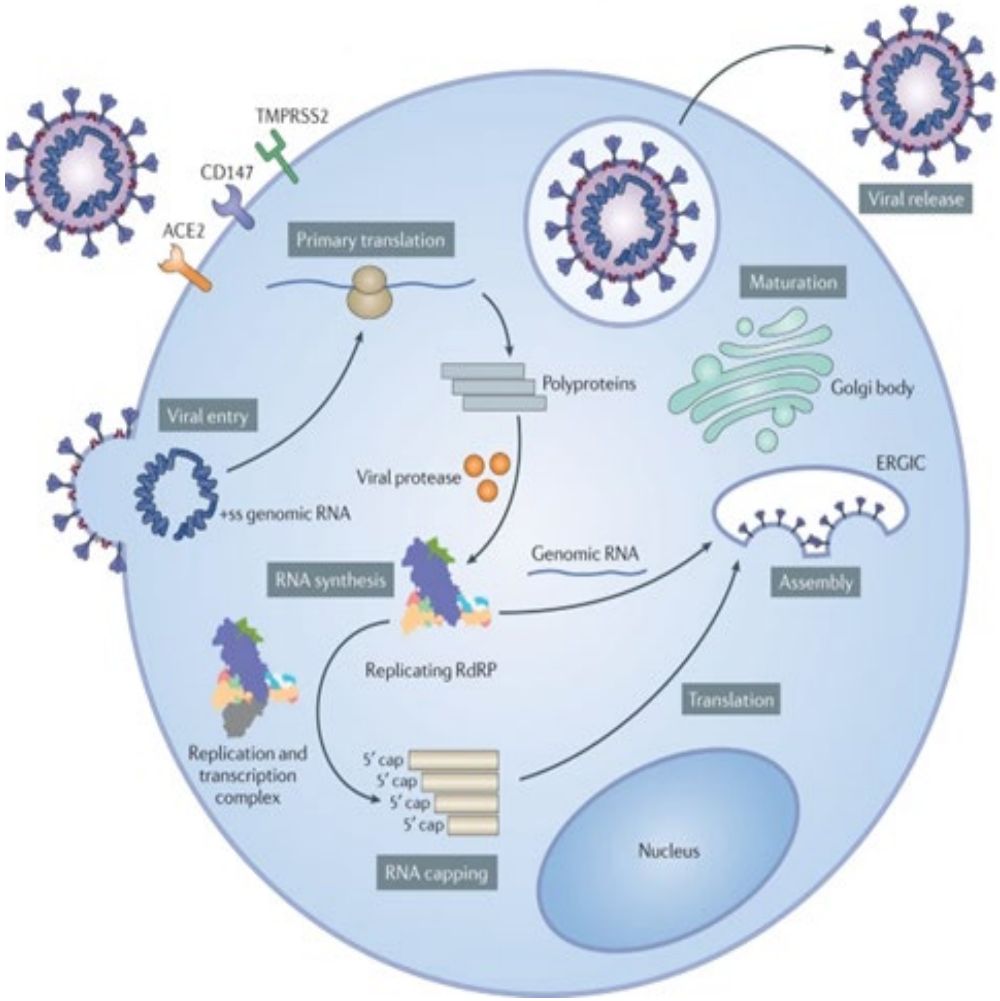
(2) Fusing the viral and host cell membranes

(3) Viral entry (start of the infection)

(4) Main target of neutralizing antibodies

(5) Vaccine and therapeutic design

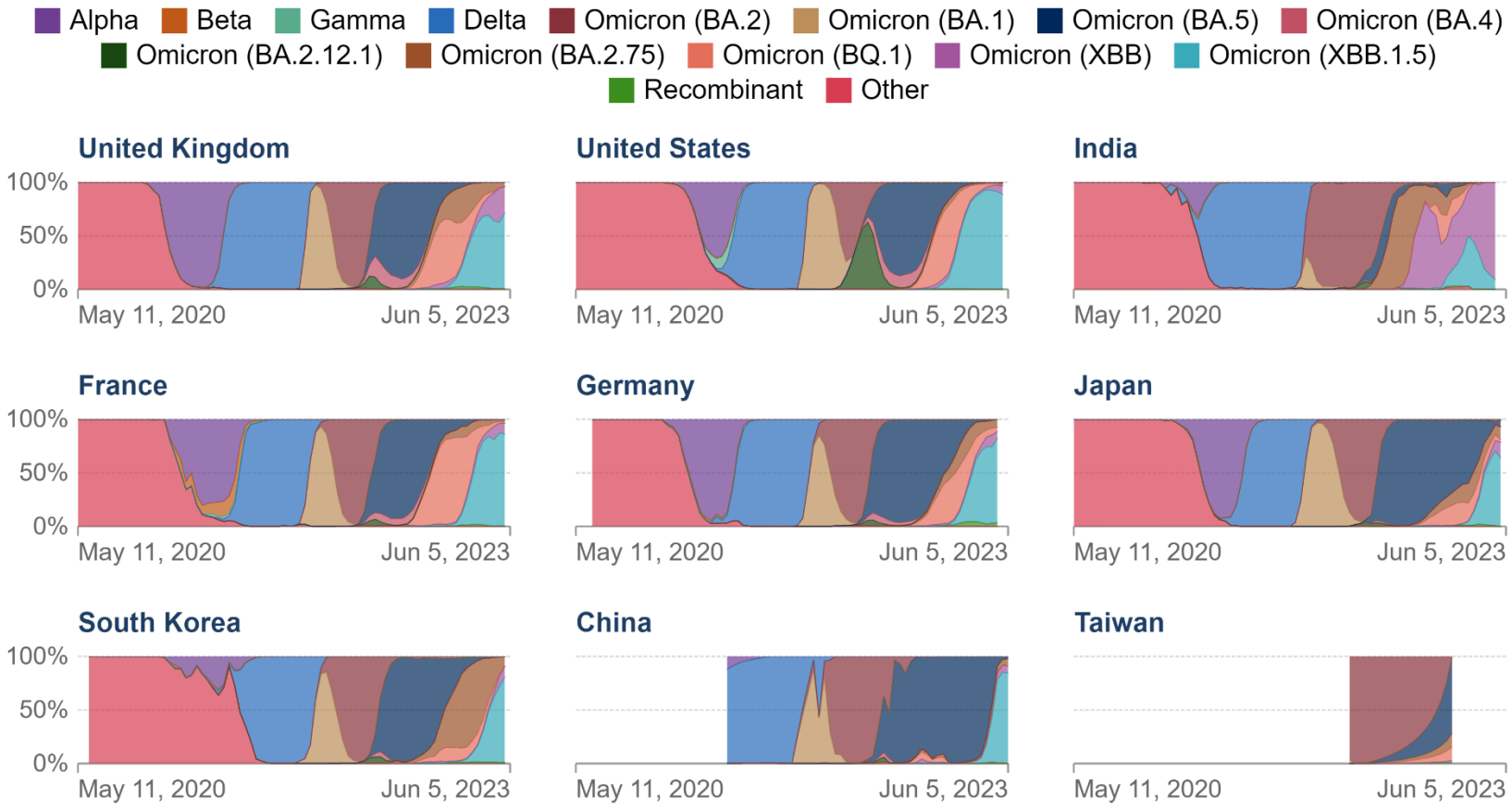
Entry pathways of SARS-CoV-2



Haitao Yang & Zihe Rao (2021, Nature Reviews Microbiology)

SARS-CoV-2 variants in analyzed sequences

The number of analyzed sequences in the preceding two weeks that correspond to each variant group. This number may not reflect the complete breakdown of cases since only a fraction of all cases are sequenced.



Source: GISAID, via CoVariants.org – Last updated 12 June 2023

OurWorldInData.org/coronavirus • CC BY

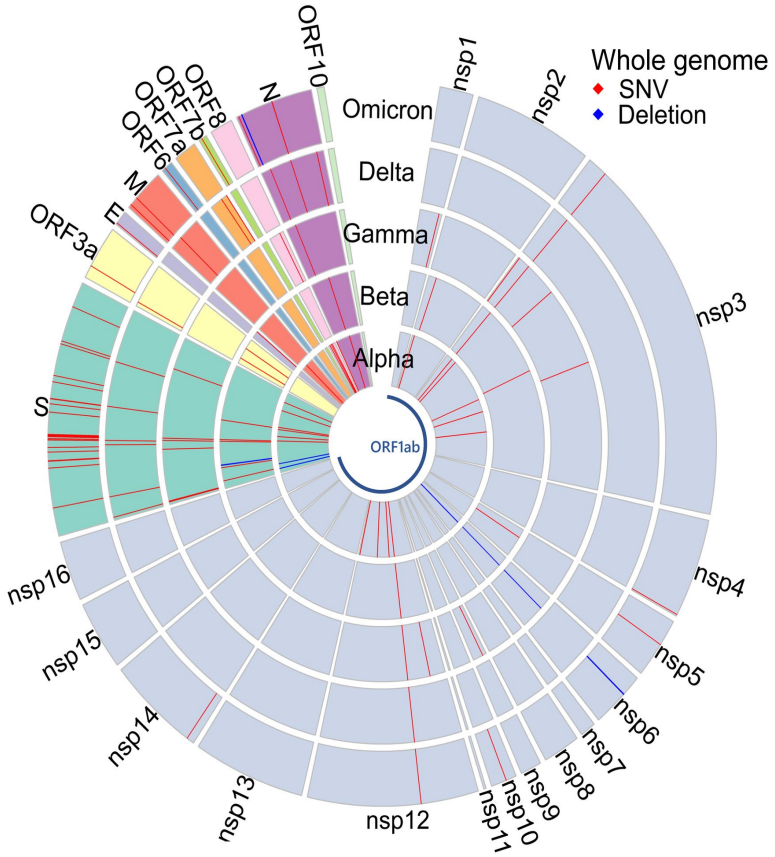
Note: Recently-discovered or actively-monitored variants may be overrepresented, as suspected cases of these variants are likely to be sequenced preferentially or faster than other cases.

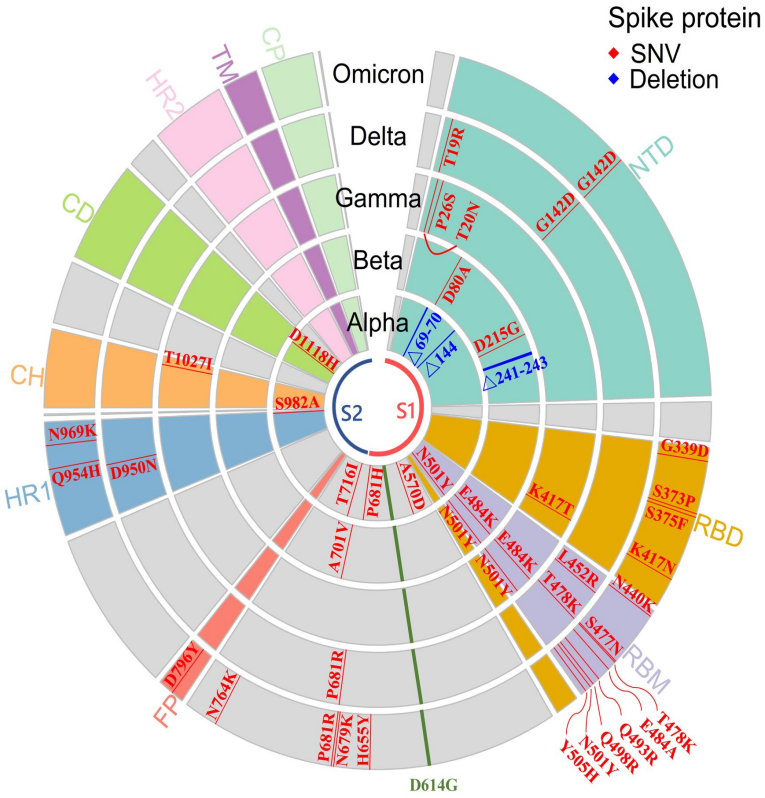
XBB.1.5 is the most transmissible Omicron sub-variant currently.

Basic reproductive number R0

- Basic reproductive number **R0**:
  - Influenza **1.3**
  - 1918 Spanish flu **1.8**
  - Wu-Han variant **2.2 – 2.6**
  - D614G **3**
  - Alpha **4 – 5**
  - Delta **5 – 8**
  - Omicorn **> Delta**
  - Early estimates of the R0 of BA.4 and BA.5 is **18.6**

Variants of SARS-CoV-2





COVID-19 diagnostic testing

- **A positive antigen test** that the person tested is **currently infected with COVID-19**, specifically during the **acute phase** of the infection.
- **A positive antibody test** suggests that the person tested **had a previous COVID-19 infection**; their immune system responded by producing antibodies (such as IgM and IgG) to combat the virus.
- **PCR tests** are considered the **"gold standard"** for COVID-19 testing because they are **highly accurate and sensitive in detecting the presence of the virus**; they are more reliable in identifying COVID-19 infections.

COVID-19 therapeutics

- **Antiviral Drugs** such as **Remdesivir** and **Molnupiravir** for inhibiting or interfering with **viral RNA replication**.
- **Immune Modulators** such as **Dexamethasone**, **Tocilizumab**, and **Baricitinib** for reducing **inflammation** and suppressing the **immune response**.
- **Monoclonal antibodies targeting SARS-CoV-2,** such as **Casirivimab and imdevimab (Regeneron)** and **Bamlanivimab and etesevimab (Eli Lilly)** for **neutralizing the virus and reducing viral replication**.
- **Convalescent plasma** for passively transferring antibodies from whom have recovered from COVID-19 to **help the recipient's immune response**.

COVID-19 vaccines

Vaccine platform	Advantages	Disadvantages
mRNA (Pfizer-BioNTech and Moderna)	Safe and well-tolerated; Highly adaptable to new pathogen; Native antigen expression	Lower immunogenicity; Requirement of low temperature storage and transportation; Potential risk of RNA-induced interferon response
Viral vector (Oxford-AstraZeneca and Johnson & Johnson/Janssen)	Stronger immune response; Preservation of native antigen; Mimicking natural infection	More complicated manufacturing process; Risk of genomic integration; Response dampened by pre-existing immunity against vector
Protein subunit (Novavax and Medigen Vaccine Biologics)	Safe and well-tolerated	Lower immunogenicity; Requirement of adjuvant or conjugate to increase immunogenicity
Inactivated virus (Sinovac and Bharat Biotech)	Stronger immune response; Safer than live attenuated virus	Potential epitope alteration by inactivation process

Li et al (ACS Cent. Sci. 2021)

Non-Pharmaceutical Interventions (NPIs)

- NPIs, such as **social distancing**, **wearing masks**, **lockdowns**, and **quarantine measures**, are a range of measures and actions that can be taken to
  - **slow the transmission**
  - **protect vulnerable populations**
  - **ease the burden on healthcare systems**
  - **buy time for vaccine development and distribution**
  - **complement vaccine effectiveness**
- **Combining vaccination efforts with NPIs** offers the most effective approach to managing and mitigating the pandemic.

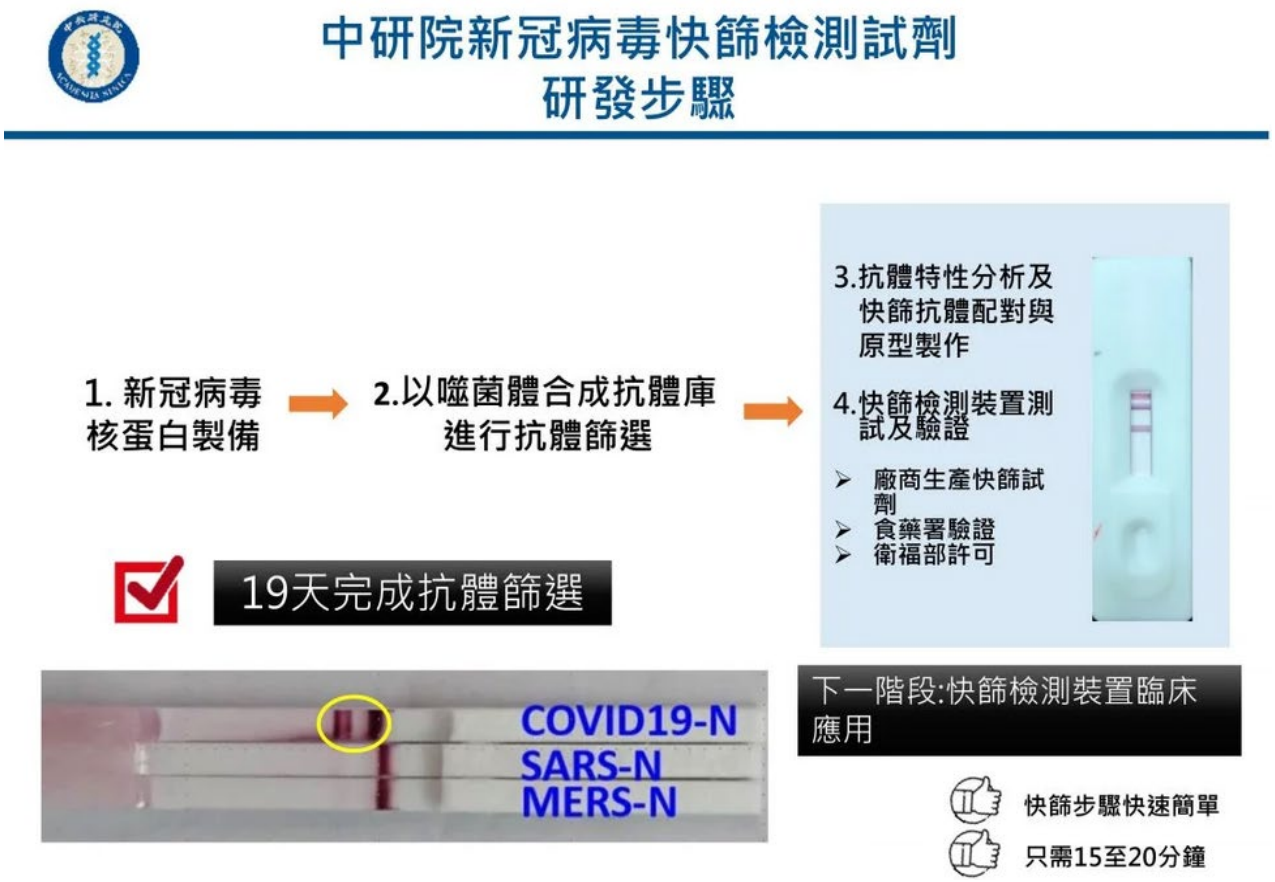
President James Liao's address on Mar 20, 2020

"…, Academia Sinica rapidly assembled a task force during the Lunar New Year period to initiate research work in **rapid viral detection**, **antibody screening**, **drug synthesis**, and **vaccine development**. In addition, we established working groups among different research organizations and academics in order to share information, materials, and methodologies for use in COVID-19 research …"

In February 2020, Academia Sinica successfully synthesized Remdesivir at the "hundreds of milligrams level" with a purity of 97%, and further improved it to the "grams level" with a purity of 99%.

https://www.facebook.com/sinicaedu/photos/a.1671785293137244/2463057814009984/?type=3

In March 2020, Academia Sinica discovered antibodies capable of detecting viral antigens, which can be applied as rapid screening reagents.



https://newsletter.sinica.edu.tw/21564/

When the SARS outbreak occurred in Taiwan, Academia Sinica promptly constructed two P3 negative-pressure laboratories for developing COVID-19 rapid screening, viral testing, and vaccine and therapeutics.

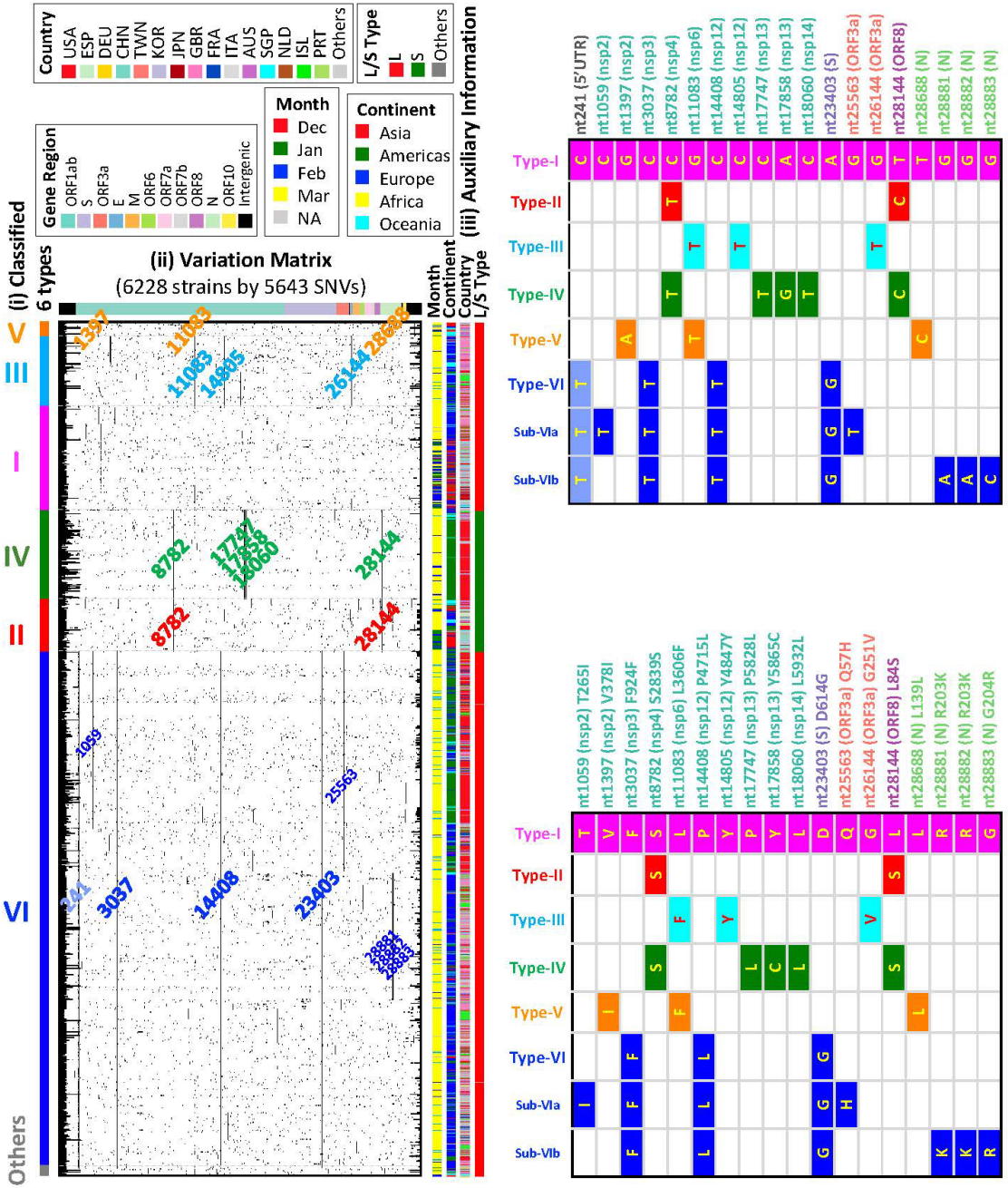
https://research.sinica.edu.tw/covid19-p3lab-academiasinica/

In January 2021, Academia Sinica repurposed existing medicines (mefloquine, nelfinavir, and extracts of Ganoderma luciudum, Perilla frutescens, and Mentha haplocalyx) as anti-COVID-19 virus agents

In June 2023, Academia Sinica and Moderna jointly launch the Forward-looking Innovation Award to accelerate mRNA research in Taiwan

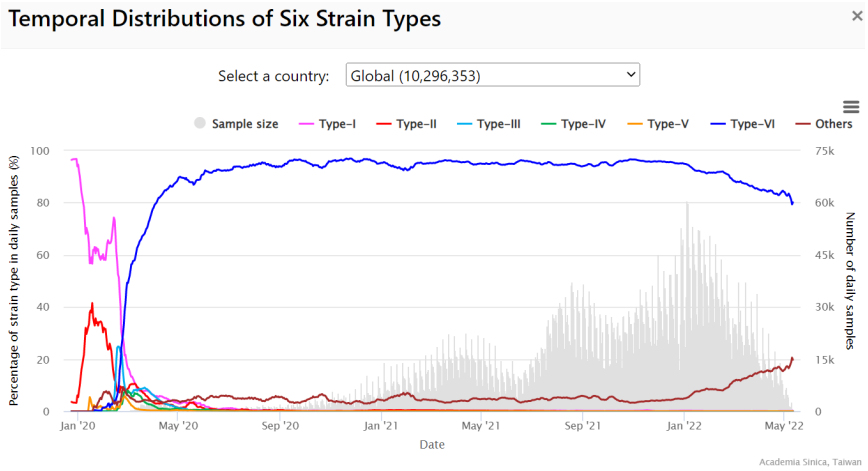
https://newsletter.sinica.edu.tw/31631/

In April 2020, Academia Sinica identified six major types of COVID-19 virus and Type VI becomes the dominant strain in the world.

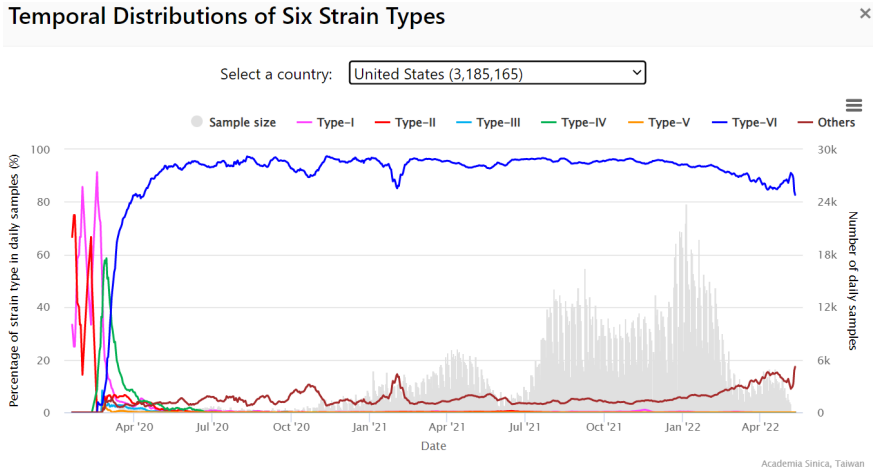


https://www.pnas.org/doi/10.1073/pnas.2007840117

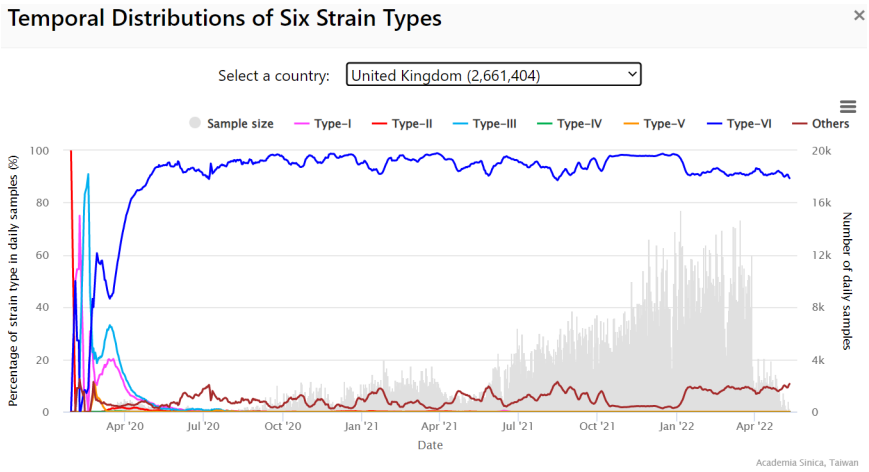
Type VI became the dominant strain in the world



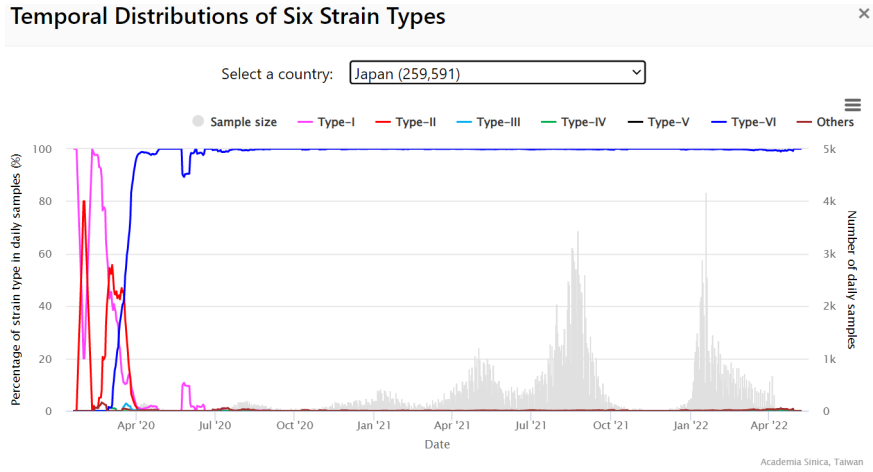
Distribution of Strain Types over time: Global



Distribution of Strain Types over time: United-States



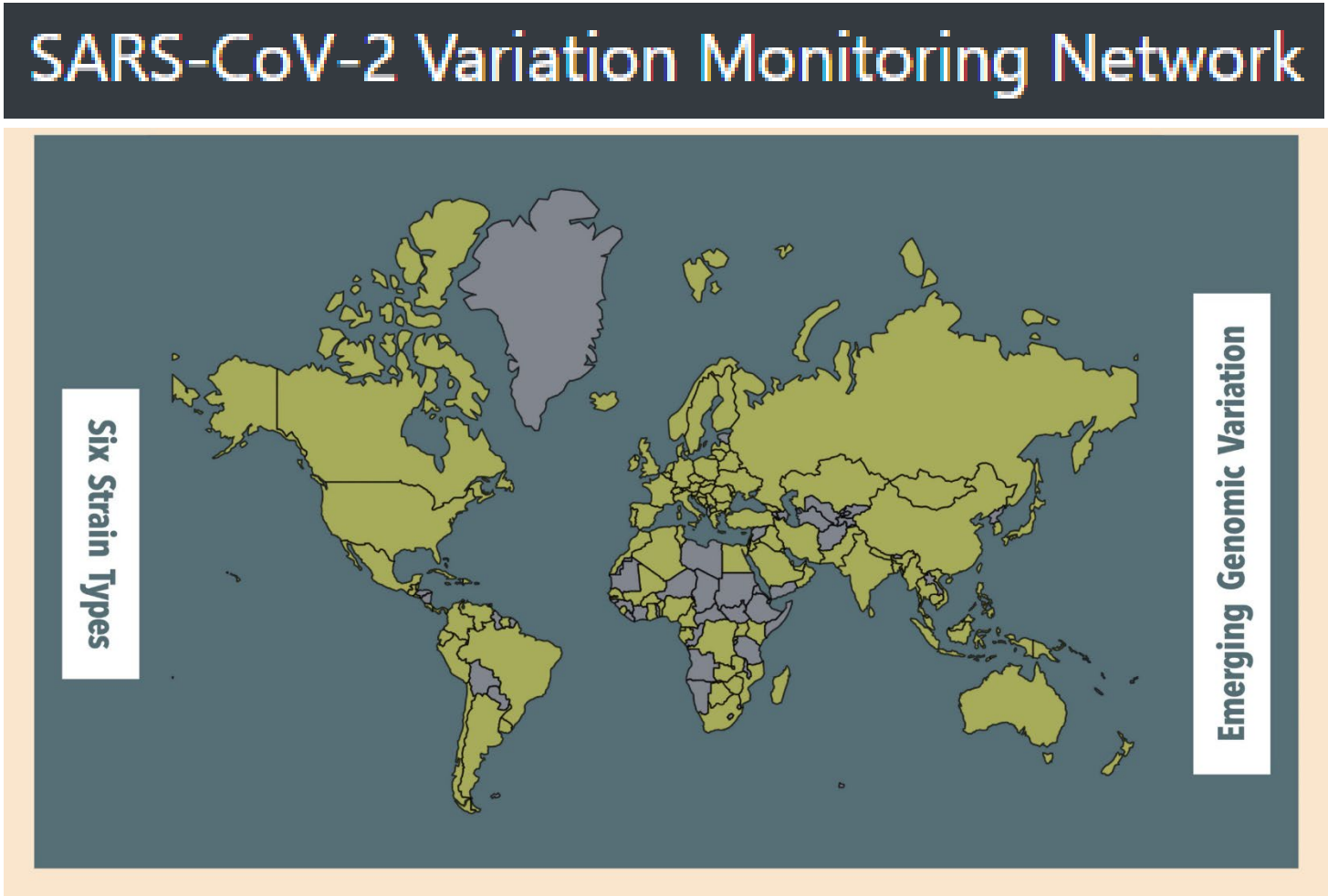
Distribution of Strain Types over time: United-Kingdom



Distribution of Strain Types over time: Japan

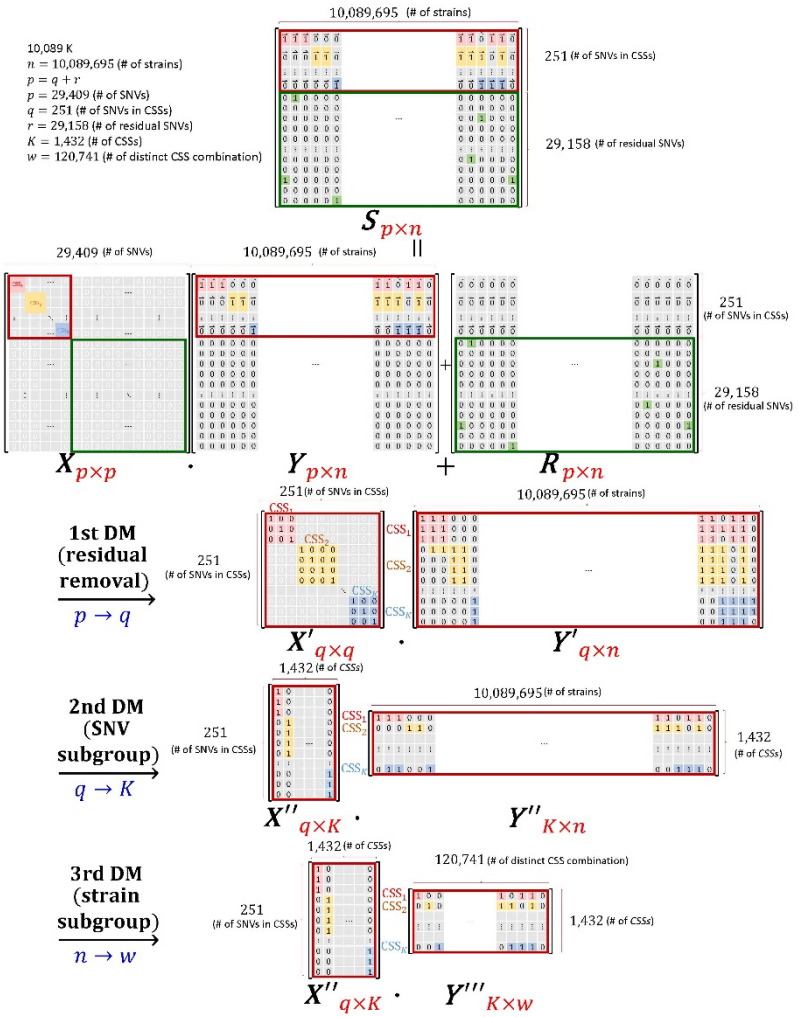
https://sarscov2.sinica.edu.tw/tracking.html

In December 2020, Academia Sinica established the SARS-CoV-2 Variation Monitoring Network to track the transmission dynamics and evolution of SARS-CoV-2 variants.



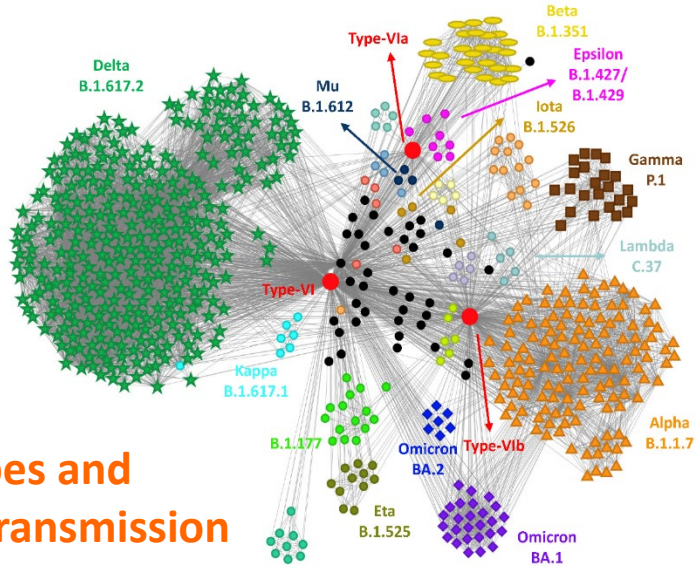
https://sarscov2.sinica.edu.tw/tracking.html

Subtyping of major SARS-CoV-2 variants reveals different transmission dynamics based on 10 million genomes

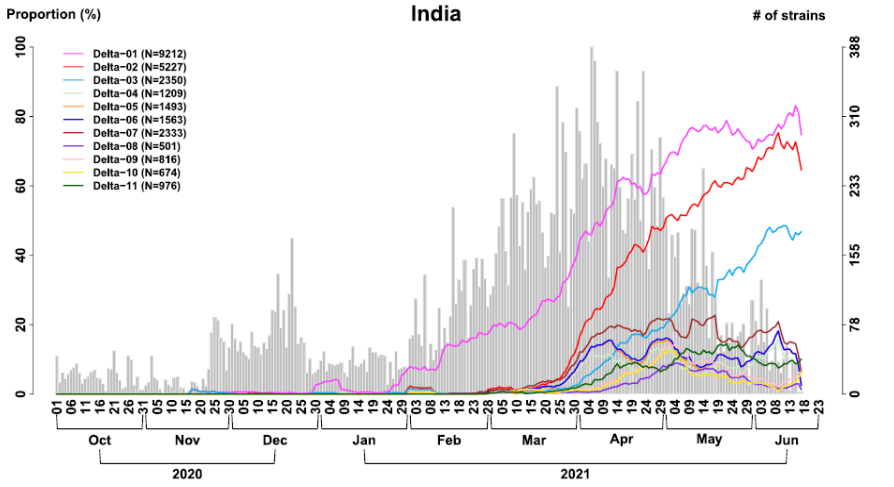


(A) An efficient data dimensionality reduction

(B) Virus network analysis



(C) Subtypes and dynamic transmission of Delta variant



Taiwan's experience with the COVID-19 pandemic (1)

Lessons from SARS in 2003:

- Regular reviews for **infection control** and **drills** in the medical care system have been held periodically. The hospitals could **activate immediate measures** such as triage, quick isolation, strictly controlled crowd flow, medical task force, and epidemic prevention materials to **maintain the normal operation of the medical care system**.
- Residents remained **self-alert** during the disease pandemic, voluntarily put on **face masks**, **wash hands** properly, and practiced **social distancing**.

Taiwan's experience with the COVID-19 pandemic (2)

- In January 2020, when news of a "new and unknown respiratory disease emerging in China" was first disclosed, an inter-ministerial **Central Epidemic Command Center** was activated, providing four important principles — **Rapid measures**, **Early deployment**, **Prudent actions**, and **Transparency** for blocking virus spread into Taiwan.
- **Taiwan CDC** began to implement relevant prevention strategies, including **Surveillance and laboratory diagnosis**, **Border control**, **Control of community transmission**, **Medical system response and preparedness**, and **Health education and fighting disinformation**.
- When the supply of face masks met the domestic demand, Taiwan began to **donate medical supplies to more than 80 countries worldwide** to assist them in combating COVID-19 and to realize the spirit of "**Taiwan Can Help, and Taiwan is Helping!**"

Chen (2021, Nature Immunology)

Lessons Learned from the Global COVID-19 Pandemic

- Preparedness and Early Response
- Importance of Global Cooperation
- Healthcare System Strengthening
- Vaccine Development and Distribution
- Importance of Public Health Measures
- Health Inequities and Vulnerable Populations
- Digital Transformation and Telemedicine
- Risk Communication and Misinformation
- Economic Impact and Social Resilience

COVID-19 is not the final global health challenge we will face, highlighting the ongoing need for vigilance, preparedness, and investment in public health infrastructure to effectively respond to future infectious diseases.


Thank you for your attention!
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