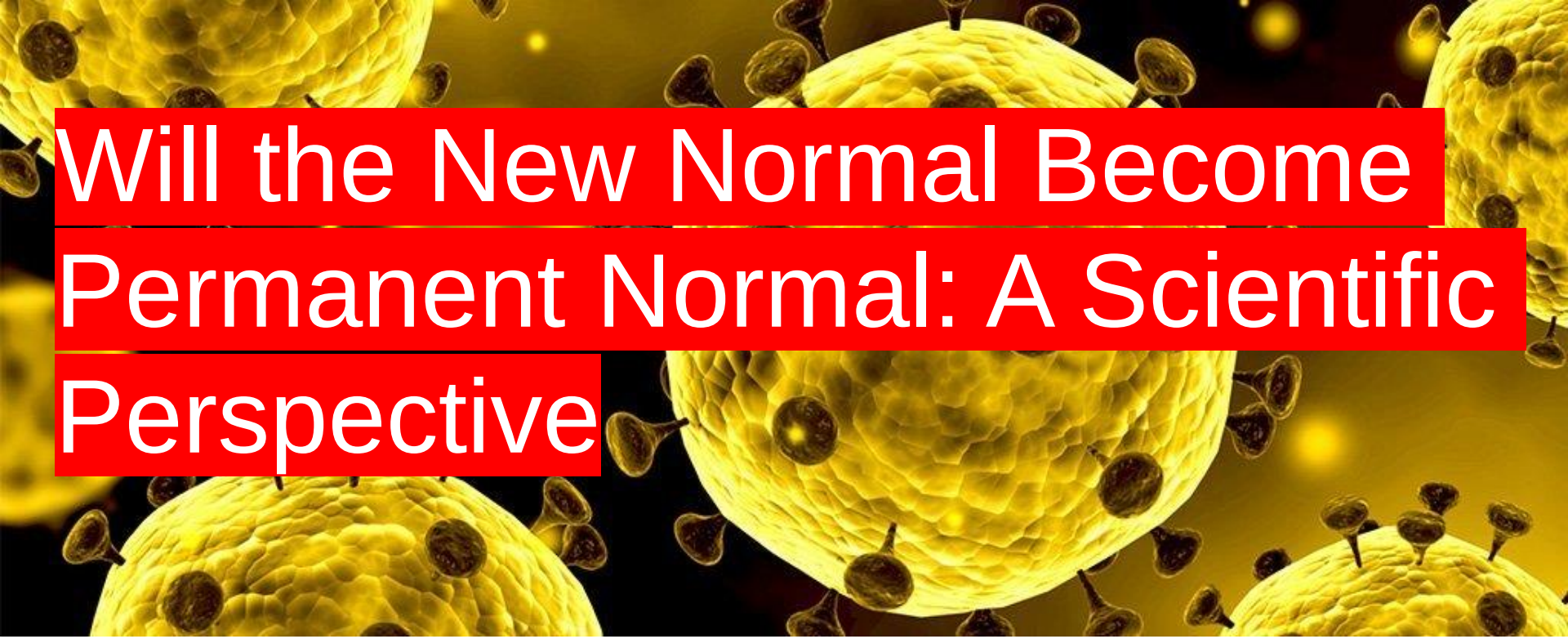


Will the New Normal Become Permanent Normal: A Scientific Perspective

Bimo A. Tejo, Ph.D

Associate Professor

Department of Chemistry

Universiti Putra Malaysia

✉ bimo.tejo@upm.edu.my

What is Normal?

"…social and economic life can function"

WHO SEARO, Local epidemiology should guide focused action in 'new normal' COVID-19 world, 15 May 2020

NEW NORMAL

"a new way of living and going about our lives, work and interactions with other people"

TheStar, Covid-19: What does the 'new normal' mean?, 21 May 2020

Previous new normals:

New normal after World War II (1945)
New normal after *Orde Lama* (1966)
New normal after the Asian economic crisis (1998)
New normal after the global economic crisis (2008)
New normal after COVID-19 (2020)

Daily confirmed COVID-19 cases

The number of confirmed cases is lower than the number of total cases. The main reason for this is limited testing.

Our World in Data

World

160,000
140,000
120,000
100,000
80,000
60,000
40,000
20,000
0

Dec 31, 2019 Jan 21 Feb 10 Mar 1 Mar 21 Apr 10 Apr 30 May 20 Jun 24, 2020

Source: European CDC – Situation Update Worldwide – Last updated 24th June, 11:00 (London time)

Daily confirmed COVID-19 deaths

Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.

Our World in Data

Source: European CDC – Situation Update Worldwide – Last updated 24th June, 11:00 (London time)

COVID-19 mutations helping virus spread in humans: UK scientists

A police officer wears a thermal headgear to monitor the temperature of commuters in New Delhi.

Latest Updates

Coronavirus pandemic threatens Saudi progress on energy transition, says WEF
1373

Pompeo lands in Israel for talks on West Bank annexations
2431

RAK ruler grants expat boy's wish to be reuinited with mother after COVID-19 pandemic
1017

Dubai allows reopening of hotel beaches, but only for guests
3528

What We Are Reading

Arab News, COVID-19 mutations helping virus spread in humans: UK scientists, 12 May 2020

LATEST ON CORONAVIRUS OUTBREAK

COVID-19 mutations could risk vaccine: UK researchers

London School of Hygiene & Tropical Medicine say mutations could impact vaccine, drugs being developed against virus

Karim El-Bar | 11.05.2020

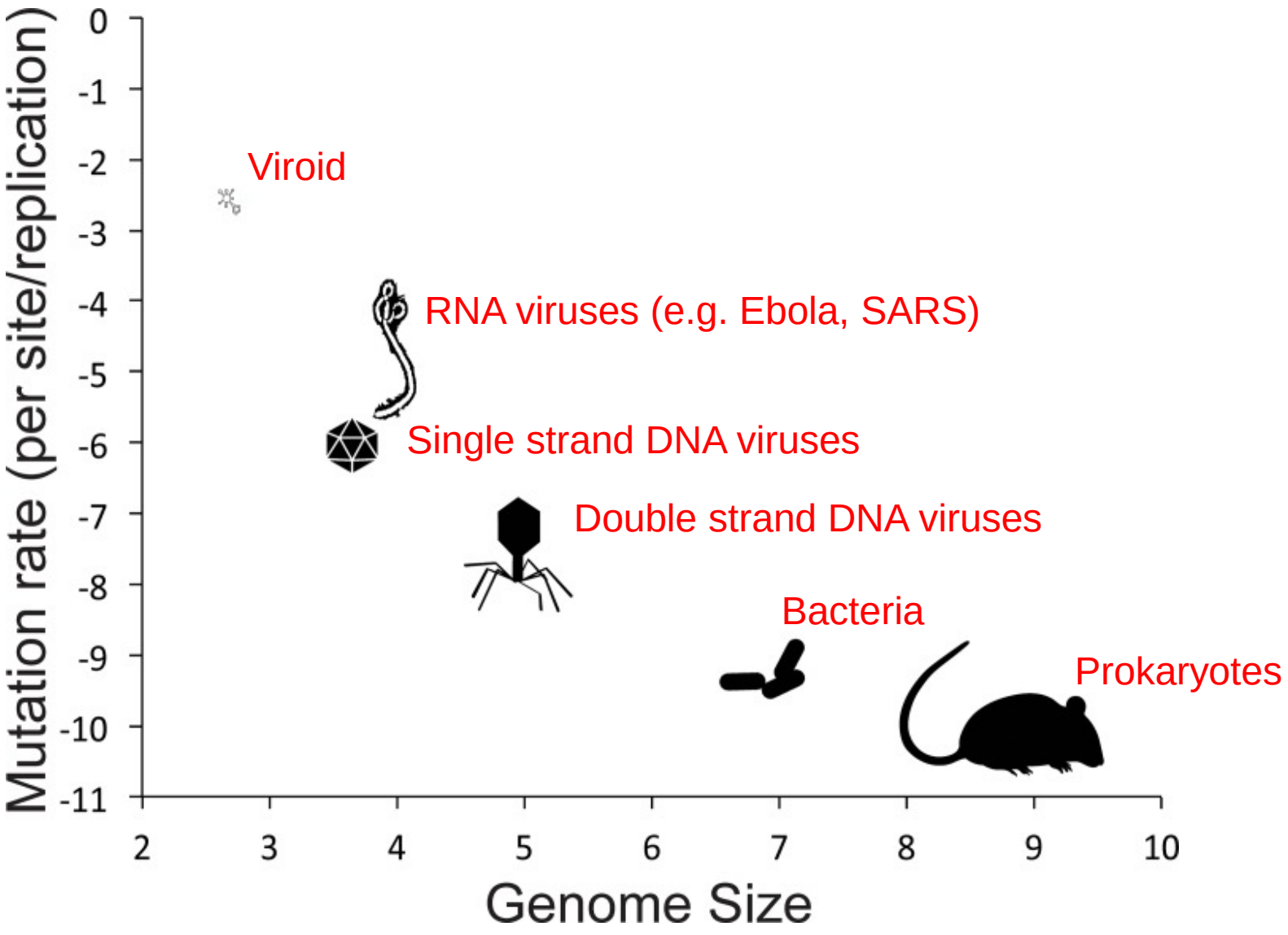
Coronavirus

'9,647 Turkish citizens in virus quarantine'

Anadolu Agency, COVID-19 mutations could risk vaccine: UK researchers, 11May 2020

SARS-CoV-2 Mutations

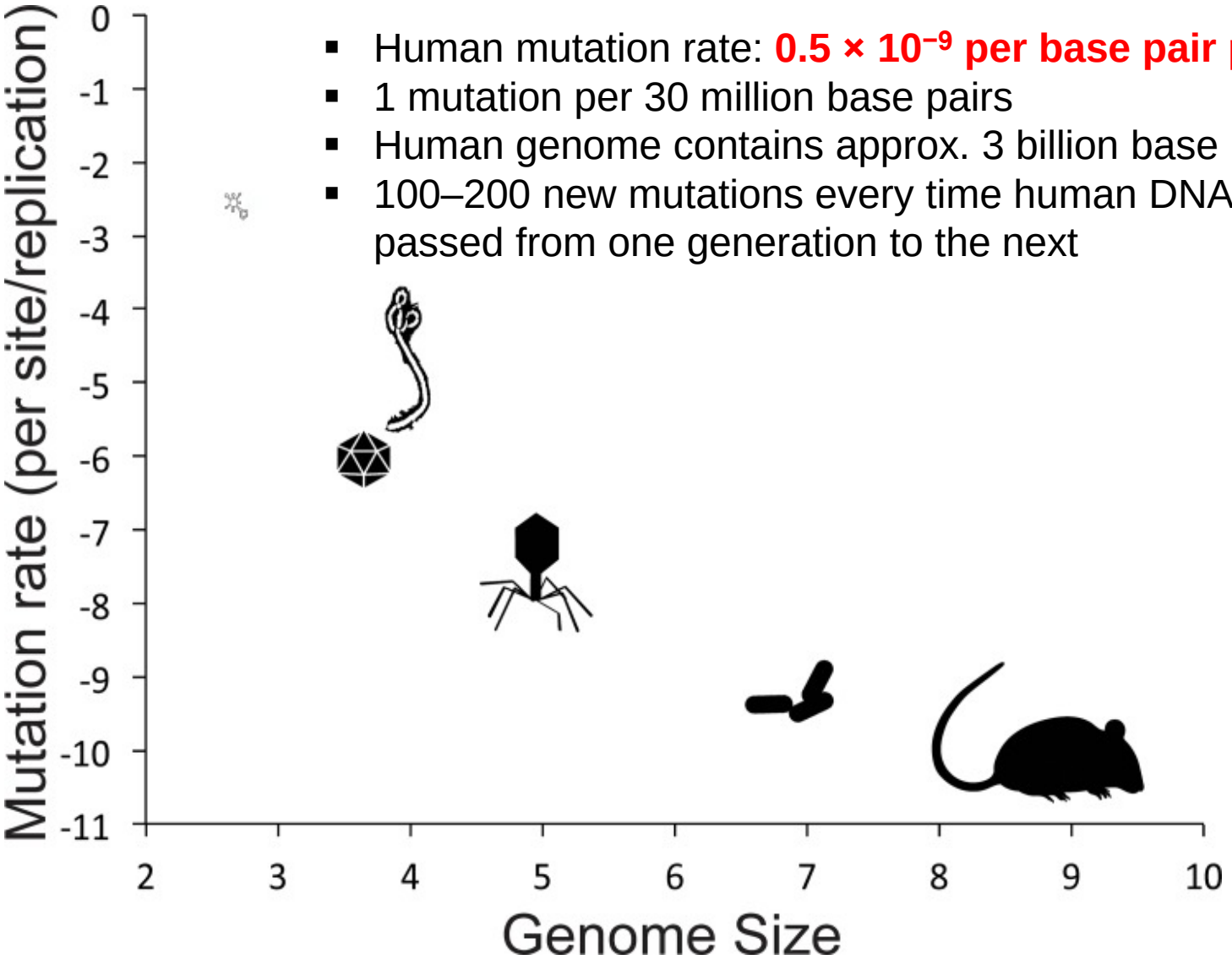
Mutation Rate vs Genome Size



Duffy S. Why are RNA virus mutation rates so damn high? PLoS Biol. 2018 Aug 13;16(8):e3000003

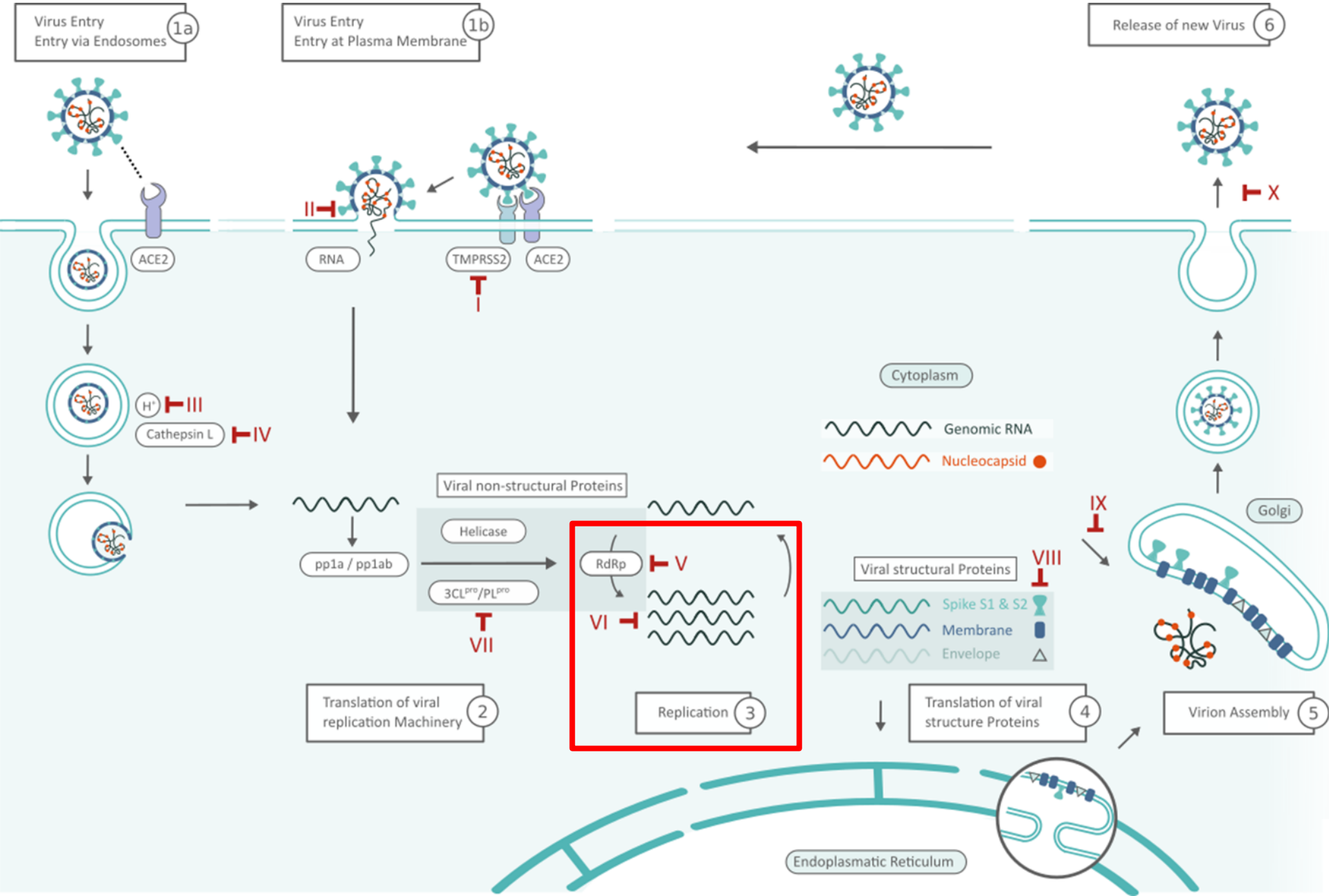
Mutation Rate vs Genome Size

- Human mutation rate: **0.5×10^{-9} per base pair per year**
- 1 mutation per 30 million base pairs
- Human genome contains approx. 3 billion base pairs
- 100–200 new mutations every time human DNA is passed from one generation to the next

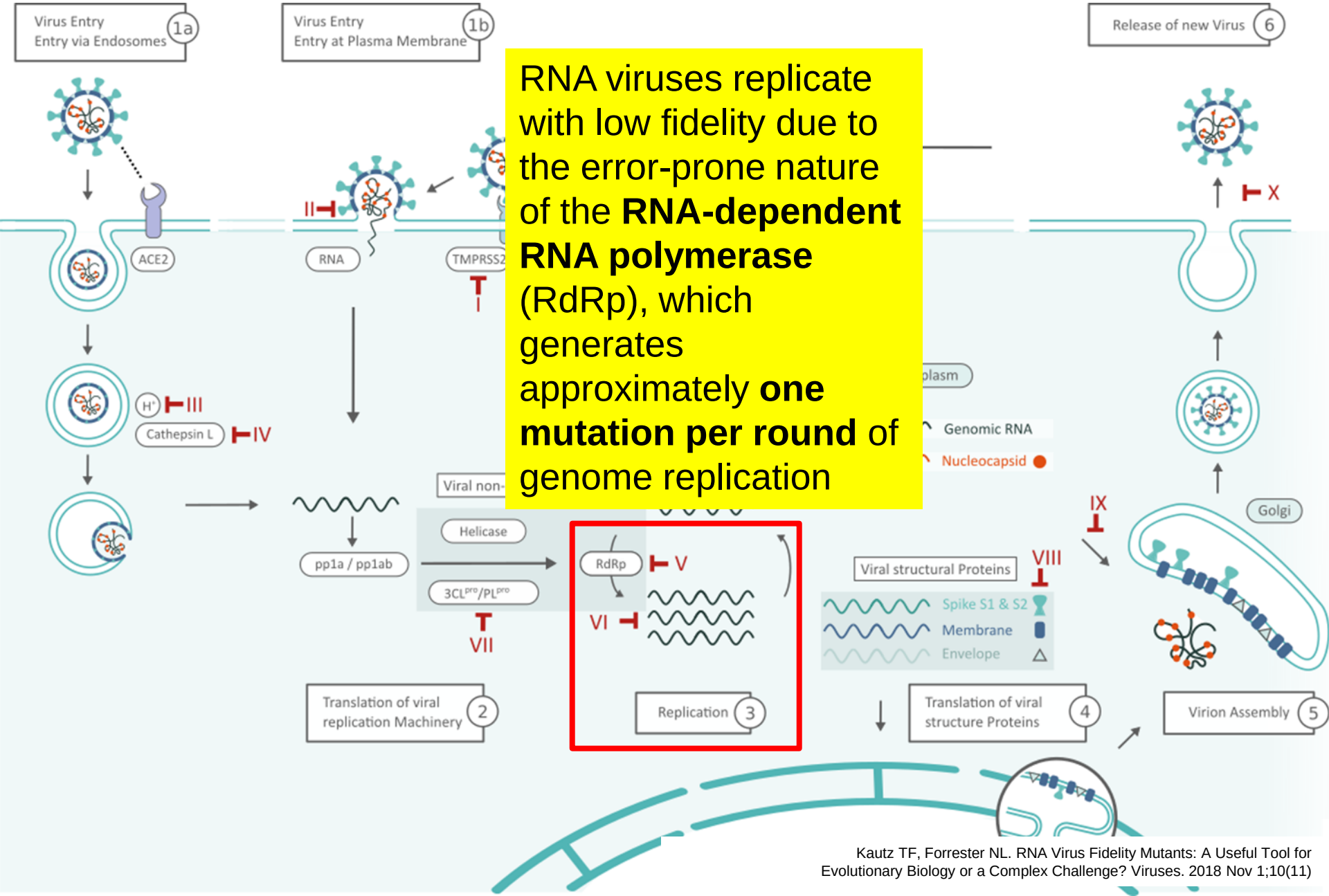


Dolgin, E. Human mutation rate revealed. *Nature*. 2009 Aug 27

Why are RNA virus mutation rates so damn high?



Why are RNA virus mutation rates so damn high?



RNA viruses replicate with low fidelity due to the error-prone nature of the **RNA-dependent RNA polymerase** (RdRp), which generates approximately **one mutation per round** of genome replication

Kautz TF, Forrester NL. RNA Virus Fidelity Mutants: A Useful Tool for Evolutionary Biology or a Complex Challenge? Viruses. 2018 Nov 1;10(11)

SARS-CoV Mutation Rate

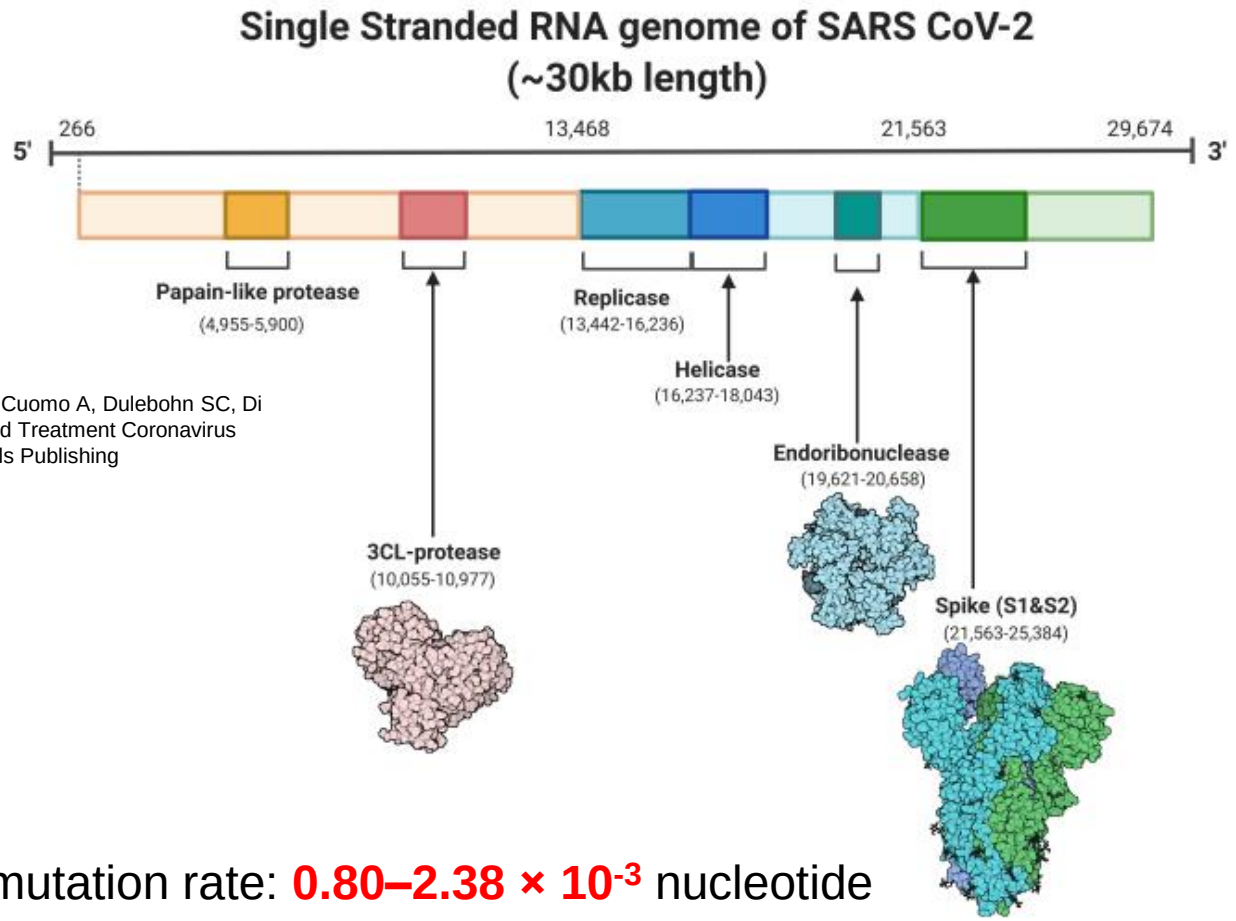


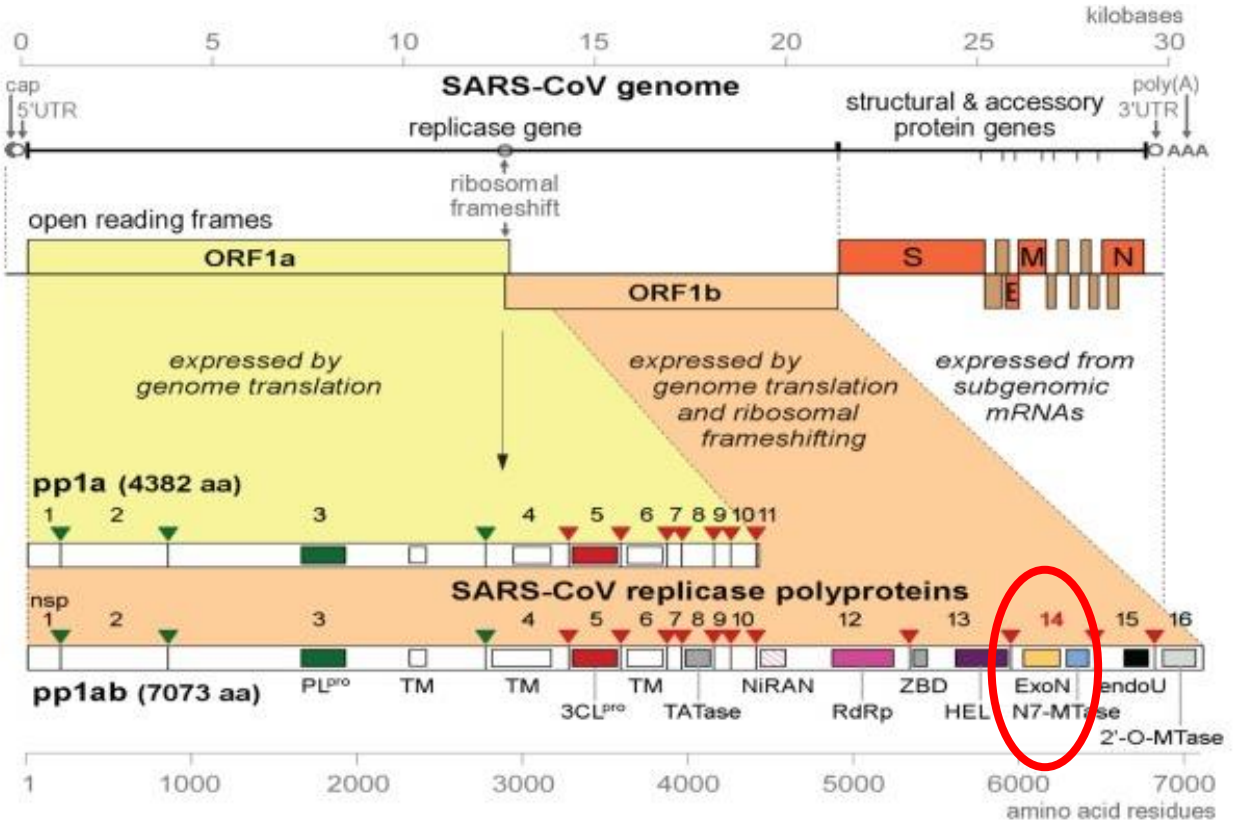
Figure from Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, Evaluation and Treatment Coronavirus (COVID-19). 2020 Apr 6. StatPearls Publishing

- SARS-CoV mutation rate: **$0.80–2.38 \times 10^{-3}$** nucleotide substitution per site per year
- SARS-CoV contains approx. 30,000 nucleotides
- 24–71 new mutations/year **(*moderate*)**

Zhao Z, Li H, Wu X, Zhong Y, Zhang K, Zhang YP, Boerwinkle E, Fu YX. Moderate mutation rate in the SARS coronavirus genome and its implications. BMC Evol Biol. 2004 Jun 28;4:21

SARS-CoV has a proofreading mechanism…

Among RNA viruses, coronaviruses stand out for including viruses with the largest RNA genomes currently known.



ExoN (exoribonuclease, nsp14) may enhance the fidelity of RNA synthesis by correcting nucleotide incorporation errors made by the RNA-dependent RNA polymerase (RdRp).

Ogando NS, Ferron F, Decroly E, Canard B, Posthuma CC, Snijder EJ. The Curious Case of the Nidovirus Exoribonuclease: Its Role in RNA Synthesis and Replication Fidelity. Front Microbiol. 2019 Aug 7;10:1813

Tables are empty at St. Mark's Square in Venice after the Italian government adopted emergency measures to contain the novel coronavirus. MANUEL SILVESTRI

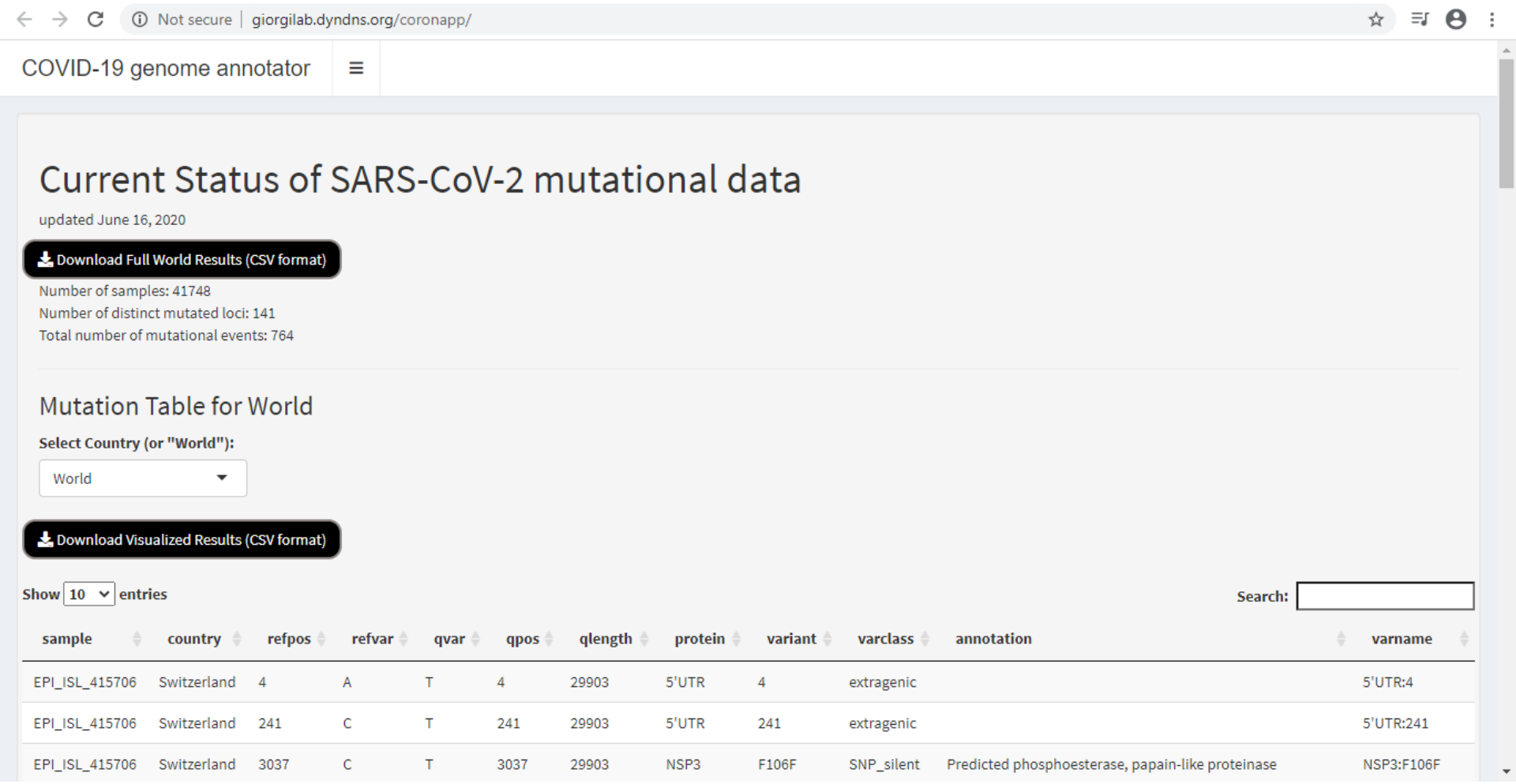
Mutations can reveal how the coronavirus moves—but they're easy to overinterpret

By Kai Kupferschmidt | Mar. 9, 2020 , 1:00 PM

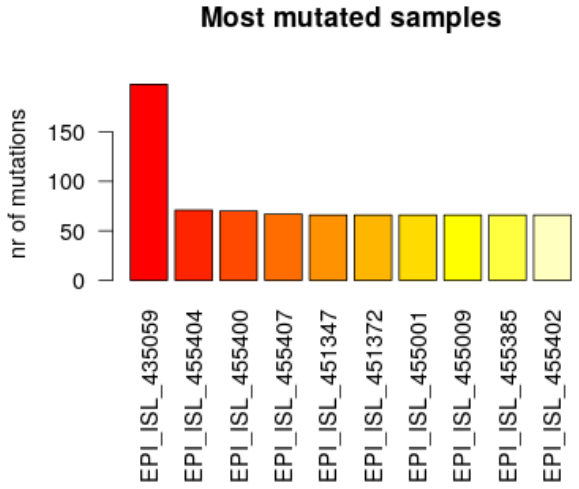
*"…SARS-CoV-2 accumulates an average of about one to two mutations per month. It's about **two to four times slower than the flu**."*

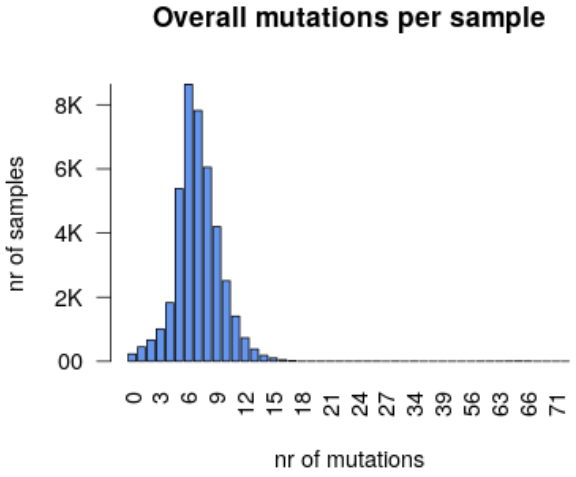
What is the bad and good news?

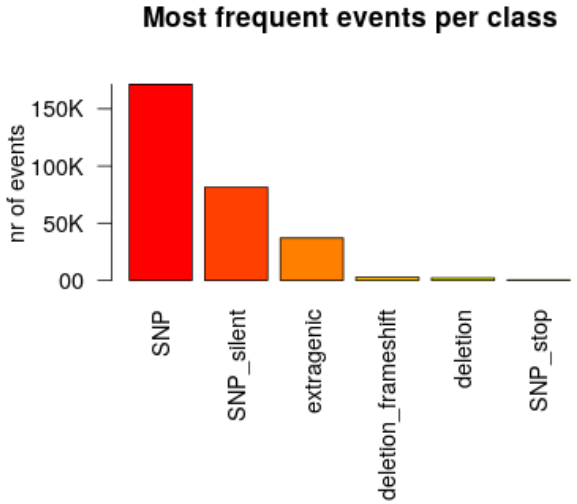
coronapp: A Web Application to Annotate and Monitor SARS-CoV-2 Mutations

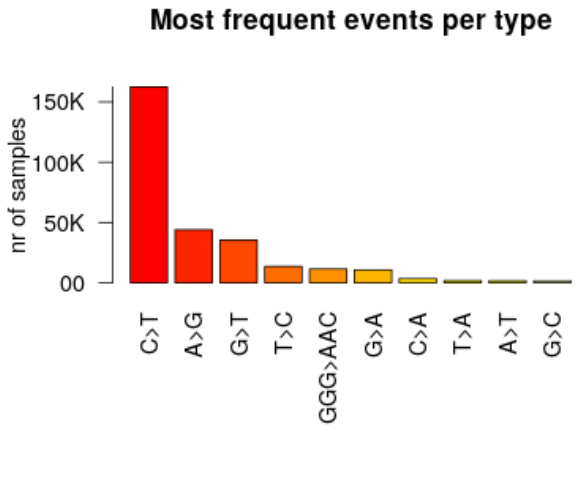


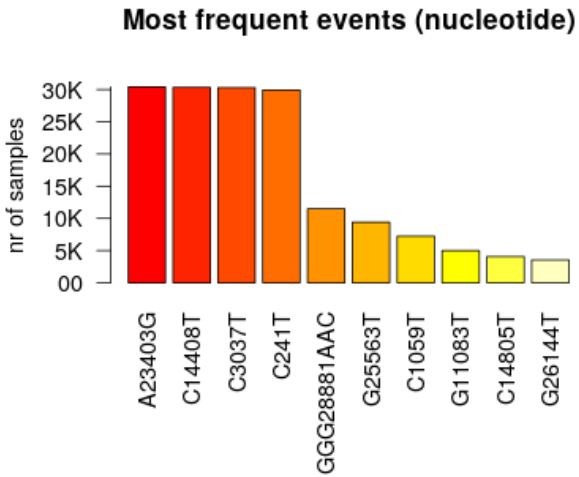
Mutational Overview for World

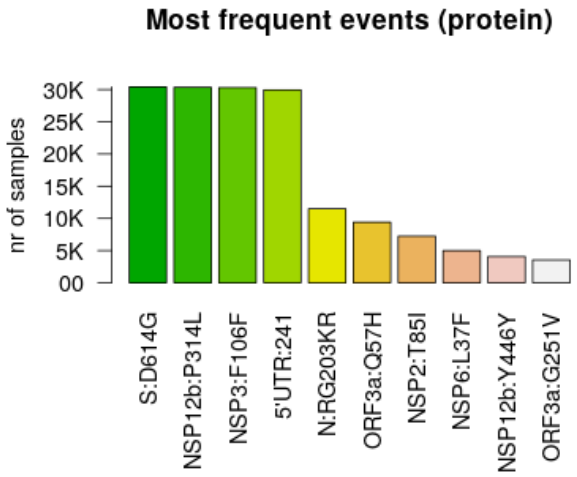




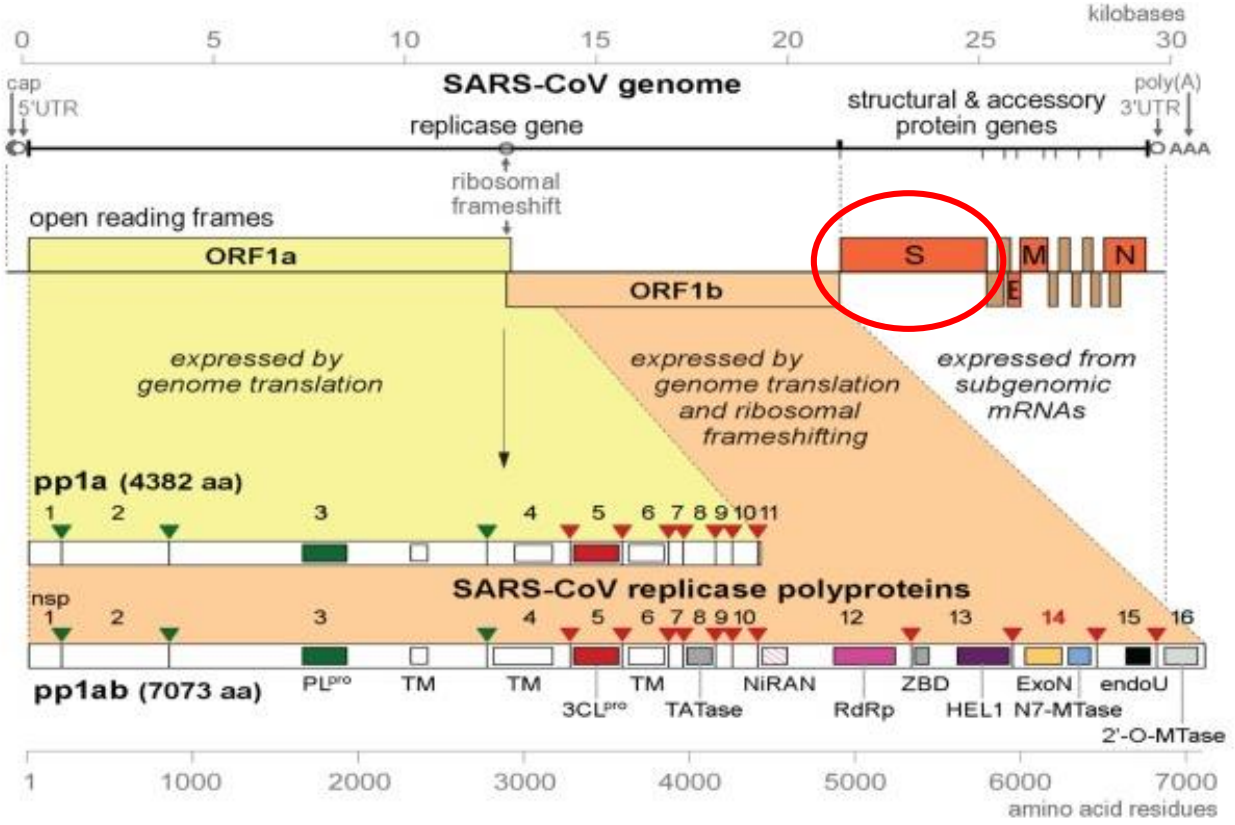


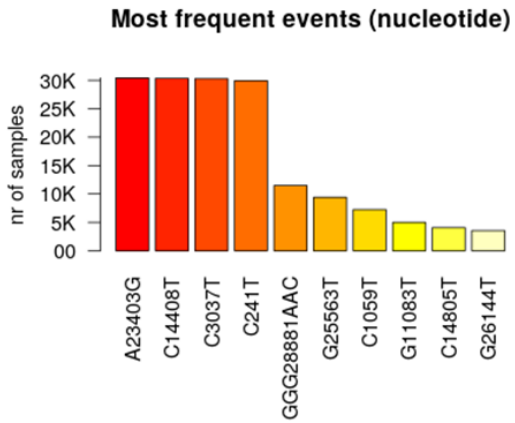


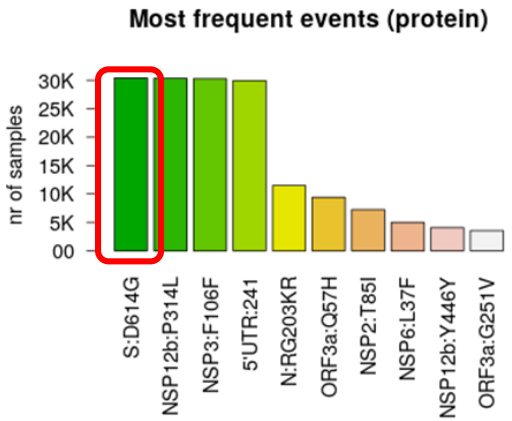


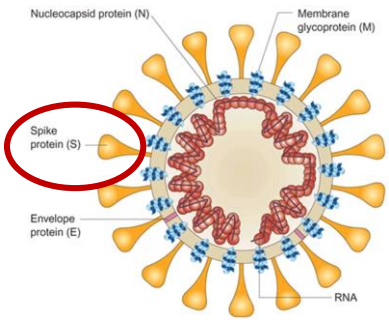


Mutational Overview for World

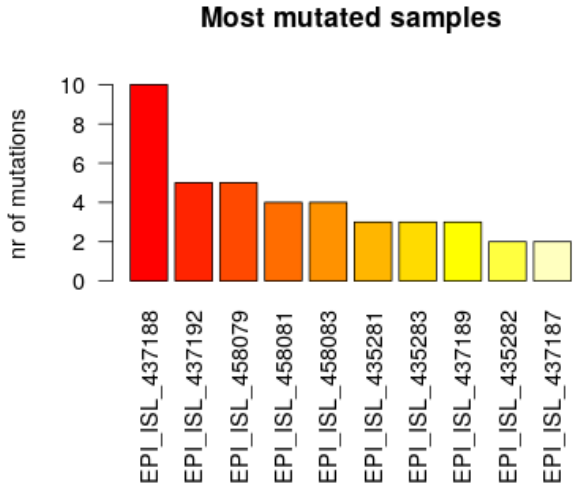


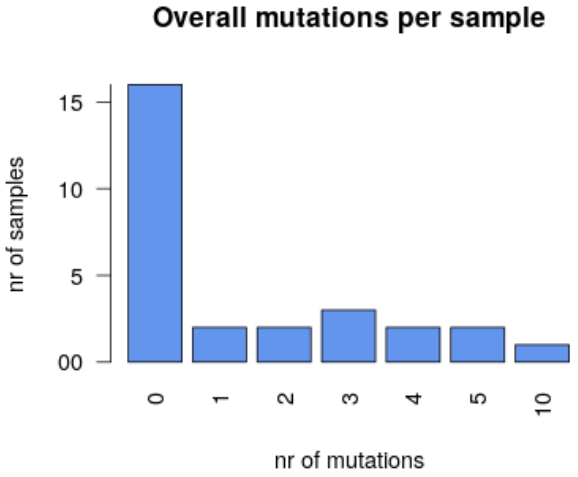


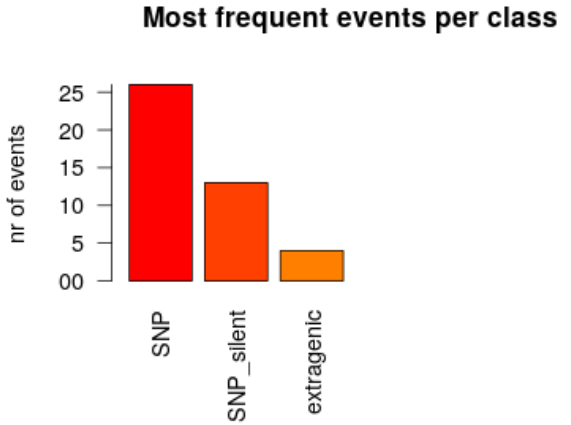


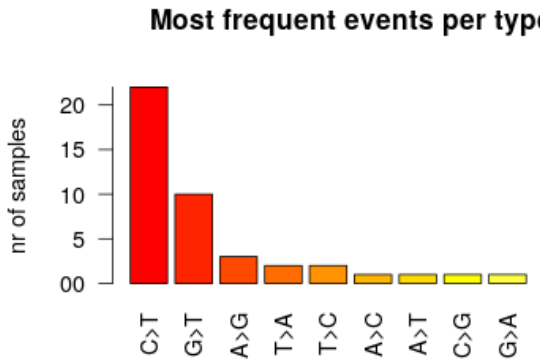


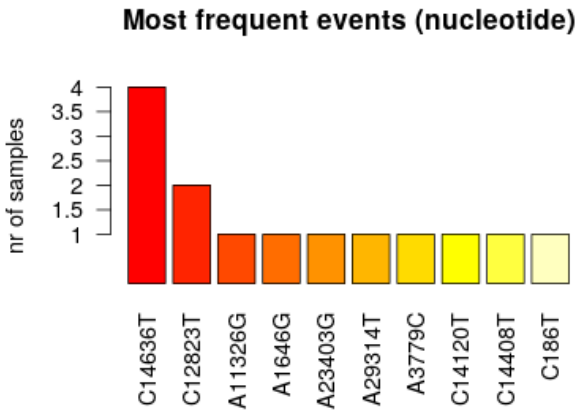
Mutational Overview for Indonesia

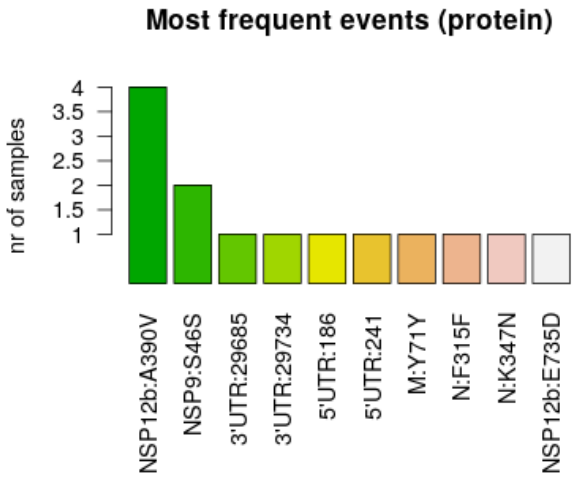




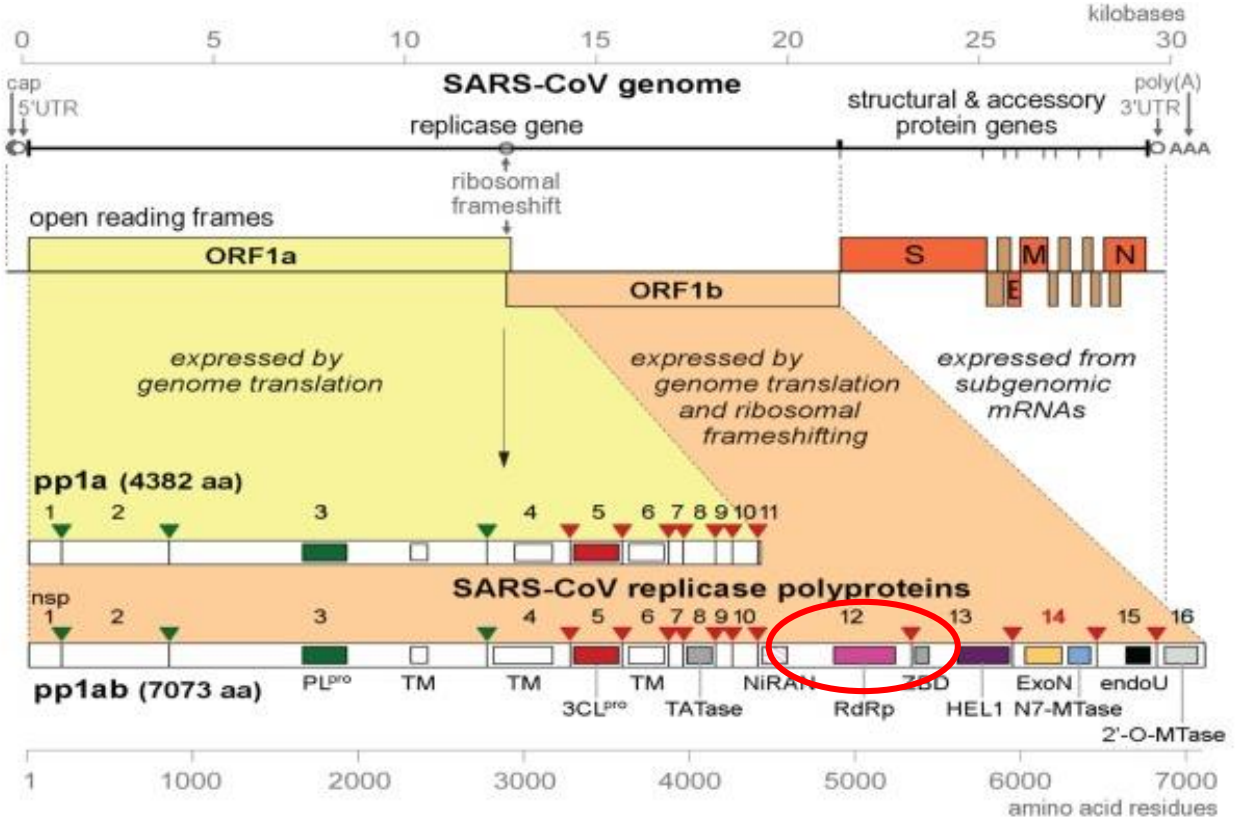


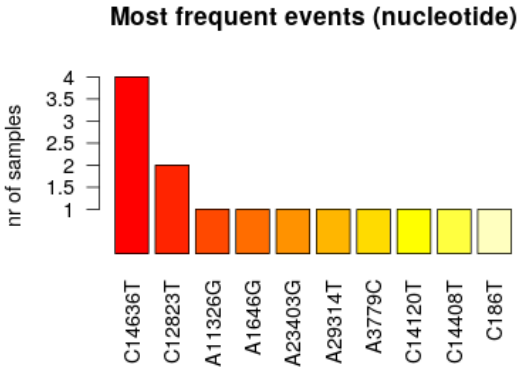


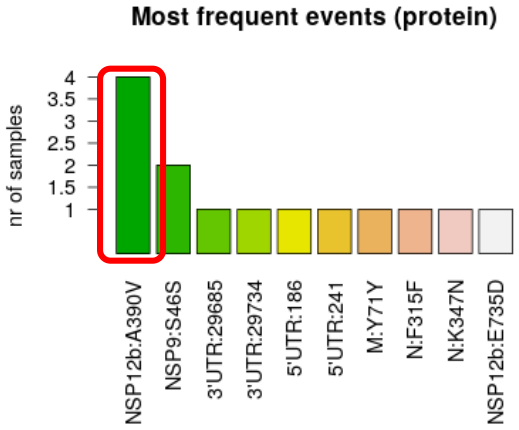




Mutational Overview for Indonesia







Coronaviruses have a slower mutation rate than the flu due to the enhanced fidelity of RNA replication. Therefore, coronaviruses may retain its pathogenicity and transmissibility longer.

Social distancing may be here to stay…

'No vaccine is not an issue'

NATION

Monday, 08 Jun 2020

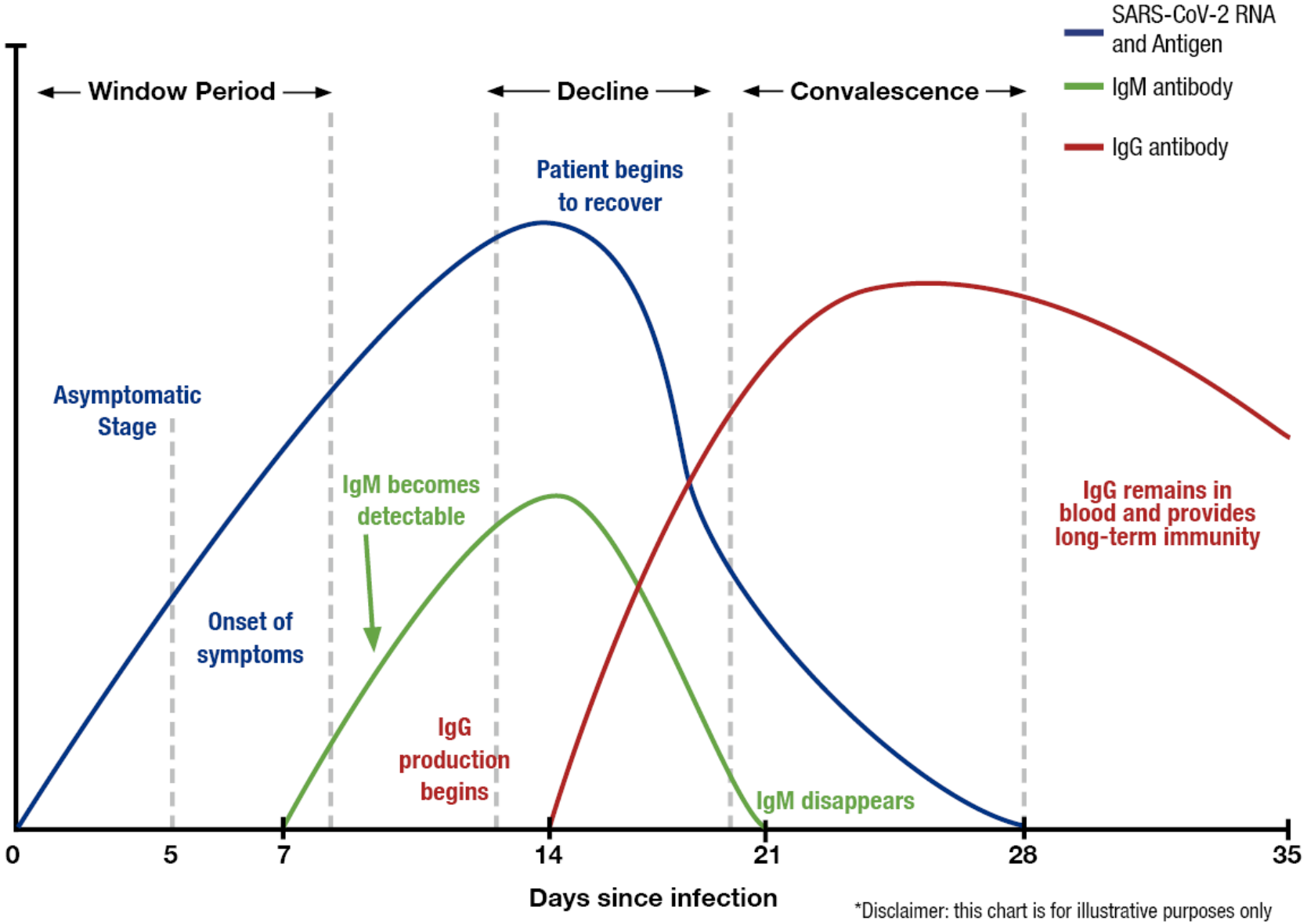
By CLARISSA CHUNG and JUSTIN ZACK

PUTRAJAYA: As the country transitions into the recovery movement control order (MCO) period, there is a possibility the Covid-19 pandemic can be beaten even without a vaccine as long as Malaysians maintain strong health discipline, says the Health Ministry.

Its director-general Datuk Dr Noor Hisham Abdullah said while a Covid-19 vaccine is desirable, he noted that past experience with other coronaviruses, such as the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS), showed that the chain of infection could be stopped without a vaccine.

TheStar, 'No vaccine is not an issue', 8 June 2020

Reinfection?



http://www.diazyme.com/covid-19-antibody-tests

JOURNAL OF GENERAL VIROLOGY

REVIEW

Kellam and Barclay, *Journal of General Virology*

DOI 10.1099/jgv.0.001439

MICROBIOLOGY SOCIETY

OPEN MICROBIOLOGY

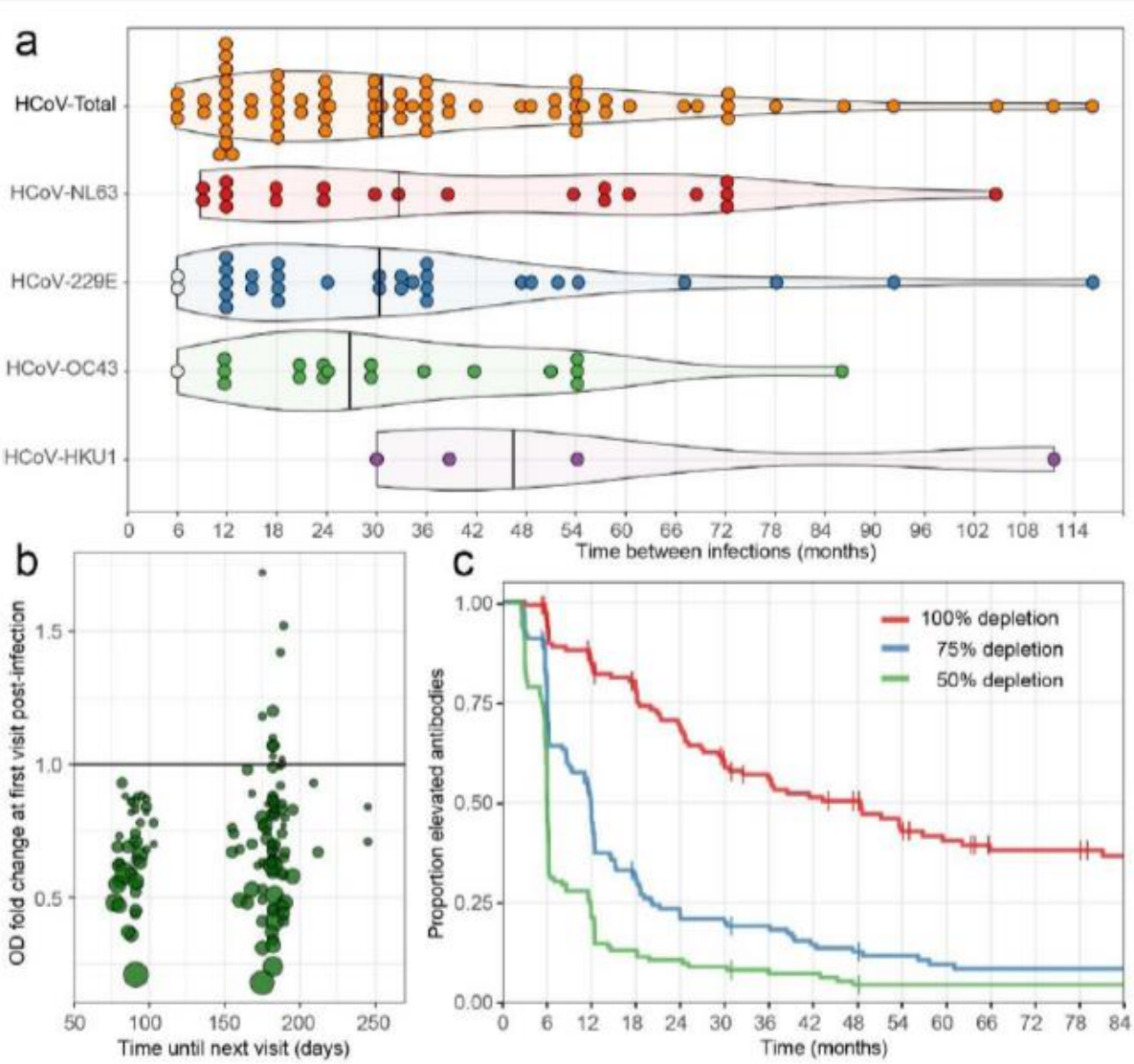
The dynamics of humoral immune responses following SARS-CoV-2 infection and the potential for reinfection

Paul Kellam[1,2,*] and Wendy Barclay[1,*]

- Four species of seasonal coronaviruses: **NL63** and **229E** (alphacoronaviruses), **HKU1** and **OC43** (betacoronaviruses).
- Three species of severe coronaviruses: **MERS-CoV**, **SARS-CoV-1** and **SARS-CoV-2** (all betacoronaviruses).
- Everyone previously infected with **SARS** and **MERS** will have minimal detectable antibody response after 2−3 years. Those suffering more severe disease have the highest antibody responses for longer.
- Antibody to **NL63** can protect from infection by **229E** (both alphacoronaviruses). Antibody to **OC43** can protect from infection by **HKU1** (both betacoronaviruses). However, *no reciprocal protection* (**229E** protects against **NL63** and **HKU1** against **OC43**).
- Immunity to **OC43** and and **HKU1** remains for 45 weeks. Immunity to **229E** remains for 52 weeks.

Kellam P, Barclay W. The dynamics of humoral immune responses following SARS-CoV-2 infection and the potential for reinfection. J Gen Virol. 2020;10.1099/jgv.0.001439.

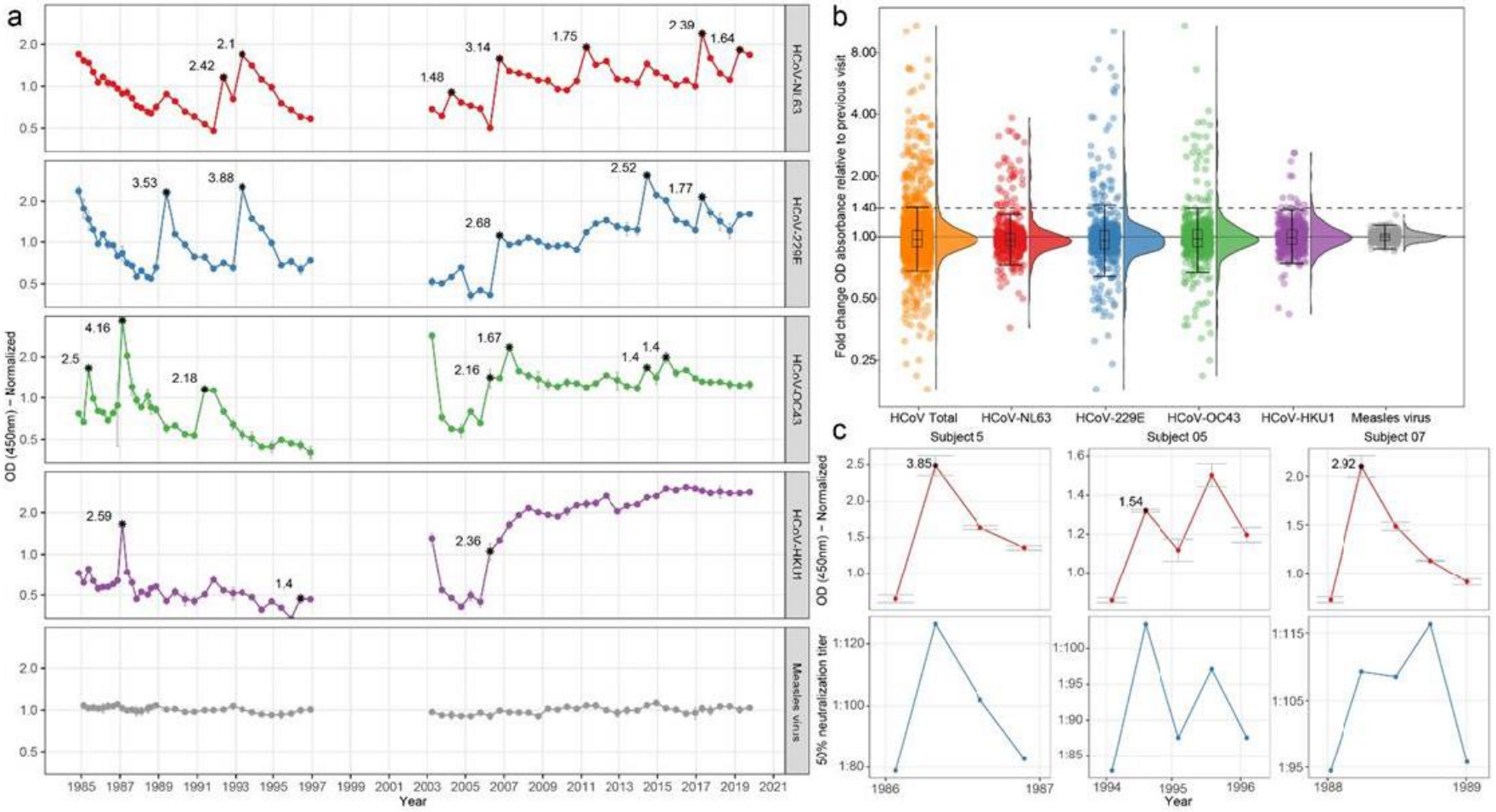
Reinfection Characteristics for Seasonal Coronaviruses



- Reinfections occur frequently in a 12-month period. On average there were 13 infections.
- Patients experienced an antibody drop as early as 50 days post-infection.
- Patients loss 50% of the antibodies after 6 months, 75% after 1 year, and 100% antibody loss after 4 years.

Edridge, AWD., Kaczorowska, JM., Hoste, ACR., Bakker, M., Klein, M., Jebbink, MF., Matser, A., Kinsella, C., Rueda, P., Prins, M., Sastre, P., Deijs, M., van der Hoek. Coronavirus protective immunity is short-lasting. medRxiv 2020.05.11.20086439

Antibody Dynamics for Seasonal Coronaviruses



For subject #9, total 22 coronavirus infections during 1985−2019:
NL63 (7), **229E** (5), **OC43** (7), **HKU1**

Edridge, AWD., Kaczorowska, JM., Hoste, ACR., Bakker, M., Klein, M., Jebbink, MF., Matser, A., Kinsella, C., Rueda, P., Prins, M., Sastre, P., Deijs, M., van der Hoek. Coronavirus protective immunity is short-lasting. medRxiv 2020.05.11.20086439

nature medicine

LETTERS

https://doi.org/10.1038/s41591-020-0965-6

Check for updates

Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections

Quan-Xin Long[1,8], Xiao-Jun Tang[2,8], Qiu-Lin Shi[2,8], Qin Li[3,8], Hai-Jun Deng[1,8], Jun Yuan[1], Jie-Li Hu[1], Wei Xu[2], Yong Zhang[2], Fa-Jin Lv[4], Kun Su[3], Fan Zhang[5], Jiang Gong[5], Bo Wu[6], Xia-Mao Liu[7], Jin-Jing Li[7], Jing-Fu Qiu[2]✉, Juan Chen[1]✉ and Ai-Long Huang[1]✉

- Asymptomatic COVID-19 patients have a longer duration of viral shedding (19 d) than the symptomatic patients (14 d).
- Asymptomatic group has a lower antibody level than the symptomatic group.
- Antibody levels of most recovered patients start to decrease within 2−3 months after infection.

Long, Q., Tang, X., Shi, Q. et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med (2020). https://doi.org/10.1038/s41591-020-0965-6

Implications

- Annual vaccination is needed?
- Herd immunity is challenging to accomplish?
- Repeat testing is needed?
- *The new normal becomes permanent normal?*

Ultimately, it's the virus that sets the timeline!

Q & A