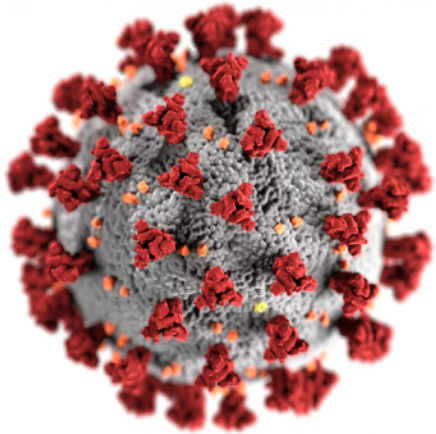

Update on the New Variant of SARS-CoV-2

Jan. 7, 2021

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Professor
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HiPAM
Hawai'i Pandemic Applied Modeling

UNIVERSITY OF HAWAI'I
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THREAT ASSESSMENT BRIEF

Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom

20 December 2020

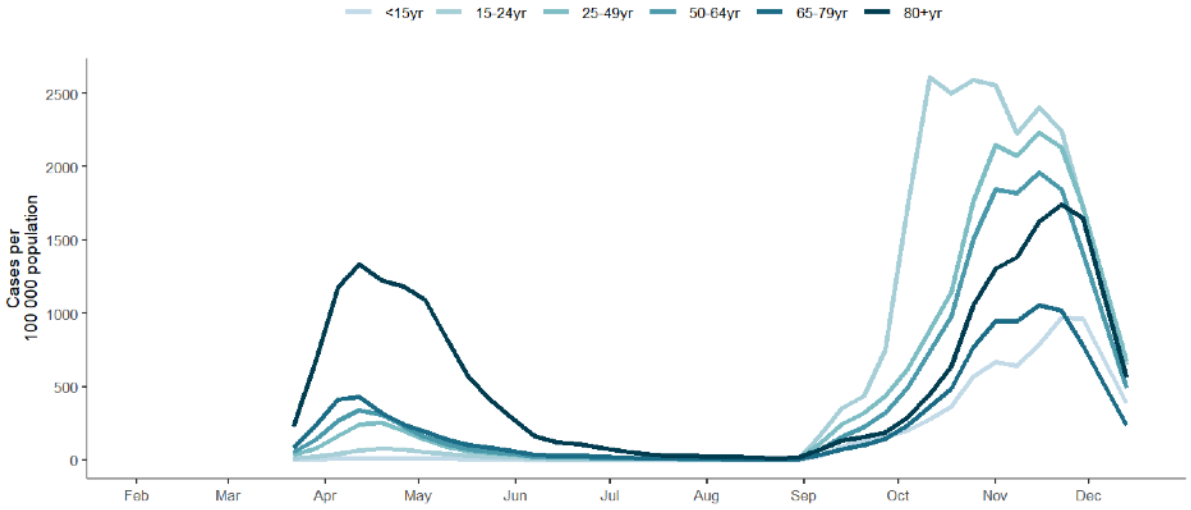
- Cases of COVID-19 rising rapidly in south of UK over the last several weeks
- Analysis of genomic sequencing data identified majority (>50%) belong to a new variant (UK has a massive genomic surveillance effort)
- New Variant has 17 mutations that appeared to arise in concert: 9 are in the Spike region
  - Estimated increase in transmission by 70%
  - Potential to increase viral Reproductive number by 0.4
  - No indication of increased virulence (no increase in disease severity or mortality)
  - 9 mutations in Spike: deletion 69-70, deletion 144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H

Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom

20 December 2020

EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

England (UK): 14-day age-specific COVID-19 case notification rate



ECDC. Figure produced 16 December 2020.
Source: TESSy COVID-19, national weekly data

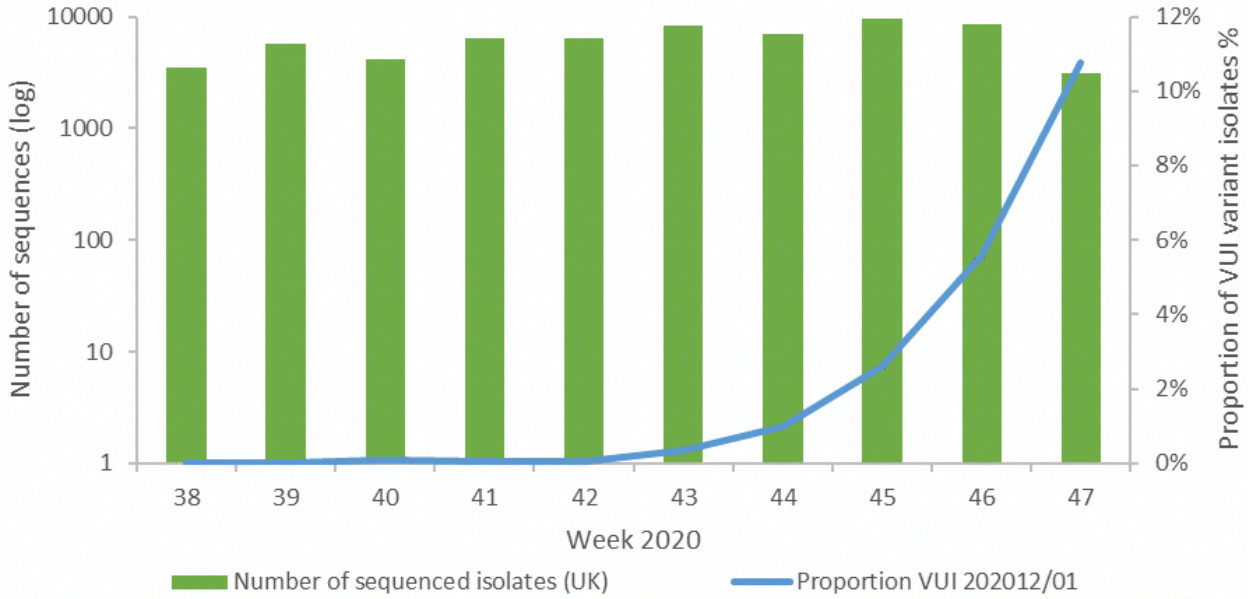
Cases rose sharply

Greatest rise in teens/young adults

THREAT ASSESSMENT BRIEF

Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom

20 December 2020



New variant is replacing other genotypes

Questions

Will there be wider spread or greater disease severity?

Will the vaccine still work on this new variant?

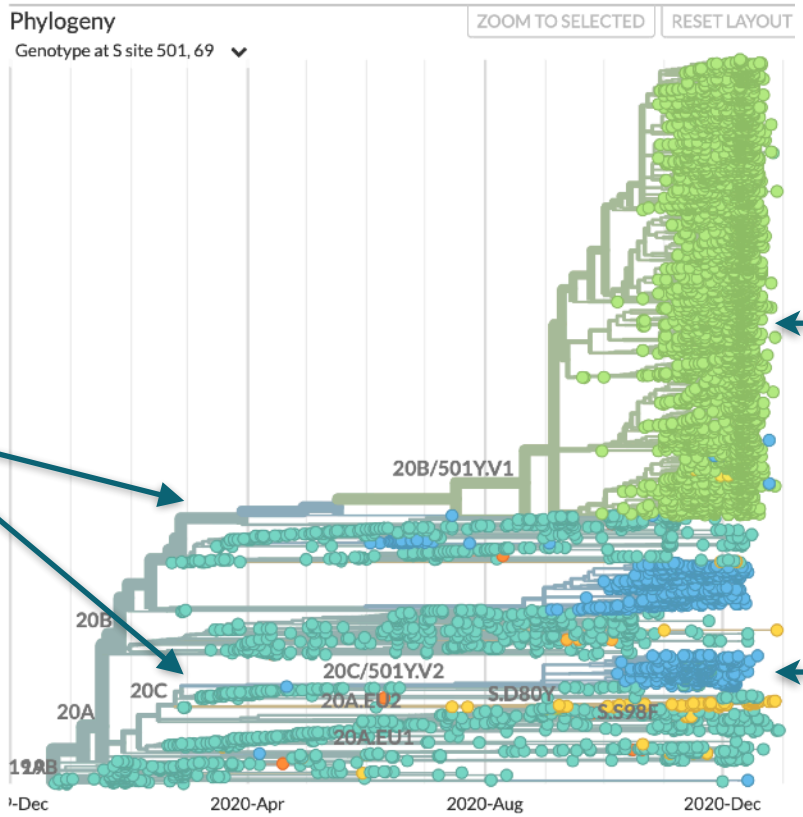
Can the new variant escape detection by PCR, etc.?

Increased potential for reinfections?

Is the UK Strain (B.1.1.7) the same as the South Africa Strain (501Y.V2 or B.1.351)?

Is the UK Strain (B.1.1.7) the same as the South Africa Strain (501Y.V2 or B.1.351)?

No, they arose Independently



UK strain

SA strain

Dr. Emma Hodcroft @firefoxx66

https://nextstrain.org/groups/neherlab/ncov/S.N501?c=gt-S_501,69&p=grid&r=country

Is the UK Strain (B.1.1.7) the same as the South Africa Strain (501Y.V2 or B.1.351)?

Dr Emma Hodcroft
@firefoxx66

Replying to @firefoxx66

Importantly!:
In Europe, the UK & Denmark are the most regular & prolific sequencers. So the variant could be elsewhere & not detected yet.
In Africa, same is true for South Africa.

More coordinated sequencing efforts regionally & globally would help us monitor variants

8/N

8:15 AM · Dec 19, 2020 · Twitter Web App

210 Retweets **49** Quote Tweets **755** Likes

Update from January 6, 2021

Is the UK Strain (B.1.1.7) the same as the South Africa Strain (501Y.V2 or B.1.351)?

Spike Mutations

	UK strain	SA strain	
Two shared	**N501Y**	**N501Y**	**Receptor Binding Domain**
		K417N	
		E484K	
Many distinct Spike mutations	-69-70	L18F	**N-terminal Domain**
	-144	D80A	
		D215G	
		-242-244?	
		R246I	
	A570D		
	D614G	**D614G**	
	P681H	A701V	
	T716I		
	S982A		
	D1118H		

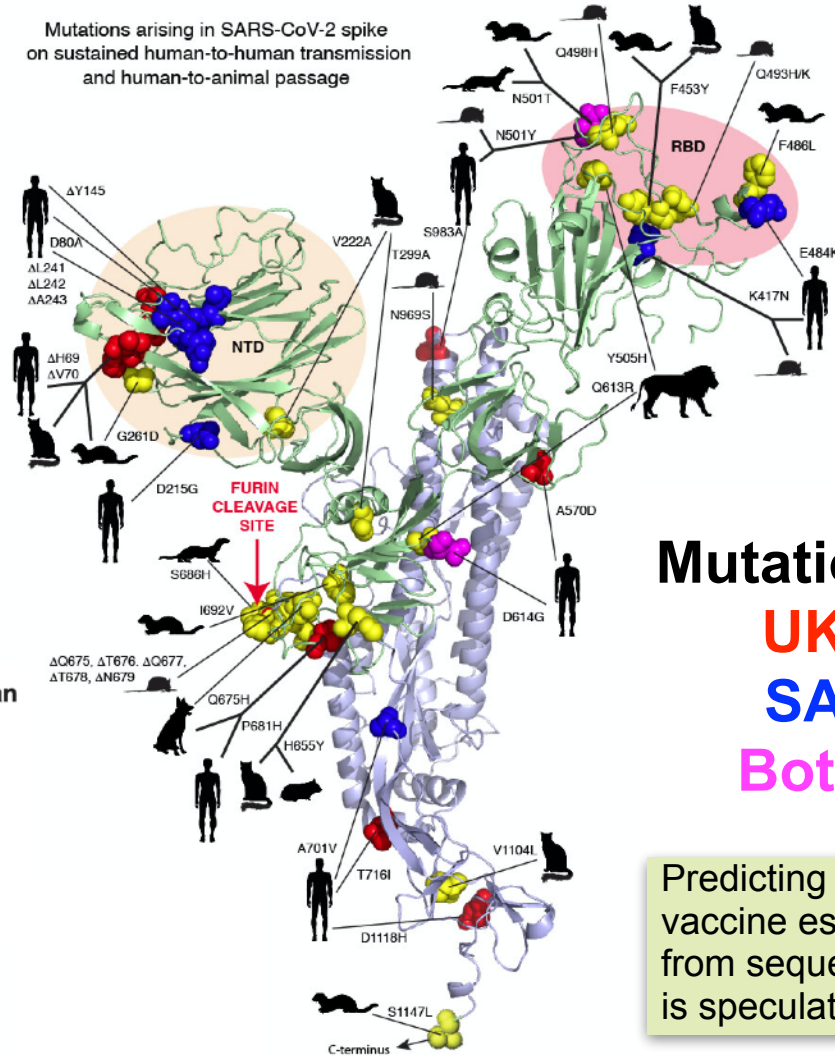
Viruses mutate frequently!

Mutations are intensively studied

Most mutations have no functional effect

Sometimes they do - and selection is strong for increased transmission

Amino-terminal domain



Receptor binding domain

Mutations:

UK

SA

Both

Predicting vaccine escape from sequences is speculative

Mutations arising in SARS-CoV-2 spike on sustained human-to-human transmission and human-to-animal passage

SARS-CoV-2 coronavirus

R rfgarry 5d

Mutations arising in SARS-CoV-2 spike on sustained human-to-human transmission and human-to-animal passage

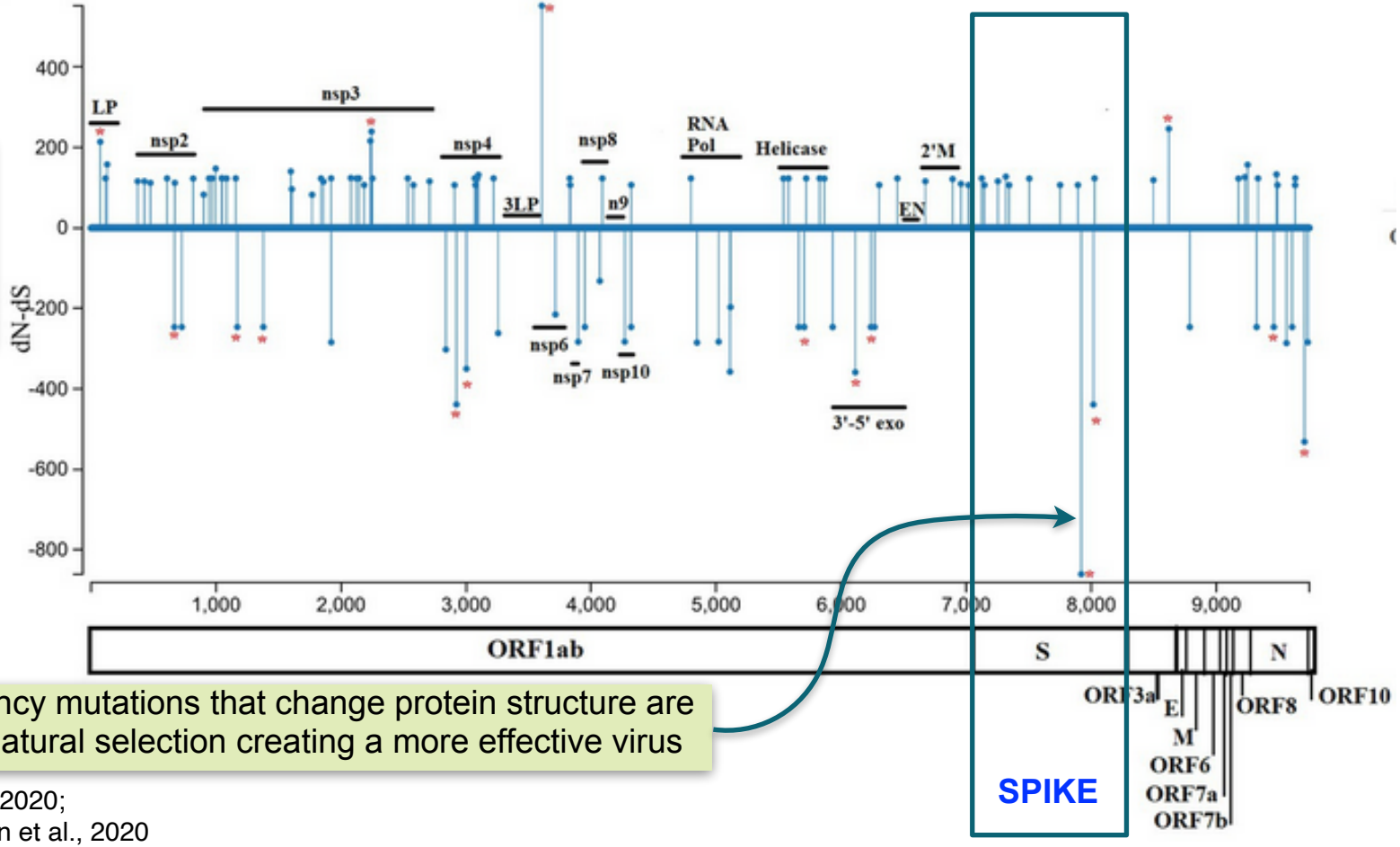
Robert F. Garry1,2

1Department of Microbiology and Immunology, Tulane University Medical Center, 1430 Tulane Avenue, New Orleans, Louisiana 70112 USA; E-Mail: rfgarry@tulane.edu

https://virological.org/t/mutations-arising-in-sars-cov-2-spike-on-sustained-human-to-human-transmission-and-human-to-animal-passage/578

SARS-CoV-2 Mutations Occur All The Time

Thousands of mutations have been documented for SARS-CoV-2

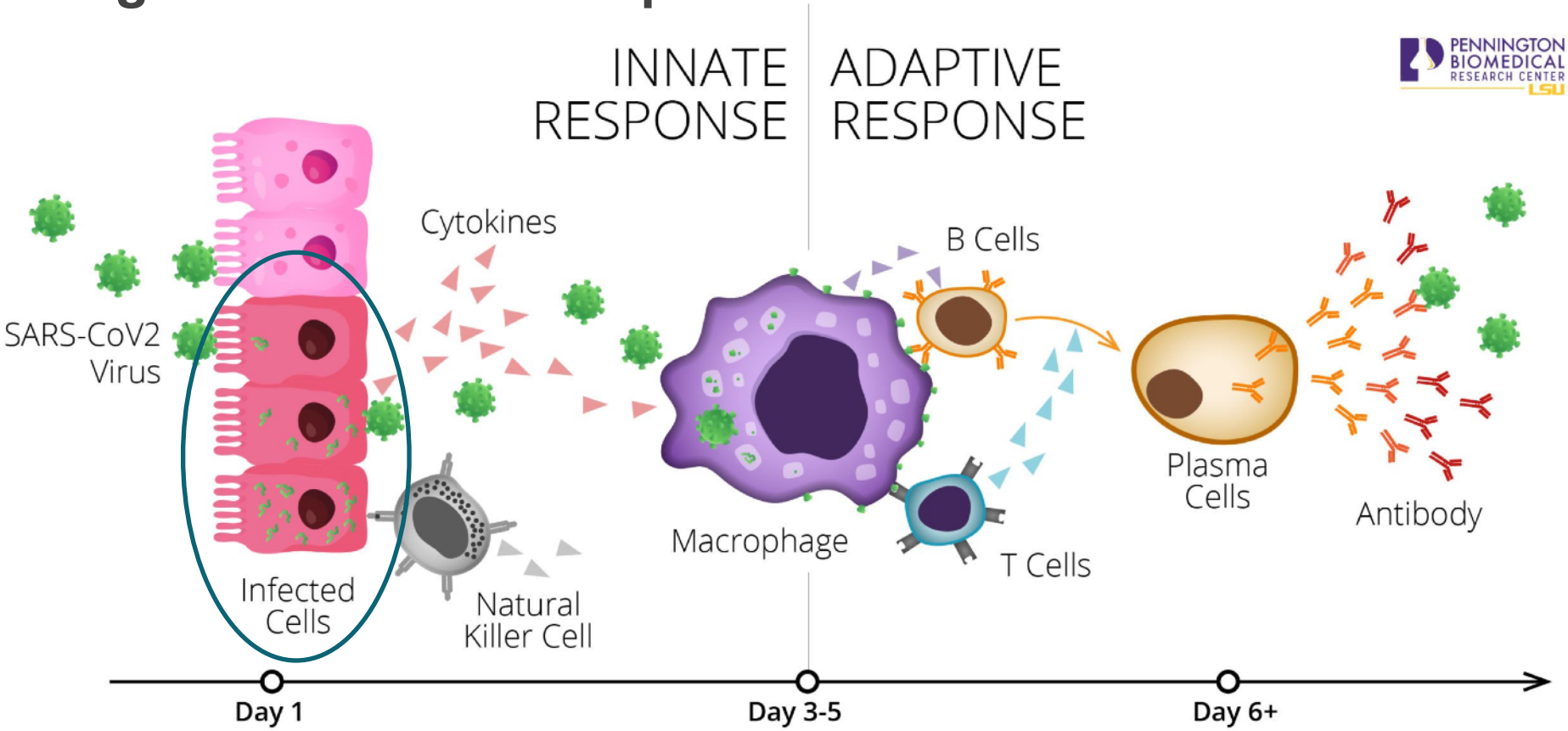


High frequency mutations that change protein structure are a signal of natural selection creating a more effective virus

Velazquez-Salinas et al., 2020;
Cagliani et al., 2020; Zhan et al., 2020

Will the vaccine remain effective against new variants?

Background: Immune responses to viral infection



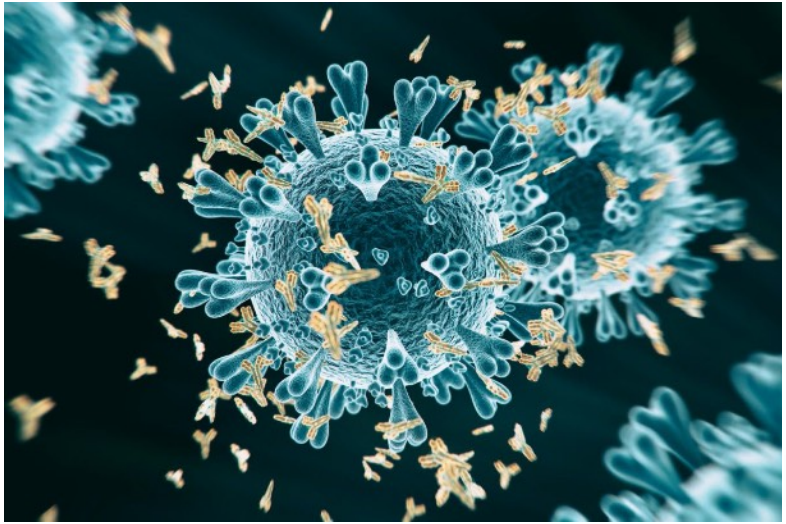
Kappen and Cole (accessed Jan 6, 2021)
https://pbrf.org/covid19/what-is-immunity-against-the-virus-and-how-can-i-become-immune/

Antibodies: Multiple Ways They Block Coronaviruses

Antibodies stick to SPIKE

- **Blocking SARS-CoV-2 receptor binding site**

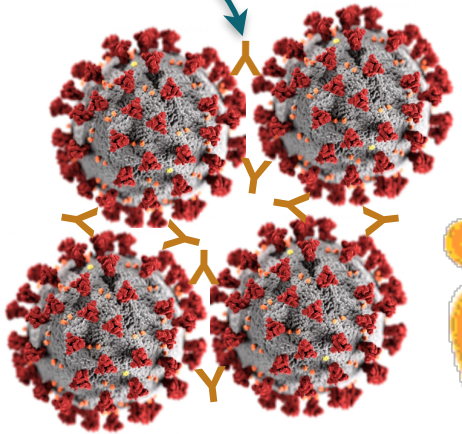
SARS-CoV-2 cannot enter



Source: koto_feja / Getty Images

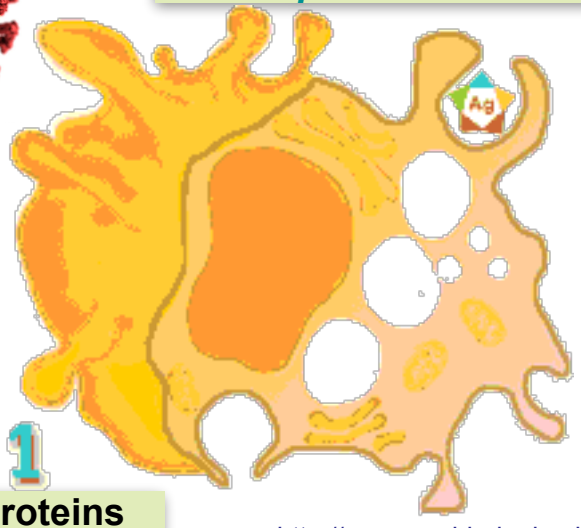
- **Cause agglutination**

Virus clumps together - cannot enter



- **Signals macrophage**

'Eats' Virus - aids B and T cell responses



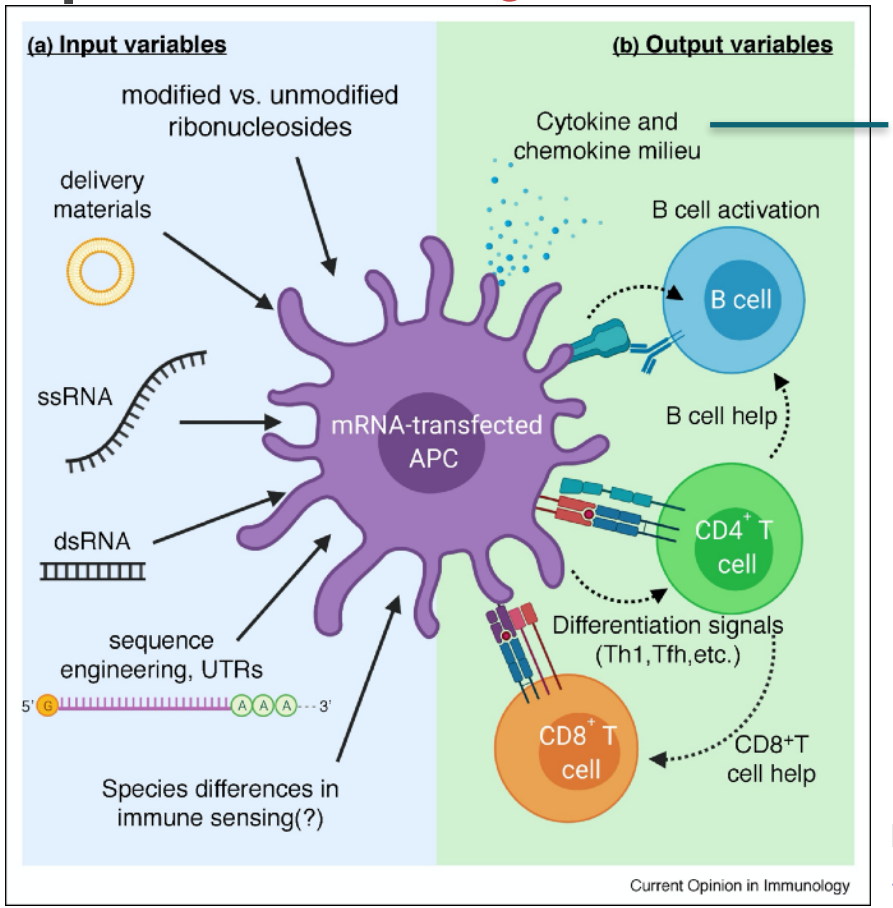
http://apps.sanidadanimal.info/cursos/immunology/ca071.htm

- **Attract Complement Proteins**
- **Coat virus**, make sticky

mRNA vaccines contain information for SPIKE —

Immune response produces many of types of antibodies to SPIKE

But there‘s more… mRNA vaccines elicit multiple immune responses *Creating a robust immune response*



Cytokine response -> alerts immune system

B cell activation-> Humoral (antibody) response

Memory B cells

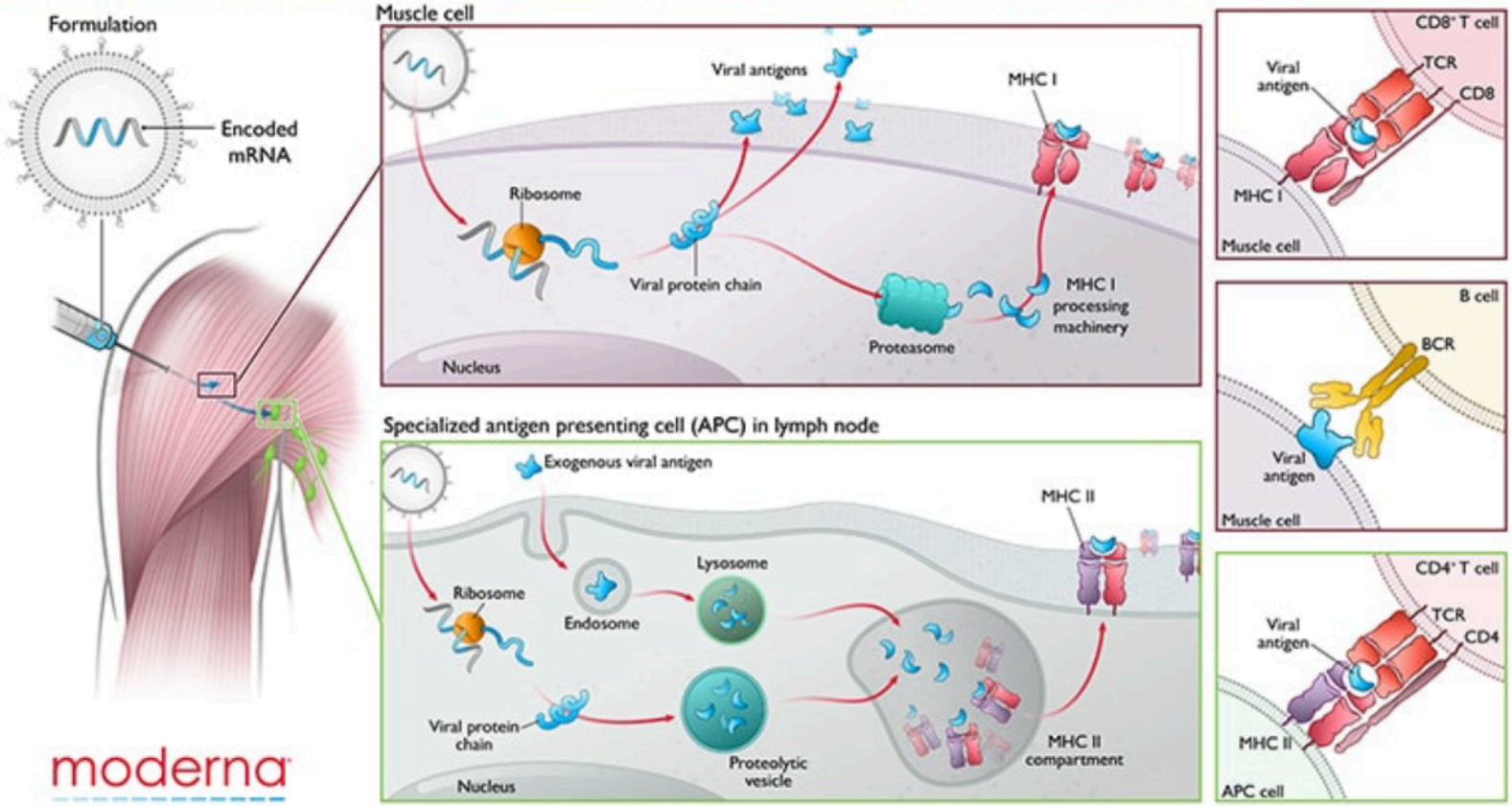
T cell activation-> Cellular response

Memory T cells

Pardi, Hogan, Weissman 2020
https://doi.org/10.1016/j.coi.2020.01.008

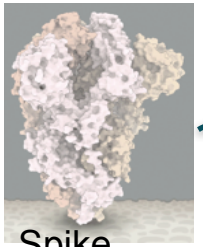
Moderna's mRNA Vaccine Approach

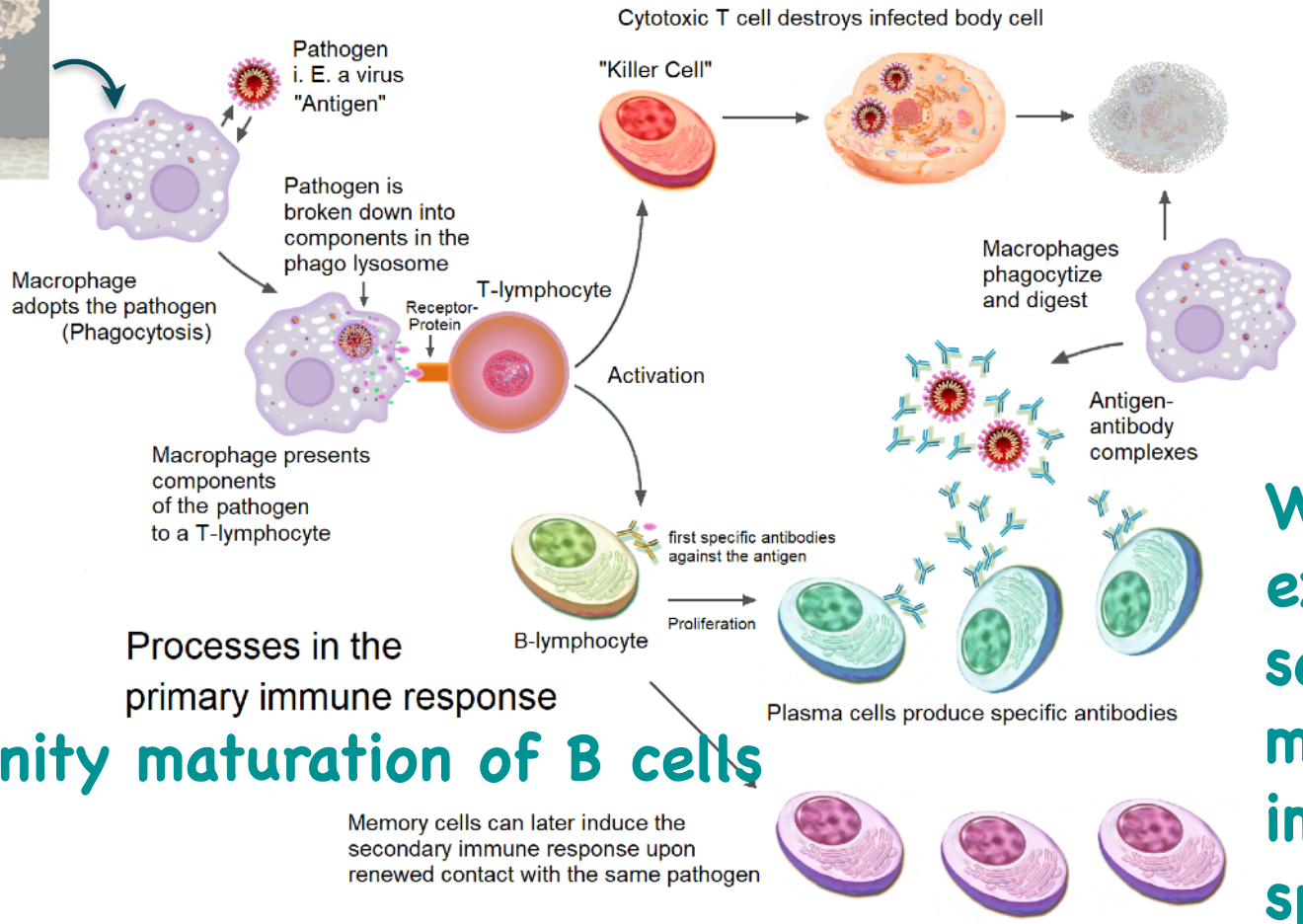
Closely mimics a native viral infection leading to B and T cell responses



© 2017 Moderna Therapeutics

https://www.modernatx.com/moderna-blog/shedding-light-our-prophylactic-vaccines-moa





Processes in the primary immune response

Affinity maturation of B cells

With repeated exposure, somatic mutations improve fit to spike

https://www.nature.com/articles/d41586-020-02544-6#ref-CR2

Summary Antibody Response:

Adults produce naive B cells in random combinations

- 100‘s of millions of variants a day
- A handful will match

B cells will undergo affinity maturation

- Somatic mutations to improve fit to SPIKE
- Becomes memory B cells

Adaptive memory is not set in stone - maturation will happen with every exposure

- Our immune system **will keep evolving** for better fit

mRNA vaccine also recruits other components of immune response

- Cytokine and some inflammatory response
- T cell response
- Alerts Macrophage and other non-specific immune responses

REPORT

Robust neutralizing antibodies to SARS-CoV-2 infection persist for months

Ania Wajnberg[1,*], Fatima Amanat[2,3], Adolfo Firpo[4], Deena R. Altman[5], Mark J. Bailey[1], Mayce Mansour[1], Me...
+ See all authors and affiliations

Science 04 Dec 2020:
Vol. 370, Issue 6521, pp. 1227-1230
DOI: 10.1126/science.abd7728

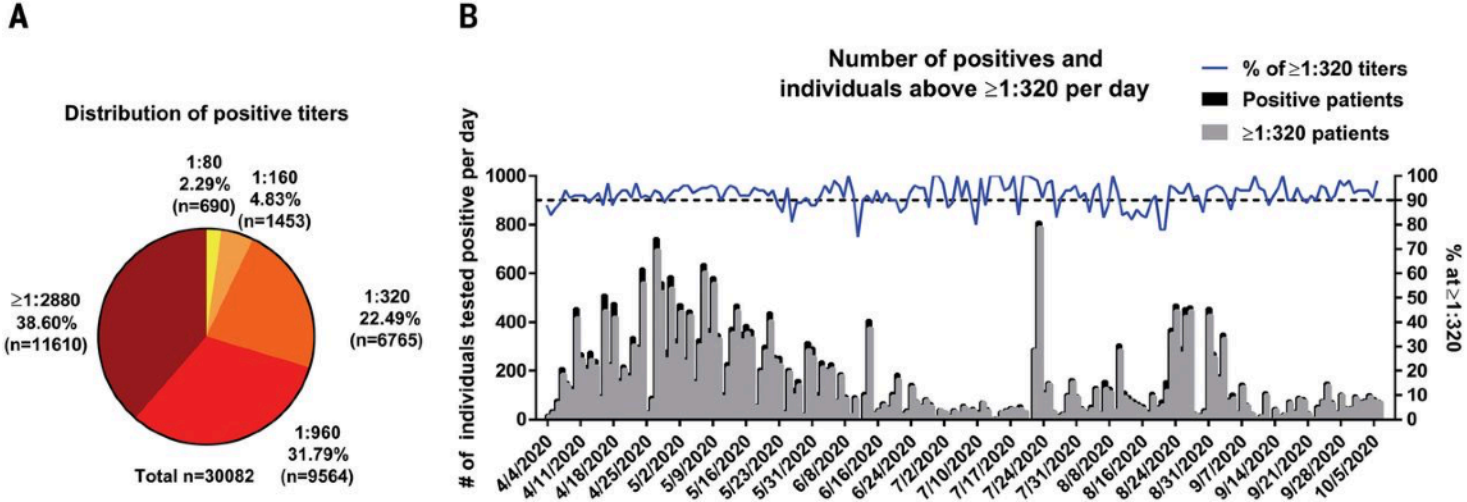
Article | Figures & Data | Info & Metrics | eLetters | PDF

GREAT NEWS!

Natural infection study -
Cases with **Mild to Moderate** symptoms

Followed >30,000 infected individuals

SARS-CoV-2 antibodies persist



Vast Majority of individuals showed:
- Strong neutralizing Antibody titers
- Antibodies persisted for > 5 months

How did the UK strain arise with 17 mutations “at once”?

How did a new variant arise with 17 mutations at once?

Shoppers wear face masks on Regent Street in London on 19 December, the day the U.K. government imposed new restrictions to curb a rapidly spreading new SARS-CoV-2 variant. AP PHOTO/ALBERTO PEZZALI

U.K. variant puts spotlight on immunocompromised patients' role in the COVID-19 pandemic

By **Kai Kupferschmidt** | Dec. 23, 2020 , 2:30 PM

https://www.sciencemag.org/news/2020/12/uk-variant-puts-spotlight-immunocompromised-patients-role-covid-19-pandemic

Typically mutations accumulate one at a time

medRχiv

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Neutralising antibodies drive Spike mediated SARS-CoV-2 evasion

Posted December 19, 2020.

SA Kemp, DA Collier, R Datir, S Gayed, A Jahun, M Hosmillo, IATM Ferreira, C Rees-Spear, P Mlcochova, Ines Ushiro Lumb, David Roberts, Anita Chandra, N Temperton, The CITIID-NIHR BioResource COVID-19 Collaboration, The COVID-19 Genomics UK (COG-UK) Consortium, K Sharrocks, E Blane, JAG Briggs, MJ van Gils, KGC Smith, JR Bradley, C Smith, RA Goldstein, IG Goodfellow, A Smielewska, JP Skittrall, T Goulliouris, E Gkrania-Klotsas, CJR Illingworth, LE McCoy, RK Gupta

doi: https://doi.org/10.1101/2020.12.05.20241927

Download PDF

Author Declarations

Supplementary Material

Data/Code

The new variant arose with 17 mutations, and is highly transmissible

"Given both vaccines and therapeutics are designed around Wuhan-1 Spike, this raises the theoretical possibility of viral escape"

This preprint (not yet peer reviewed) explores how the new variant arose

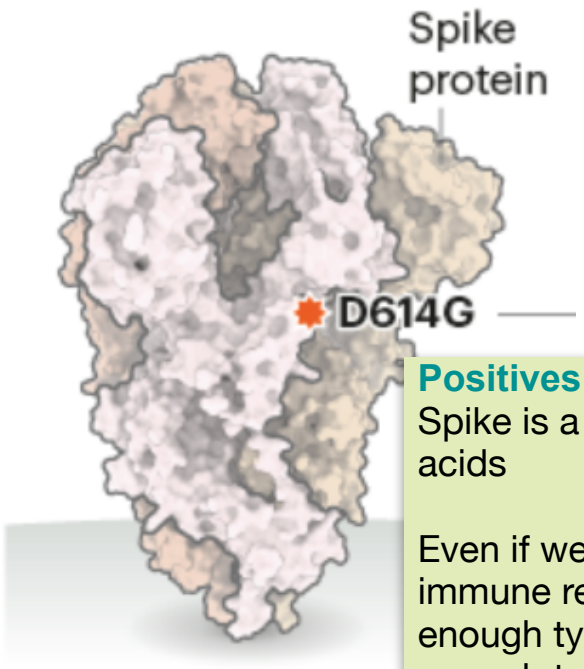
Preprint Summary: The SARS-CoV-2 virus mutates at a rate of 1-2 mutations per month on average
However, immunocompromised individuals offer the virus opportunity for multiple replication cycles in same host

Cancer patient infected for 101 days, sampled 23 times
No change over 65 days with 2 doses of Remdesivir
Following convalescent plasma treatment, variant strain emerged with several mutations and waned
A final, unsuccessful dose of convalescent plasma was given, followed by rise of the variant strain

In vitro the Spike escape variant has decreased sensitivity to plasma and is highly infective
Suggests that convalescent plasma treatment on immunocompromised individual created positive selection environment on SARS-CoV-2

https://www.medrxiv.org/content/10.1101/2020.12.05.20241927v2.supplementary-material

B.1.1.7: The New Variant contains 9 mutations in Spike



- deletion 69-70
- deletion 144
- N501Y*
- A570D
- D614G
- P681H
- T716I
- S982A
- D1118H

Concerns:

Deletions/mutations may interfere with PCR or other diagnostics

- labs should remain vigilant

Although not likely, there is a risk of immune escape if the mutations allow the virus to "hide" from the immune system

- genomic surveillance to monitor genotypes in populations, especially patients at risk of reinfection or vaccine failure

Positives:

Spike is a large, conserved protein 1273 amino acids

Even if we have 10, or 20 mutations etc. our immune response should produce more than enough types of antibodies so that we will have enough to be protected from infection

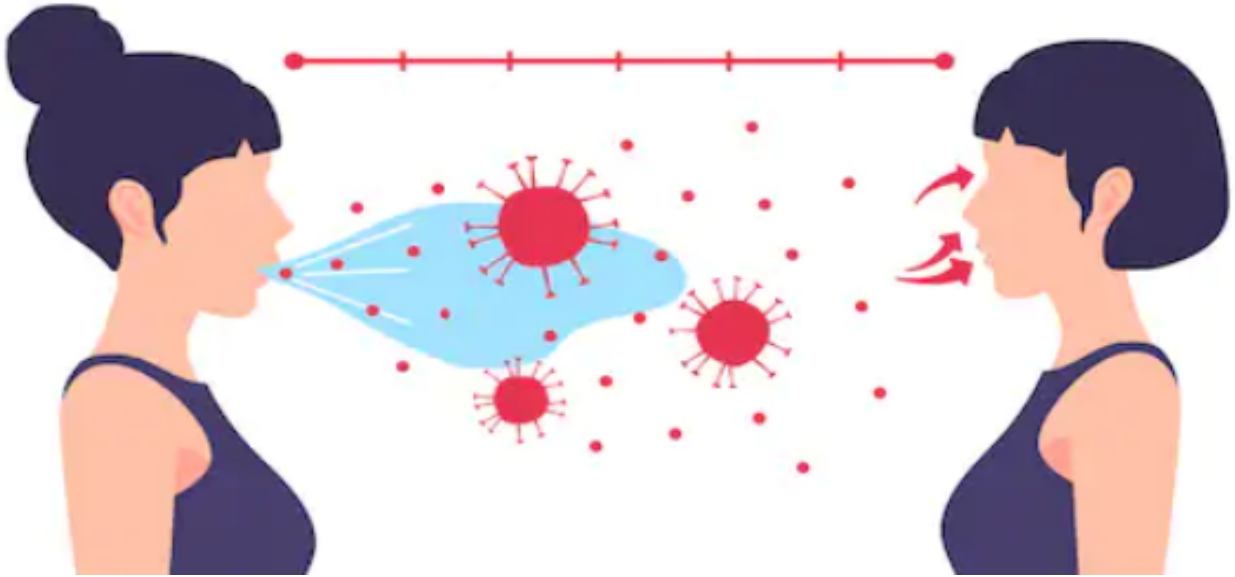
mRNA vaccines are easy to modify and update

The new variant B.1.1.7 has been found in Canada, France, Japan, Spain, Sweden, and Norway, despite lockdown in the UK. The US is behind on genomic sequencing.

Another variant 501.V2 with some of the same mutations arose in South Africa. Speculation that it may be even more transmissible and has now been found in the UK (?- no one knows)

https://www.nature.com/articles/d41586-020-02544-6#ref-CR2

The Opportunity for Mutation Arises when Cases Proliferate



Stop the Spread

Get Vaccinated

Wear a Mask

Social Distance

https://www.shutterstock.com/image-vector/coronavirus-contamination-during-communication-between-two-1721817907

Thank you!

Special thanks to Dr. Howard Chen at UHM

HiPAM

Hawai'i Pandemic Applied Modeling

UNIVERSITY OF HAWAI'I

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UA MAU KE EA O KA 'ĀINA I KA PONO