LOGBOOK

Feb 26:
I am trying to choose a topic which is based around “what is a gene/viral mutation and how are they cured". I am picking a topic which will dive deeper into a particular aspect of this topic rather than a broad topic. The ideas I want to research will arise from either different types of vaccine development, why viruses mutate and why variants are formed. Some of the possible questions consist of
1. Can Mutations helps us be immune to viruses
2. Can we stop virus mutations i.e Covid-19 vs the Variant version
3. Can we stop the genesis of new viruses like COVID?
4. What is a viral mutation and are we able to stop them the same way as the original virus i.e Covid 19?
5. Which vaccine is the most effective
6. Difference between influenza and covid 19

I ended up choosing the fourth one. This is because as of right now vaccines are being distributed all throughout Canada and other countries in the world. It is important to know if this vaccine is able to have the same effect on patients with original coronavirus vs the variant (both UK variant and African Variant).

The background research helps the viewer understand a little bit about gene mutation before I get into viruses and viral mutations.

Background Research:

- A gene mutation is a permanent alteration in the DNA sequence (genetic material) that makes up a gene, making it different from what is found in most people.
- It can be transmitted to the cell's or the virus’s descendants
- Mutations occur in different sizes and they can affect anywhere from a single DNA building block to multiple genes and large sections of chromosomes
- <u>Gene Mutations can be classified in two ways</u>

- **<u>Hereditary mutations:</u>** This is inherited from a person’s ancestors and is present in every cell in the body. Mutations are present in the parent’s egg or sperm cells (germ cells), which is why they are also called germline mutations. When an egg and a sperm cell unite, the fertilized egg cell receives DNA from both parents. If this DNA contains a mutation, the child that grows from the fertilized egg will have the mutation in each of their cells.
- **Acquired (or somatic) mutations**: These occur at any time in a person’s life and are not present in every cell in the body. Environmental factors are the major cause for this, for example, ultraviolet radiation from the sun, or can occur if an error is made as DNA copies

itself during cell division. Acquired mutations in somatic cells cannot be passed to the next generation.

Problem:
What is a viral mutation and are we able to stop them the same way as the original virus i.e Covid 19?
Research:
Viruses are microscopic parasites, which are even much smaller than most bacteria that lack the capacity to survive and reproduce outside of a host body. When it attaches itself to a host body (depending on the specific proteins molecules on the cell) it uses the cell to create more virions. It destroys the cell and goes into more cells, repeating the process
Viral Mutations:

- Mutations are changes to the sequence of an organism's genetic code when there is a small error in the copying process
- Mutations can alter the structure of the viral envelope and choose which organs the virus attacks for example lungs or throat and if the genetic change causes the virus to spread, it prevails. It is proven that the higher transmission rate the less likely any new mutations will add any improvement
- Viruses tend to mutate more rapidly than human cells do. This is because human cells are able to proofread the genome and also contain mechanisms that are able to repair a sequence in the genetic code if an error is found. Mutations can vary in severity from having zero consequence to completely changing a protein and its function.
- Once a mutation occurs, if it changes the function of a resulting protein and as a result, a virus or organism is then fully altered.
- Some of the reasons why Virus Mutations are increasing rapidly is due to natural selection, random genetic drift, or features of recent epidemiology.
- Viruses with RNA-based genomes (HIV) mutate faster than viruses with DNA-based genomes.
- The higher mutation rates in RNA viruses evolve faster and could evolve resistance to drugs more than DNA-based viruses
- Average mutation rates in RNA based mutations are 100 times higher than DNA based mutations
- RNA virus mutations is because of the lack of proofreading activity in polymers
- SARS-CoV-2 is changing much more slowly as it spreads compared with HIV
- In the issue of Cell, Korber et al. found that an amino acid change in the spike protein D614G quickly became common early during the pandemic and in april, viruses containing G614 are now spreading throughout the world. Korber saw the mutation appearing again and again in samples from people with COVID-19. It started off in Europe but now has spread to multiple countries like Canada, America, Australia etc. D614G is represented as a "more transmissible form of SARS-CoV-2"
- clinical samples from G614 infections have a greater level of viral RNA present

- Viruses that encode their genome in RNA, such as SARS-CoV-2, HIV and influenza, pick up mutations quicker as they are copied inside their hosts. This is because enzymes that copy RNA are more likely to make errors as mentioned earlier
- data suggests that coronaviruses transform more slowly than most other RNA viruses, most likely because of a 'proofreading' enzyme that corrects potential mistakes
- When Scientists examined clinical data from 999 COVID-19 cases diagnosed in the United Kingdom, Korber et al. (2020) came to a conclusion that patients infected with viruses containing G614 had higher levels of virus RNA, however there was no difference in hospitalization numbers.
- This variant also affected how t-cells function which have the job of killing virus-infected cells and help control the infection
- In the past and to this day, Flu or Influenza is a fast mutator and there is a new strain every year which results in yearly vaccines.
- When researchers were studying the novel coronavirus SARS-CoV-2 they came to the conclusion that the genomic mutation rate is lower than the flu. This is good as a lower mutation rate makes a vaccine effective for a longer period of time
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- **We can use antibodies as a source to cure coronavirus**
- Antibodies are laboratory made proteins that mimic the immune system's ability to fight off harmful pathogens like viruses. They latch onto surfaces of the virus and inactivate or neutralize it.
- An advantage of this is that antibodies target the SARS-CoV-2 virus because they originate in the blood of people who have fully recovered from covid 19 which makes it more effective than other drugs
- it can help those who are at high risk of severe disease because of weak immunity or a medical condition
- On Wednesday, Eli Lilly said that the combination of two antibodies, bamlanivimab and etesemivab, reduced hospitalisations and deaths in high-risk patients recently diagnosed with COVID-19 by 87 per cent in trials
- The monoclonal antibody known as VIR-7831 had an 85 per cent efficacy in reducing hospitalisation or death from Covid-19 compared to a placebo.
- However this is only effective for the original strain of coronavirus
- <u>How are they made?</u>
- First, scientists attract the relevant antibodies from human blood. Then they replicate and replicate in large quantities. Majority of monoclonal antibodies are made in Chinese hamster ovary cells which are typically grown in around 10 to 15 days. The resulting antibody is then cleaned thoroughly and packaged.
- Antibodies provide rapid protection against covid 19 infection as they enter the bloodstream straight away and offer immediate protection for a few weeks or months. This is a short term protection however antibodies provide immediate protection meanwhile vaccines take weeks to be in effect
- **<u>Vaccine:</u>**
- Vaccines are chemicals that help the body develop antibodies
- Biotech firm Moderna in Cambridge, Massachusetts, has invented an RNA-based vaccine and is expected to fight against the UK variant

- Scientists found a way to swap vaccines' old versions of the spike protein (original coronavirus) for an updated molecule that has the specific changes in amino-acid that antibody responses. But researchers are required to determine whether any such changes will change how an average person's immune system reacts to the vaccine. Another idea scientists came up with is called multivalent vaccine which consists of both new and old forms of the spike protein. However these are still being studied
- COVID-19 vaccines, including ones made by Moderna, Pfizer and AstraZeneca, instruct cells to produce the virus's spike protein (the immune system's prime target for coronaviruses). Variants carry spike mutations that alter regions targeted by neutralizing antibodies.
- For samples collected at Emory University, collection and processing were performed under approval from the University Institutional Review Board
- **Moderna and Pfizer/ BioNTech Vaccine:** These vaccines are proven to provide protection against virus variants. However it has shown a decrease in the antibody response from the South African Variant
- A study showed that 16 people who received Pfizer vaccines came into contact with 10 mutations found in B117 were easily neutralized by antibodies in the samples, keeping vaccine efficiency high for this variant. This same vaccine was ⅔ less effective against the south african variant
- Pfizer vaccine has effectively and successfully neutralized the coronavirus strain in Brazil and the UK variant as well. It has a "robust but lower" effectiveness against the South Africa variant according to the letter to the New England Journal of Medicine
- **The AstraZeneca/oxford vaccine** is said to have "minimal protection" against mild to moderate African variant cases. This means it will give protection from this variant however there is a chance one might contract it. It is only 10 percent effective against it. Studies show it is 74.6 percent effective against the UK variant
- **The Novavax vaccine** is 95.6 percent effective overall and 85.6 percent effective against B117 and 60 percent effective against the African Variant.
- Biotech firm Novavax released data from clinical trials showing that its experimental vaccine, designed for the original virus, was about 85% effective against a variant identified in the United Kingdom but 50% less effective against African Variant.

- Conclusion: The original question that I asked was diving into what viral mutation was and if we were able to stop them the same way as the original virus i.e Covid 19. I was able to fully come to a conclusion that a mutation is the change to the sequence of an organism's genetic code when there is an error in the copying process. Viruses attach themselves to a host body and use it to create more virions. This then completely destroys the cell and goes into more cells, repeating the cycle. During this process it is possible to make an error as viruses are not able to proofread the genome the same way human cells are able to. RNA based genomes mutate faster than DNA based genomes. SARS-CoV-2 is an RNA

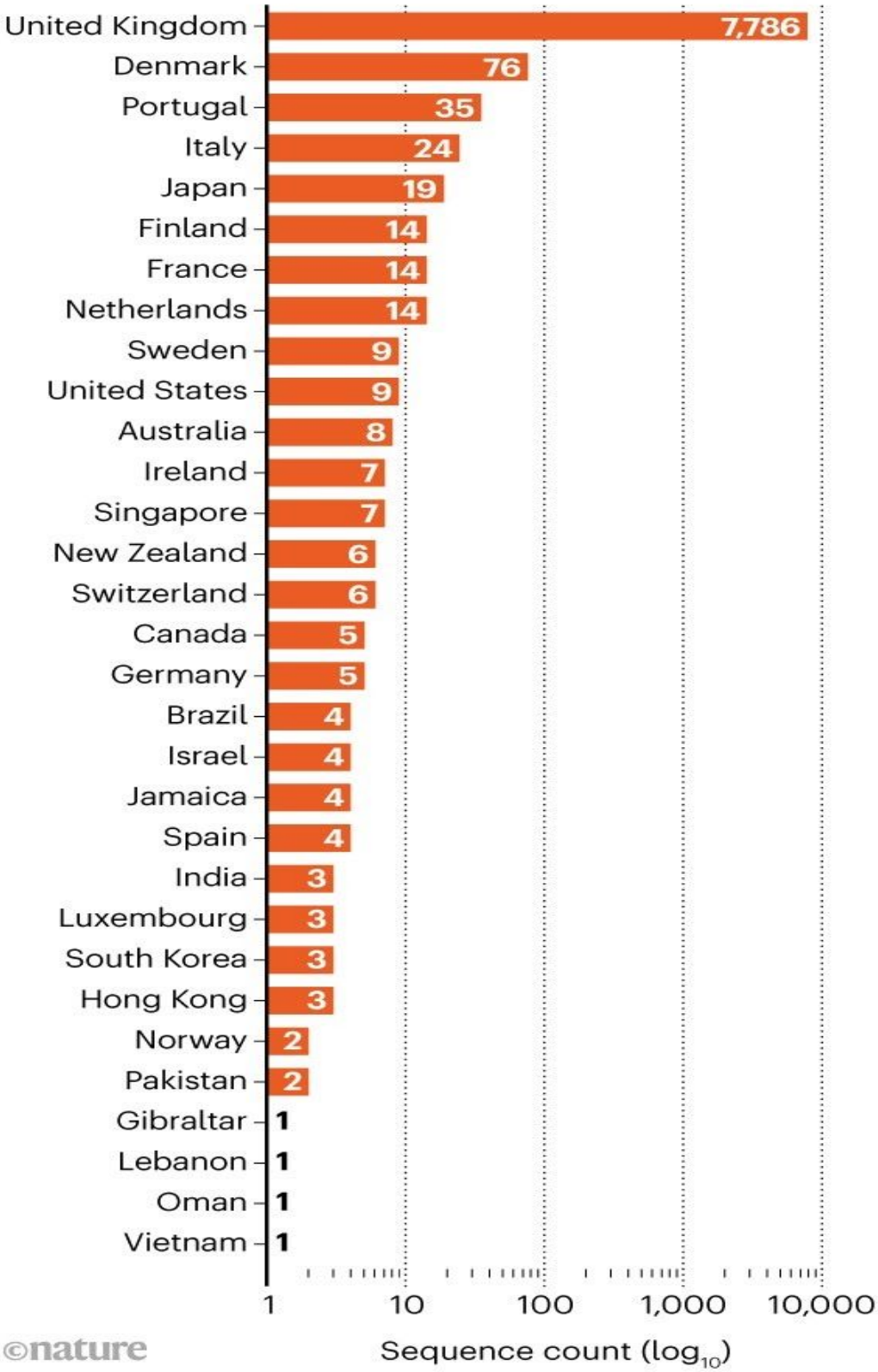
genome and picks up mutations faster. The mutated version of this virus had an even greater number of RNA. In addition to this, scientists have found ways to cure coronavirus using vaccines and antibodies. Antibodies are developed by the body's immune system to fight pathogens like viruses while vaccines are chemicals injected into the body to help it develop antibodies. However we have come to a conclusion that due to the multiple different strains of the virus, these strategies will not work the same way. Many of the vaccines were less effective especially for the African variant. Research also proves that the UK variant is affected with most of the vaccines. I have concluded that the original vaccine can be used on the variants however its effect will not be the same as the original.

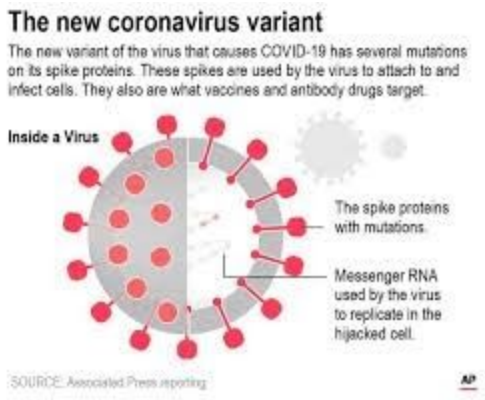
- **What's next?**

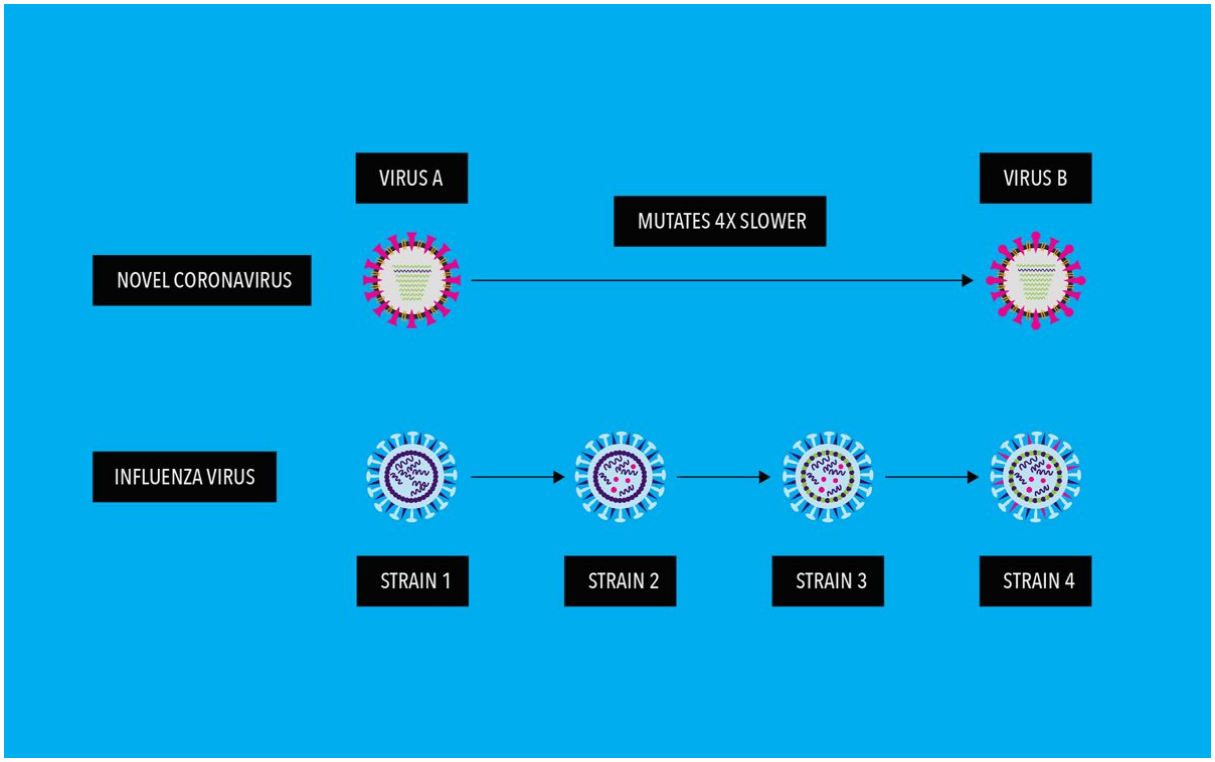
If I were researching this furth and delved deeper into this I would research more about vaccine development. I would learn more about more types of vaccines and how they are being developed by scientists.

VIRAL SEQUENCES

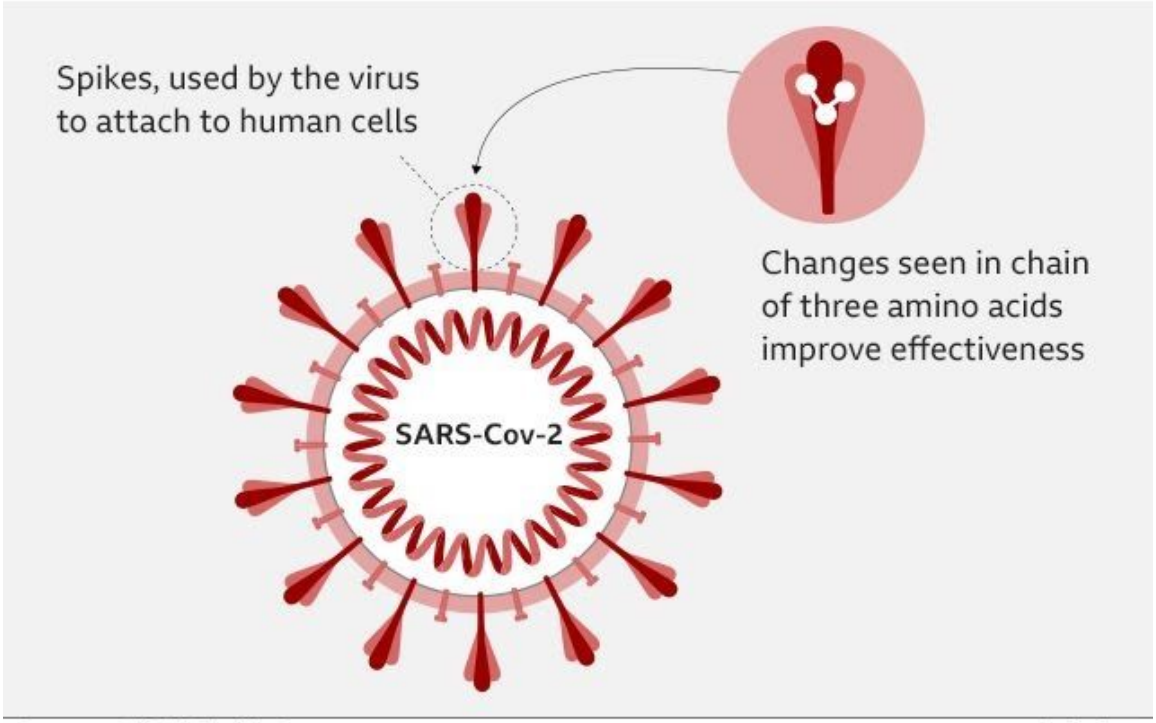
Genome-sequencing efforts are crucial to understanding how the SARS-CoV-2 coronavirus is mutating. A fast-spreading variant, called B.1.1.7, was identified by a UK-wide COVID-19 genomics effort, and 31 countries or regions have now uploaded sequence data to the GISAID website.




The new coronavirus variant
The new variant of the virus that causes COVID-19 has several mutations on its spike proteins. These spikes are used by the virus to attach to and infect cells. They also are what vaccines and antibody drugs target.
Inside a Virus
The spike proteins with mutations.
Messenger RNA used by the virus to replicate in the hijacked cell.
SOURCE: Associated Press reporting
AP


VIRUS A
VIRUS B
MUTATES 4X SLOWER
NOVEL CORONAVIRUS
INFLUENZA VIRUS
STRAIN 1
STRAIN 2
STRAIN 3
STRAIN 4

One coronavirus mutation has become dominant



Source: GISAID Initiative

BBC