TEAM YOKOVID

Geneseo COVID-19 Study Group Report IV: Zoonotic Transmission and Variants of SARS-CoV-2

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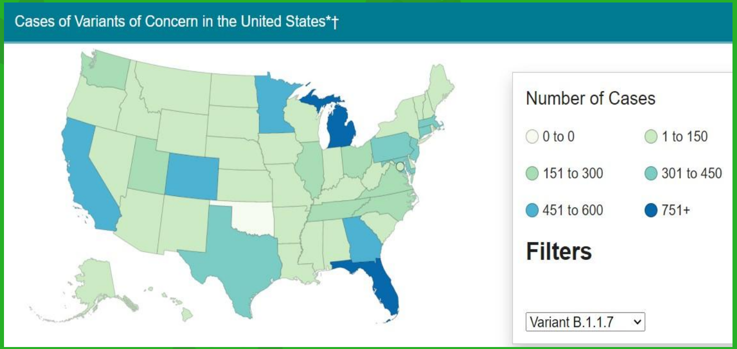
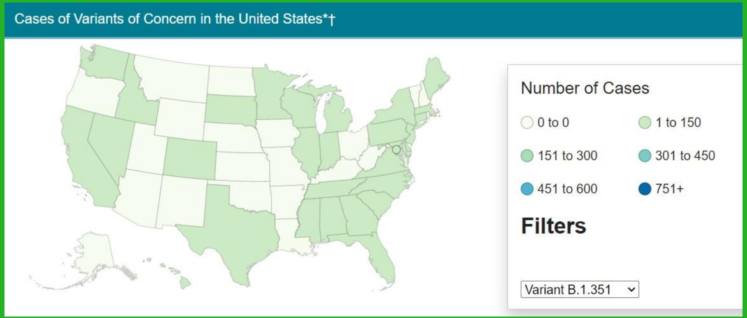


Filters

Variant B.1.1.7

This image shows the prevalence of the B.1.1.7 (UK) variant in the US as of 3/30/21



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Variant B.1.351

This image shows the prevalence of the B.1.351 (South Africa) variant in the US as of 3/30/21

Variants of COVID-19

- When a virus mutates or changes its genetic code a new strain/variant of the virus is formed. This has been seen with COVID-19, currently we know of 3 major variants, the B.1.1.7 (UK) strain, the P.1.351 (South Africa) strain, and the P.1 strain (Brazil). The data on these variants is still very limited as they are new and are currently being studied.
- Virus' mutate due to random changes in their genetic code, and these changes can happen almost anywhere and at any time. For example, the B.1.1.7 variant first identified in the UK has 17 changes to its genetic code.
- The overall consensus on these variants is that all of them are transmitted more easily, most likely due to changes of the spike protein that binds to the ACE2 receptors. This could lead to more deaths simply as a result of more infections.
- Both the South Africa and Brazil variants have shown the ability to prevent neutralization by antibodies from a previous infection, or in other words, if you previously had Covid-19 then those antibodies would not be as effective against these strains.
- The B.1.1.7 (UK) variant was first identified in the US in December 2020.

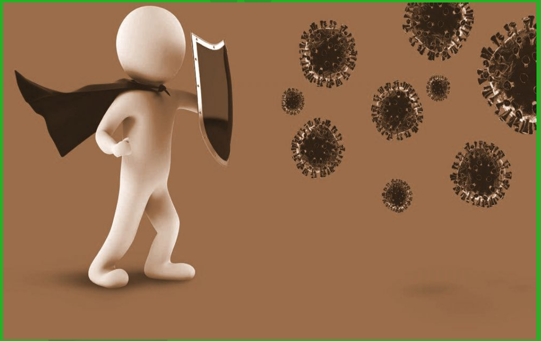
These new variants have slight effect on vaccine efficacy

What is a zoonotic disease?

A zoonotic disease is a virus, bacteria or other organism that is transmitted from animals to humans. To be classified as zoonotic, it must be able to replicate within a human. A reservoir organism is the typical organism that the zoonotic disease resides in. In most cases this is an animal. A host is an organism that does not typically harbor a particular pathogen. In most cases of zoonotic diseases the host is a human. A vector is a different organism that is able to transmit the zoonotic disease to other organisms. In most cases a vector is another animal. There is a special type of vector called an intermediate host. The intermediate host can transmit a zoonotic disease that is not developmentally mature. This zoonotic disease does not have the ability to reproduce, therefore it technically should not be considered a zoonotic disease. Intermediate hosts are also typically animals.

Zoonotic diseases are very common in new emerging diseases, but it is very difficult biologically to achieve. When exposed to new viruses from animals, human's immune systems can deter most viruses. If the virus is able to make it past the body's viral protections then most viruses are not able to replicate within a human host. Most viruses that are able to replicate are not able to replicate in numbers that are able to produce disease or eventually illness. All these factors cause a bottleneck in the viral population that has potential to become zoonotic.

Complications of a virus becoming Zoonotic



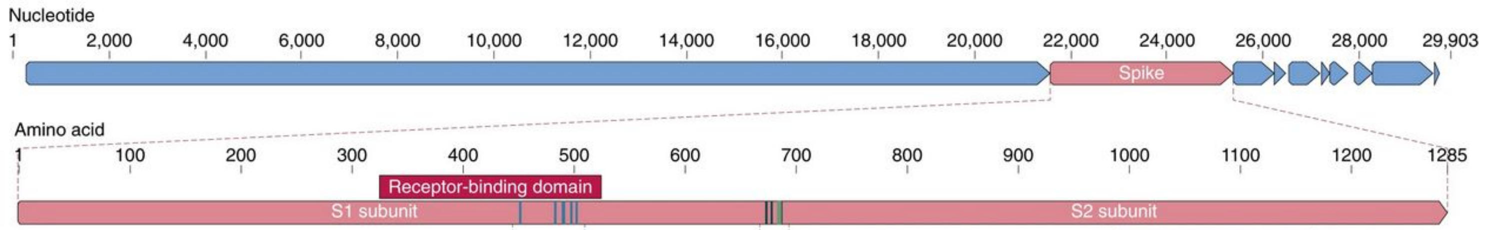
Replication of a virus is very host specific because the virus must navigate its way through hundreds of protein interactions. These interactions can be deterred by changes in pH, temperature, and even a simple change in amino acid in a single protein. The virus must be able to successfully replicate within a new host with a different environment. The virus must be able to utilize host proteins specific for replication including transcription factors, cell surface proteins, and transport proteins. If the virus is not complementary with the host's proteins or a couple mutations away from being complementary, then the virus will not be able to replicate; therefore it is not considered zoonotic.

Viruses from the *Coronaviridae* family have been historically monitored for zoonotic potential. Most viruses in the *Coronaviridae* family only require one mutation to their surface protein to be able to utilize the human ACE2 receptor. Once a virus has all required mutations to infect a host's cell it can begin to mutate and further adapt to the new environment. Humans become an alternate host when a virus becomes zoonotic. This virus can now replicate in the reservoir as well as within the host. Once the numbers of the virus increase in the first infected individual, then there is the possibility for the virus to spread to other members of the population

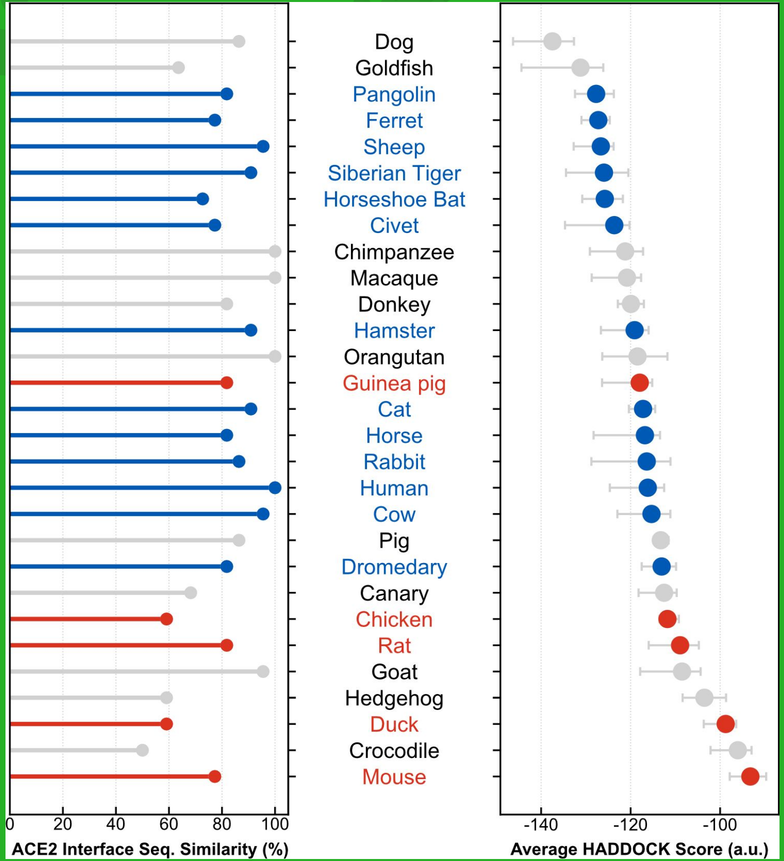
What animal did the COVID-19 virus come from?

It not a surprise that SARS-CoV-2 is responsible for the current pandemic of COVID-19. The SARS-Cov-2 virus is the seventh zoonotic virus arising from that family of viruses. There have been some claims that the virus did not come from an animal and it was made within a laboratory. The Coronaviruses have very similar homology except for a receptor binding domain (RBD) region that is more variable. This RBD is found within the spike proteins of the virus that binds with the ACE2 receptor in human cells. The RBD region on the SARS-CoV-2 virus is completely unique to the that virus. The SARS-CoV-2 binds with high affinity to the ACE2 receptors in the host cell. Computational analysis shows that this unique RBD sequence should not have a high affinity for the ACE2 receptors, but the fact that they do suggests that natural selection occurred within this virus. This is good evidence to suggest the virus was not made within a laboratory, although that could never be proven. To think of it plainly, to manufacture this virus, a laboratory would need to take the genetics from a previous organism to allow it to have a high affinity for binding, but this is not the case. The researchers found that the RBS is completely unique to anything that had been previously found.

Many of the early cases of COVID-19 were associated with a meat market in Wuhan, China. The bat species present at Wuhan market was *Rhinolophus affinis which when* genetically sequenced has 96% similar genetic code to SARS-CoV-2. The genetic codes differed within the RBD. Pangolins, *Manis javanica,* that were illegally imported into that region of China also were proposed as a reservoir. The genetic code of *Rhinolophus affinis* are very homologous, but it is missing a polybasic cleavage site sequence unique to SARS-CoV-2. It is possible that either of these species could be an intermediate host for the virus. The exact reservoir organism is unknown.



The first line represents the entire genetic sequencing of the SARS-CoV-2 virus. The pink region is what encodes for the spike proteins which includes the RBD region. The second line is a magnification of the spike protein region. As you can see by the five vertical lines within S1 subunit, most mutations occur within the RBD.



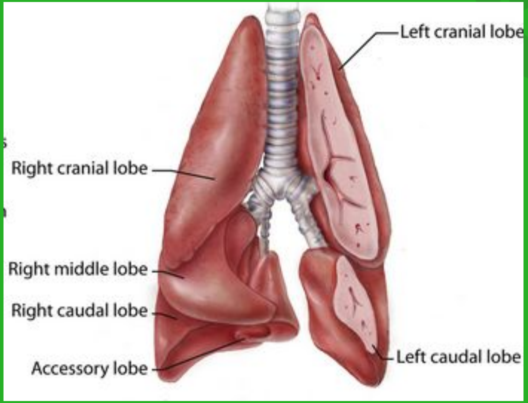
A HADDOCK score ranks the molecule interactions between proteins, therefore binding affinity. Species shown in red have low binding affinity, Species in blue have higher binding affinity, and species in black need to undergo more testing.

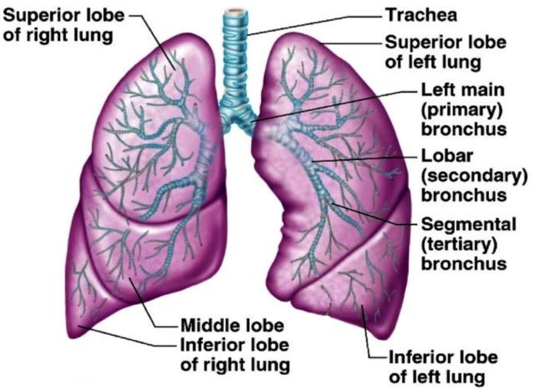
Can our pets get COVID-19?

As of March, animals play an insignificant role in spreading SARS-CoV-2 to people. As previously mentioned, it is likely that either a pangolin or a bat initiated the spread of SARS-CoV-2 to people. Those who are concerned that they themselves may have COVID-19, should refrain from having contact with animals, both domestic and wild. This is due to the few cases that have occurred in animals. As mentioned, the high binding affinity for SARS-CoV-2 to our ACE2 receptor is responsible for Covid-19 infections in our bodies. In other species, this is also the case. We can attribute the infections found in animals to the ability for their ACE2 receptor to bind to SARS-CoV-2 leading to COVID-19 cases being documented in a few animals. Using an ELISA assay and RNA analysis the presence of SARS-CoV-2 in the animal hosts was evaluated. It has been found that cats, civets, camels, horses, sheep and rabbits can be infected with COVID-19 as their ACE2 receptors bind to the virus very similarly to ours in a laboratory setting. Though there have been a few cases of COVID-19 occurring in dogs, and this is still being evaluated to determine why. While these dogs can have symptoms when infected, their ACE2 receptors bind with a weaker affinity to SARS-CoV-2, making them a less suitable host for the virus. This means that while dogs may shed the virus, they are far less likely to spread it. Animals such as pigs, chickens, mice, guinea pigs and ducks do not have ACE2 receptors that bind well to the virus and as such, they have not been shown to contract the virus in a laboratory setting. As such, it is very possible that domestic animals can become infected with SARS-CoV-2, though how they affect the transmission to humans is still under review.

What animals have been infected?

There have been minimal positive dogs and cat cases (U.S. - 67 cats, 47 dogs) as of february. Various minks and one ferret did contract Covid-19. Ferrets are often used as animal models for respiratory diseases seen in animals because their anatomy is similar. Ferrets are often recipients of viral diseases such as the common flu that their owners contract and pass on. Additionally, several large animals, including lions, tigers, pumas, snow leopards and gorillas in zoos have contracted Covid-19 from humans and displayed symptoms. Unfortunately, there is no cure for these animals, and the only care that can be provided is palliative care and quarantine.





Ferret lungs(above) and human lungs (below) have the same number of lung lobes as well as main bronchial patterns.

This project is a part of an outreach project to thank the Geneseo community for making Geneseo such a great place. This will be reproduced as part of a booklet that will be provided for the community to promote science. We would appreciate any feedback on our poster!

Citations

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