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Literature Review of COVID-19 Biochemistry

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Introduction

Coronaviruses (CoVs) are viruses with a single-strand, positive-sense RNA genome that is approximately 30 kilobases, the largest known RNA virus genome.
The genome of SARS-CoV-2, the virus responsible for the current pandemic, contains 82% nucleotide identity with human SARS-CoV, and 88% nucleotide identity with 2 bat derived SARS-like coronaviruses. Therefore the virus is thought to have originated in bats but transmitted to humans through some intermediate mammal. Human SARS-CoV-2 was sequenced against the Pangolin-CoV virus to determine whether the pangolin could be the intermediate for human SARS-CoV-2, however the bat CoV was more similar to human SARS-CoV-2 than Pangolin-CoV. Human SARS-CoV-2 was also shown to have a unique peptide sequence insertion that the Pangolin-CoV does not share. Therefore, human SARS-CoV-2's intermediate host is still unknown.

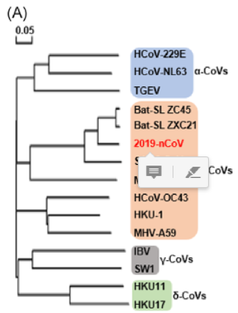


Figure 1: Current phylogenetic tree for known coronaviruses
Y. Chen, Q. Liu and D. Guo, "Emerging coronaviruses: Genome structure, replication, and pathogenesis," Journal of Medical Virology, vol. 92, no. 4, pp. 418-423, 2020.

SARS-CoV-2, like SARS-CoV, enters T lymphocytes using its spike protein to interact with the human angiotension-converting enzyme 2 (ACE2) as its receptor. SARS-CoV-2 was found to have a unique peptide sequence that could contribute to the proteolytic cleavage of the spike protein, therefore potentially impacting host range and transmissibility. In previous research of SARS-CoV, it was found that in order for the virus to enter a host cell, an endocytic, protease-primed cleavage event must occur. This is different from most coronavirus fusion proteins in that most are primed during assembly of the virus or upon release from the cell.

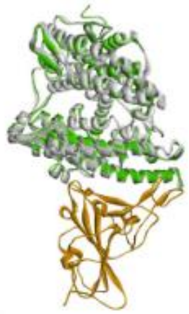
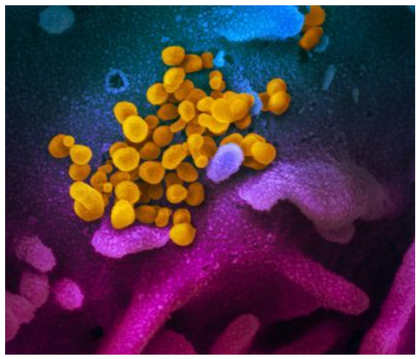


Figure 2: Docking conformation of SARS-CoV-2 spike protein (gold) with wild-type ACE2 (green) and its allelic variants (gray)
M. Hussain, N. Jabeen, F. Raza, S. Shabbir, B. A. A., A. Amanullah and B. Aziz, "Structural variations in human ACE2 may influence its binding with SARS-CoV-2 spike protein," Journal of Medical Virology, pp. 1-7, 2020.

Introduction Continued

Though human coronavirus infections generally involve the upper respiratory tract, SARS-CoV-2 patients do not tend to show prominent upper respiratory tract symptoms, indicating that SARS-CoV-2 target cells are in the lower respiratory tract. The most common symptoms of COVID-19 appear to be fever, cough, and fatigue, with pneumonia often developing as well. The virus has been found to be primarily transmitted through person-to-person contact, particularly through those that are infected, but asymptomatic.

Patients with SARS-CoV-2 test positive, starting from the onset of symptoms, for a median of 16 days, with 26.3% testing positive after 4 weeks. This indicates that the viral replication in SARS-CoV-2 has a relatively long period compared to that of SARS-CoV. Studies also show that SARS-CoV-2 can be detected in the fecal matter of a recovered patient up to 10 days after the nasal test comes back negative, indicating the patient can stay contagious longer than originally thought.



Scanning electron microscope image of SARS-CoV-2 (yellow) emerging from cells (blue and pink)

https://www.niaid.nih.gov/news-events/novel-coronavirus-sarscov2-images

Diagnosis

The most common means of diagnosis for COVID-19 is real time quantitative polymerase chain reaction, or RT-qPCR using a nasal swab. Unfortunately, the sensitivity of RT-qPCR is only 50%-79%, meaning there are quite a few false negatives. Chest CT scans are far more sensitive for diagnosis of COVID-19, however they also come with shortcomings such as not being able to distinguish between COVID-19 or some other viral pneumonia. ELISA kits are also being developed by some companies and studies show that the ELISA is much more sensitive than RT-qPCR as well, but they are still being tested.

Potential Treatments

One theory on a treatment for COVID-19 is angiotension-converting enzyme inhibitors (ACE inhibitors). ACE inhibitors block ACE2 receptors, which could protect against a SARS-CoV-2 infection. ACE inhibitors have both pros and cons, however. For example, ACE inhibitors inhibit ACE which leads to decreased angiotension I levels. This can cause a negative feedback loop which would ultimately increase ACE2 receptors, leading to more binding sites for the SARS-CoV-2 virus.
Some argue, however, that ACE inhibitors are beneficial. Some arguments are that the stimulation of negative feedback in ACE would reduce inflammation, while some argue that ACE inhibitors impair the ACE receptor pathway, making it harder for SARS-CoV-2 to bind to the receptor.
Another study showed no detectable difference in the virus progression between those treated with ACE inhibitors and those not treated with ACE inhibitors.

Another potential treatment that has been explored is the binding affinity of 27 ligands occurring naturally in many cuisines to SARS-CoV-2 proteases. If any bind successfully, they could potentially prevent the virus from replicating. This study found that 15 of the 27 ligands were successful in binding to the viral proteases and therefore successful in hindering viral replication. More research would need to be done to recommend these natural ligands as a viral treatment, but the preliminary research was positive.

Antibody Testing

A blood test for SARS-CoV-2 specific antibodies would be simple, rapid, and sensitive option for diagnosis of COVID-19 as well as determining if one has been exposed to the virus and has been able to develop the antibodies to the virus. IgM can be detected in the blood 3-6 days after exposure to SARS-CoV, and IgG can be detected after 8 days. Since SARS-CoV-2 is so similar to SARS-CoV, a SARS-CoV-2 IgG-IgM combined antibody test was developed under the assumption that SARS-CoV-2 follows the same pattern. The combined IgG-IgM test also allows for widespread testing for asymptomatic carriers.

Conclusion

SARS-CoV-2 is the virus responsible for the current COVID-19 pandemic. SARS-CoV-2 is a betacoronavirus with a genome that is 82% identical to SARS-CoV. The virus enters T lymphocytes using its spike protein with the human angiotension-converting enzyme 2 as its receptor. COVID-19 is diagnosed through a nasal swab SARS-CoV-2 RT-PCR assay and the most common symptoms appear to be fever, cough, and fatigue. The median amount of time an individual will be contagious with the virus is 16 days. Many possible treatment methods have been explored including a SARS-CoV-2 specific antibody that could be potentially therapeutic against the virus, natural remedies, and ACE inhibitors. There are also IgM-IgG tests being developed that detect the antibodies against SARS-CoV-2 virus in the blood that could help determine transmission of the virus in the population as well as lead to more rapid, sensitive diagnosis.

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