The Race to Drug Discovery for COVID-19 treatments



Image Source

As 2020 comes to an end, let's reflect this year. Three months into 2020, we did not imagine a pandemic would happen. The pandemic led to mandatory mask wearing, school closures, lost jobs, and employee furloughs. Work and school was moved online. Gatherings were hosted in small groups. The pandemic challenged us emotionally, socially, financially but through these tough times brings resiliency.

The last reported pandemic caused by a respiratory virus was the H1N1 virus in 2009. The H1N1 virus was a type of influenza virus; patients experienced chills, fever, nasal secretions, low appetite, and low respiratory tract disease. Adults under 60 including children, young and middle aged adults were at high risk of infection. Some adults over 60 carried the antibodies from previous exposure to another version of the H1N1 virus. Between April 12, 2009 to April 10, 2010, there were nearly 60.8 million cases and 13 thousand deaths.



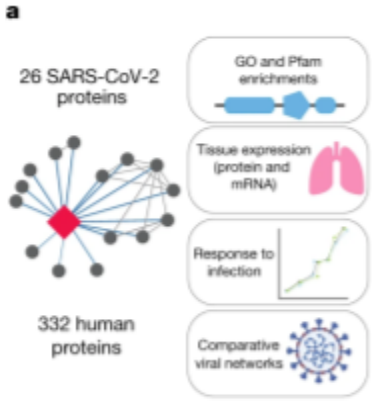
Global Spread of the COVID-19 pandemic as of December 14, 2020.
Source: John Hopkins Coronavirus Resource Center

On January 4th, 2020, the World Health Organization (WHO) reported a high number of pneumonia cases in Wuhan and the cause was unknown. Five days later, the WHO was informed the influx of pneumonia cases was caused by a novel coronavirus. At the time, little was known about the novel coronavirus and medical professionals only knew patients were experiencing severe respiratory problems like

pneumonia. Questions about how the disease was transmitted and what symptoms should be broadcasted to the public were still uncertain as scientists were still understanding about the novel coronavirus.

On January 21, the Chinese National Health Commission reports increased cases and the disease is transmitted from person to person. The Chinese government enforced a lockdown in Wuhan on January 23. The lockdown involved travel transactions within the area, but international flights were still allowed. As the number of cases and death tolls increase, global efforts are seeking to reduce the spread of COVID-19. Some policies may include travel restrictions, mask mandates, and accessibility to handwashing or disinfectants.

On March 11, 2020, WHO recognized SARS CoV-2 as a pandemic because at this point, SARS CoV-2 had over 118,000 cases in 114 countries. The first COVID-19 case in the US was reported on February 26 and 28. On March 13, the US declared that SARS CoV-2 was a "national emergency" since the virus was spreading like wildfire and a shutdown was in place to reduce the spread of the disease. During the shutdown, people were told to stay at home, classes and some jobs moved online, and our daily lives shifted mostly indoors; however, essential workers continued to work during the pandemic. The pandemic severely restricted travel, ordered mask wearing, and experienced medical supply shortages. The shutdown lasted two to three months depending on state reopening decisions.



General outline of the study published by published by Dr. David E. Gordon and colleagues on April 20, 2020 revealing important proteins and pathways the SARS CoV-2 interacts with for further research in drug repurposing treatments for SARS CoV-2.
Source:https://media.springernature.com/full/springer-static/image/art%3A10.1038%2Fs41586-020-2286-9/MediaObjects/41586_2020_2286_Fig3_HTML.png?as=webp

How does the novel coronavirus infect its host? The novel coronavirus is a virus and viruses are like small parasites because viruses depend on the host's cells to survive. The virus enters the host in different parts of the body and hijacks the cell by manipulating the cell's proteins to reproduce, survive, all without alerting the immune system's emergency response. Scientists can identify which proteins SARS CoV-2 interacts with by sequencing the DNA of COVID-19 infected cells.

In a study published in Nature, " A SARS-CoV-2 protein interaction map reveals targets for drug repurposing," Gordon and colleagues showed that SARS CoV-2 interacts with over 332 proteins in the host. These protein interactions suggest SARS CoV-2 regulates a number of different host cell functions and helps identify how the virus affects the host at the cellular level.

SARS CoV-2 predominantly attacks cells in the lung tissue and is why the novel coronavirus symptoms impact the respiratory system. For SARS CoV-2 to survive and proliferate in the host's cells, SARS CoV-2 regulates protein regulated pathways that control vesicle transport, immune signal proteins, nuclear transport, and the protein degradation pathways. By regulating vesicle transport, the bus that carries important proteins and signals to other cells or inside the

cell organelles, SARS CoV-2 is undetected by the immune system. SARS CoV-2 wants to regulate immune signal proteins so that the immune system does not attack the virus. SARS CoV-2 regulates the export proteins out the nucleus in order for the virus to transport its DNA to replicate in more host cells. Lastly, SARS CoV-2 regulates the degradation of proteins to prevent the accumulation of unnecessary proteins. SARS CoV-2 requires regulating a bunch of the host's proteins to survive.

In the same study, Gordon and his colleagues searched for which drugs kill or reduce virus activity based on 37 compounds. Gordon and his colleagues found two mechanisms that were effective in reducing antiviral activity. One mechanism involves repressing the reading of mRNA, a single stranded nucleic acid that carries information from DNA to instruct proteins. The second mechanism involves changing in the binding complex of two important cell receptors: sigma 1 and 2 which makes the virus undergo a bunch of mechanisms and signals cell stress to alert the immune system. In total, there were 69 drugs found to work in either of these mechanisms one of which was in a clinical trial: Remdesiver.

Drugs are commonly marketed for a particular purpose, but the current drugs on market could treat other diseases, also known as drug repurposing. One example is sildenafil, commonly known as Viagra, is used to treat erectile dysfunction but is now also used to treat high blood pressure because one of sildenafil's side effects is it increases blood vessels allowing better blood flow. Drug repurposing can save money for patients to get more accessible treatments and making new drugs can cost up to $10 million to $2 billion and may take at least 10 years for the drug to reach the market.

During March, there was no specific COVID-19 treatment and many treatments are experimental. Since March, the CDC has listed a few drugs that are used to treat COVID-19 depending on doctor's orders. Remdesivir is an FDA approved drug to treat COVID-19 and slows the spread and reproduction of the virus. For patients with a severe case of COVID-19, patients are given Dexamethasone which reduces the high immune response against COVID-19 to "prevent or reduce injury to the body of hospitalized patients."

Since March, treatment and our understanding of the virus has come a long way and the long-awaited vaccine was first administered in the UK to a 91 year old woman on December 8th. The approved vaccine was made by Pfizer and has a 95% efficacy rate. In the making of the vaccine, Drug repurposing provided possible drug treatment, Remdesiver, to COVID-19 patients to alleviate their symptoms while a vaccine or a new effective drug treatment is proposed.



Pfizer vaccine was found to have a 95% efficacy and was administered to the first recipient on December 8th. Source: https://news.usc.edu/files/2020/11/covid-vaccine-web-824x549.jpg

As 2020 comes to an end, we are still learning more about SARS CoV-2, but within one year since the disease was discovered, scientists have established better approaches to treat the disease.