NIH Director's Blog

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Structural Biology Points Way to Coronavirus Vaccine

Posted on March 3rd, 2020 by Dr. Francis Collins

Caption: Atomic-level structure of the spike protein of the virus that causes COVID-19.
Credit: McLellan Lab, University of Texas at Austin

The recent COVID-19 outbreak of a novel type of coronavirus that began in China has prompted a massive global effort to contain and slow its spread. Despite those efforts, over the last month the virus has begun circulating outside of China in multiple countries and territories.

Cases have now appeared in the United States involving some affected individuals who haven't traveled recently outside the country. They also have had no known contact with others who have recently arrived from China or other countries where the virus is spreading. The NIH and other U.S. public health agencies stand on high alert and have mobilized needed resources to help not only in its containment, but in the development of life-saving interventions.

On the treatment and prevention front, some encouraging news was recently reported. In record time, an NIH-funded team of researchers has created the first atomic-scale map of a promising protein target for vaccine development [1]. This is the so-called spike protein on the new coronavirus that causes COVID-19. As shown above, a portion of this spiky surface appendage

(green) allows the virus to bind a receptor on human cells, causing other portions of the spike to fuse the viral and human cell membranes. This process is needed for the virus to gain entry into cells and infect them.

Preclinical studies in mice of a candidate vaccine based on this spike protein are already underway at NIH's Vaccine Research Center (VRC), part of the National Institute of Allergy and Infectious Diseases (NIAID). An early-stage phase I clinical trial of this vaccine in people is expected to begin within weeks. But there will be many more steps after that to test safety and efficacy, and then to scale up to produce millions of doses. Even though this timetable will potentially break all previous speed records, a safe and effective vaccine will take at least another year to be ready for widespread deployment.

Coronaviruses are a large family of viruses, including some that cause "the common cold" in healthy humans. In fact, these viruses are found throughout the world and account for up to 30 percent of upper respiratory tract infections in adults.

This outbreak of COVID-19 marks the third time in recent years that a coronavirus has emerged to cause severe disease and death in some people. Earlier coronavirus outbreaks included SARS (severe acute respiratory syndrome), which emerged in late 2002 and disappeared two years later, and MERS (Middle East respiratory syndrome), which emerged in 2012 and continues to affect people in small numbers.

Soon after COVID-19 emerged, the new coronavirus, which is closely related to SARS, was recognized as its cause. NIH-funded researchers including Jason McLellan, an alumnus of the VRC and now at The University of Texas at Austin, were ready. They'd been studying coronaviruses in collaboration with NIAID investigators for years, with special attention to the spike proteins.

Just two weeks after Chinese scientists reported the first genome sequence of the virus [2], McLellan and his colleagues designed and produced samples of its spike protein. Importantly, his team had earlier developed a method to lock coronavirus spike proteins into a shape that makes them both easier to analyze structurally via the high-resolution imaging tool cryo-electron microscopy and to use in vaccine development efforts.

After locking the spike protein in the shape it takes before fusing with a human cell to infect it, the researchers reconstructed its atomic-scale 3D structural map in just 12 days. Their results, published in *Science*, confirm that the spike protein on the virus that causes COVID-19 is quite similar to that of its close relative, the SARS virus. It also appears to bind human cells more tightly than the SARS virus, which may help to explain why the new coronavirus appears to spread more easily from person to person, mainly by respiratory transmission.

McLellan's team and his NIAID VRC counterparts also plan to use the stabilized spike protein as a probe to isolate naturally produced antibodies from people who've recovered from COVID-19. Such antibodies might form the basis of a treatment for people who've been exposed to the virus, such as health care workers.

The NIAID is now working with the biotechnology company Moderna, Cambridge, MA, to use the latest findings to develop a vaccine candidate using messenger RNA (mRNA), molecules that serve as templates for making proteins. The goal is to direct the body to produce a spike protein in such a way to elicit an immune response and the production of antibodies. An early clinical trial of the vaccine in people is expected to begin in the coming weeks. Other vaccine candidates are also in preclinical development.

Meanwhile, the first clinical trial in the U.S. to evaluate an experimental treatment for COVID-19 is already underway at the University of Nebraska Medical Center's biocontainment unit [3]. The NIH-sponsored trial will evaluate the safety and efficacy of the experimental antiviral drug remdesivir in hospitalized adults diagnosed with COVID-19. The first participant is an American who was repatriated after being quarantined on the Diamond Princess cruise ship in Japan.

As noted, the risk of contracting COVID-19 in the United States is currently low, but the situation is changing rapidly. One of the features that makes the virus so challenging to stay in front of is its long latency period before the characteristic flu-like fever, cough, and shortness of breath manifest. In fact, people infected with the virus may not show any symptoms for up to two weeks, allowing them to pass it on to others in the meantime. You can track the reported cases in the United States on the Centers for Disease Control and Prevention's website.

As the outbreak continues over the coming weeks and months, you can be certain that NIH and other U.S. public health organizations are working at full speed to understand this virus and to develop better diagnostics, treatments, and vaccines.

References:

[1] Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, Graham BS, McLellan JS. Science. 2020 Feb 19.

[2] A new coronavirus associated with human respiratory disease in China. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Hu Y, Tao ZW, Tian JH, Pei YY, Yuan ML, Zhang YL, Dai FH, Liu Y, Wang QM, Zheng JJ, Xu L, Holmes EC, Zhang YZ. Nature. 2020 Feb 3.

[3] NIH clinical trial of remdesivir to treat COVID-19 begins. NIH News Release. Feb 25, 2020.

Links:

Coronaviruses (National Institute of Allergy and Infectious Diseases/NIH)

Coronavirus (COVID-19) (NIAID)

Coronavirus Disease 2019 (Centers for Disease Control and Prevention, Atlanta)

NIH Support: National Institute of Allergy and Infectious Diseases

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74 Comments

Linda Robinson **says:**
March 29, 2020 at 5:29 pm
Is there any chance that the corona virus we are now fighting is somehow related to nutrition? I know it sounds ridiculously simple. But if you study over the country's around the world, those having very large increase, and the ones very low. It almost seems it's not wreking havoc as much on countries that rely on a diet of rice, chicken, pork. Not nearly as much gluten as countries that rely on wheat (pasta) meals. Gluten is known to produce inflammation in the gut where our resistance begins. I know, the pandemic started in China. . . Rice capital? But it only began there. . . If it had been contained there, well I guess we'll never know because it wasn't contained. Ok. But just at least LOOK at the data and groups of countries. There may be something there. . .

Reply

John Hasty **says:**
March 30, 2020 at 5:43 am
Long term good health and a strong immune system is related to diet. People with a strong immune system will naturally handle an infection better. The problem is when a person who can handle the infection runs around town coming in contact with people with weaker immunity.

Reply

Yonis **says:**
March 30, 2020 at 9:12 am
I think that probably should be a good idea to practice with cell from animals that have high ratio of regeneration, combining them and use it against the covid19. We have to try everything.

Reply

Wayne Johnson **says:**
April 5, 2020 at 9:22 pm

That sounds reasonable Linda. Italy,spain, United states, France, Germany have a high intake of gluten and sugary junk food. Vietnam, Singapore, Taiwan,China,more rice and chicken,pork and veges.
And low death rates considering China eats bat meat.

Reply

Juan Carlos Manay **says:**
March 29, 2020 at 6:25 pm
I was thinking that sometimes Nature has its particularly ways.. since the COVID19 has now the possibility of infected animals; why not infect the bat where originally exists. Since it is the same virus but modified, we could use the immunology system of the bat to get the antibody for the COVID 19.
Where the disease was born, the solution could also be found.

Reply

Yonis **says:**
April 16, 2020 at 9:54 am
We have to think that bats are the same as rats. The urine or feces of these small rodents can infect us with unthinkable diseases for example, touching a dead mouse or bat can bring health problems, eating these animals is a risk and is even greater if the meat that was eaten was poorly undercooked or not properly cleaned.

Some of the diseases caused by rodents and probably bats are:

1. Tularemia.

2.Hantavirus.

3. Leptospirosis.

4. Teniasis.

5. Trichinosis.

6. Toxoplasmosis.

Most of them have treatment and clinical manifestations are similar or almost the same to covid19.

The treatment for tularemia is: streptomycin. It can also be treated with quinolones, gentamicin, tetracyclines, or chloramphenicol.
Please find more information about the diseases that I have shown and use it against covid19. I hope this information will help.

Reply

Mike Nuccio **says:**
March 30, 2020 at 3:07 pm
In the research, are we looking into oral or nasal inhalation as route for current (and future) antivirals? Plenty of previous studies with influenza.

Reply

sumith tito **says:**
March 31, 2020 at 12:11 am
try a mixture of turmeric and dry ginger power and u can chew raw ginger so that the sulphur group is not destroyed…

Reply

Saadullah **says:**
March 31, 2020 at 8:23 am
I think in.my own way
If reaserchers do that thing
If we combain sliymarin with chloroquin for treatment
Vaccine (combien blood plazma who recover from covid 19 pateints with silymarin.chloroquin and vitamins

Reply

Kerry B. **says:**
March 31, 2020 at 6:21 pm
Any chance breast milk containing antibodies would help? As a hospital nurse with a breastfed infant, I feel like an untapped resource.

Reply

Juan Carlos Manay **says:**
April 2, 2020 at 9:35 pm
Since COVID 19 has an affinity for ACE, how about using a medication that blocks its substrate well above the chain (angiotensinogen to angiotensin I), that is using aliskiren. Wouldn't I reduce the expressión of ACE and thus the site of binding of COVID19.

Reply

Vic Vorobieff **says:**

April 4, 2020 at 10:01 pm
The UK "The Times" newspaper of April 4, 2020, reports that once the coronavirus enters our body, our immune system develops antibodies to kill the virus and in some/most instances it succeeds and the infected person continues to live.
I am curious as to what happens to the carcass of the dead coronavirus and namely, does it remain in the body or does the body eject it by expiration, urination and/or defecation?

Secondly, there is a World Health Organisation (WHO) poster that shows COVID-19 droplets (subsequent to coughing, sneezing, etc) have a longevity lasting from 3 hours in the air, 4 hours on copper surfaces, 24 hours on carboard food containers and up 9 days on glass and mobile phones.
Government and health authorities informs us that we should use soap and water or an alcohol-based sanitizer/disinfectant to kill the COVID-19 droplets; (and I have been following such advice). However, we do not regularly wash/sanitise our air, disposed food containers and mobile phones.
But what happens when these exhaled droplets are released in the wild (ie bush land or farm lands). How does nature kill these droplets; and namely, is it through sunlight (ultraviolet light), or heat or cold or moisture (ie water) or is soil and flora poisonous to it?

Reply

***HERIEL E* says:**
April 7, 2020 at 1:49 pm
There are ideas from those who know about medical issue from different places in the world, can NIH support and working with these ideas and with those who provides their comments ?? Because I have more reasonable and suggestions of drugs which it can help prevent COVID19 ,those drugs are in the following groups first in immune system booster drugs, corticosteroids,and antibiotics,, I will cooperate if there is chance.

Reply

***Maureen Grey* says:**
April 9, 2020 at 8:30 am
Has anyone looked into the Ultraviolet Irradiation of Blood as a treatment?
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6122858/

Reply

***Katherine* says:**
April 11, 2020 at 7:45 am
I will continue to research this issue but had a question regarding the antibody test. Could patients having autoimmune issues be candidates in vaccines development.

Reply

Aguilar Rodarte Orlando **says:**
April 16, 2020 at 10:11 am
What kind of information could provide the genome of people infected with Covid-19??

Reply

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Francis S. Collins, M.D., Ph.D.

Appointed the 16th Director of NIH by President Barack Obama and confirmed by the Senate. He was sworn in on August 17, 2009. On June 6, 2017. President Donald Trump announced his selection of Dr. Collins to continue to serve as the NIH Director.

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I'm often asked what people can do to help combat #COVID19. If you've recovered from documented infection, your pla… https://t.co/zVZJQghzGK **3 hours ago**

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