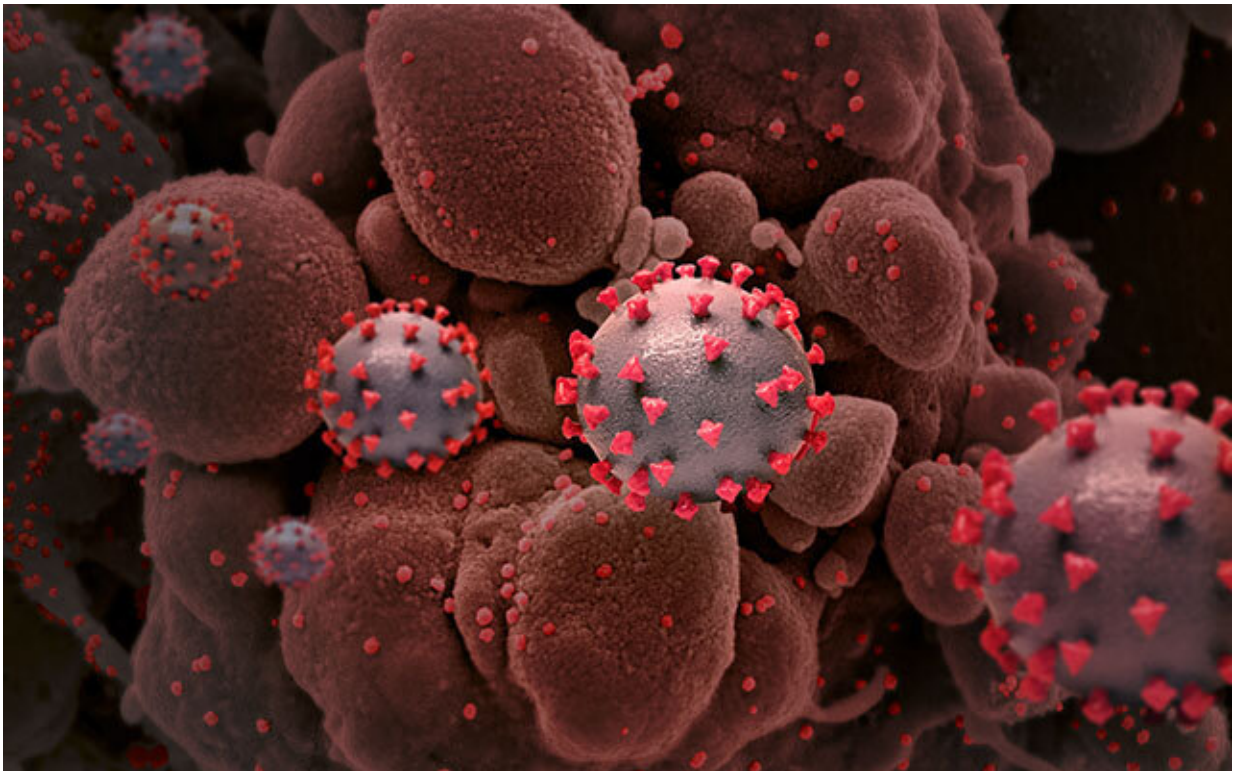


Existing drug is shown to inhibit SARS-CoV-2 virus

July 21 2021, by Emily Ayshford



Creative rendition of SARS-CoV-2 particles (not to scale). Credit: National Institute of Allergy and Infectious Diseases, NIH

A new University of Chicago study has found that the drug masitinib may be effective in treating COVID-19.

The [drug](#), which has undergone several [clinical trials](#) for human conditions but has not yet received approval to treat humans, inhibited the replication of SARS-CoV-2 in human [cell cultures](#) and in a mouse model, leading to much lower viral loads.

Researchers at UChicago's Pritzker School of Molecular Engineering (PME), working with collaborators at Argonne National Laboratory and around the world, also found that the drug could be effective against many types of coronaviruses and picornaviruses. Because of the way it inhibits replication, it has also been shown to remain effective in the face of COVID-19 variants.

"Inhibitors of the main protease of SARS-CoV-2, like masitinib, could be a new potential way to treat COVID patients, especially in early stages of the disease," said Prof. Savas Tay, who led the research.

"COVID-19 will likely be with us for many years, and novel coronaviruses will continue to arise. Finding existing drugs that have antiviral properties can be an essential part of treating these diseases."

The results were published July 20 in *Science*.

A race to find COVID-19 treatments

When COVID-19 lockdowns began in March 2020, Tay and Nir Drayman, a postdoctoral fellow who specializes in virology, began to think about how they could help. To search for a better treatment for the disease, they began by screening a library of 1,900 clinically safe drugs against OC43, a coronavirus that causes the common cold and can be studied under regular biosafety conditions. They used cell cultures to determine the drugs' effect on infection.

They then gave the top 30 [drug candidates](#) to microbiology professor Glenn Randall, who tested them in cell cultures against the SARS-CoV-2

virus at the Howard Taylor Ricketts Laboratory, a BSL-3 facility at Argonne National Laboratory. Measurements in the high-containment lab revealed nearly 20 drugs that inhibit SARS-CoV-2.

They also sent the drug candidates to other collaborators to test against the 3CL protease, the enzyme within coronaviruses that allows them to replicate inside a cell. They found that of the drug candidates, masitinib completely inhibited the 3CL viral enzyme inside the cell, a fact that was confirmed by X-ray crystallography by Prof. Andrzej Jaochimaik's group at Argonne. The drug specifically binds to the 3CL protease active site and inhibits further viral replication.

"That gave us a strong indication of how this drug works, and we became confident that it has a chance to work in humans," Drayman said.

Though masitinib is currently only approved to treat mast cell tumors in dogs, it has undergone human clinical trials for several diseases, including melanoma, Alzheimer's disease, multiple sclerosis, and asthma. It has been shown to be safe in humans but does cause side effects, including gastrointestinal disorders and edema, and could potentially raise a patient's risk for heart disease.

Drug effective against variants, other viruses

Next, the researchers worked with peers at the University of Louisville to test the drug in a mouse model. They found that it reduced the SARS-CoV-2 viral load by more than 99 percent and reduced inflammatory cytokine levels in mice.

In parallel, the researchers also began to test the drug in cell cultures against other viruses and found that it was also effective against picornaviruses, which include Hepatitis A, polio, and rhinoviruses that cause the common cold.

They also tested it in cell cultures against three SARS-CoV-2 variants, Alpha, Beta, and Gamma, and found that it worked equally well against them, since it binds to the protease and not to the surface of the virus.

Now, the team is working with the pharmaceutical company that developed the drug (AB Science) to tweak the drug to make it an even more effective antiviral. Meanwhile, masitinib itself could be taken to [human clinical trials](#) in the future to test it as a COVID-19 treatment.

"Masitinib has the potential to be an effective antiviral now, especially when someone is first infected and the antiviral properties of the drug will have the biggest effect," Drayman said. "This isn't the first novel coronavirus outbreak, and it's not going to be the last. In addition to vaccines, we need to have new treatments available to help those who have been infected."

More information: Nir Drayman et al, Masitinib is a broad coronavirus 3CL inhibitor that blocks replication of SARS-CoV-2, *Science* (2021). [DOI: 10.1126/science.abg5827](https://doi.org/10.1126/science.abg5827)

Provided by University of Chicago

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