

Designing a SARS-CoV-2 Decoy

A molecular decoy that neutralizes the SARS-CoV-2 virus by preventing it from latching onto cells protected mice against COVID-19.

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Early in the COVID-19 pandemic, monoclonal antibodies played an important role in treating some people with severe disease. A combination of antibodies was also approved as a prevention strategy for people with certain immune system problems.

As the SARS-CoV-2 virus continues to mutate, the spike protein it uses to enter human cells has changed substantially. Because of this, the monoclonal antibodies designed to bind earlier versions of the spike have become ineffective over time. Researchers have been searching for new ways to combat COVID-19 in people with a compromised immune response.

A research team from NYU Langone Health led by Dr. Nathaniel Landau developed a type of molecular decoy designed to tie up the virus in the body before it can enter human cells. The decoy includes a version of human ACE2, the protein that SARS-CoV-2 latches onto to enter cells. Since the virus needs to bind ACE2 in order to enter cells, the researchers reasoned that this aspect of the virus's function, and therefore structure, is unlikely to change much.

The team fused ACE2 to a piece of antibody that helps the immune system attack the virus and clear it from the body. A harmless version of a virus called AAV was engineered to carry the gene for the decoy. The virus could then infect cells and instruct them to produce copies of the decoy. The team tested this new decoy in cells and in mice. Their results were published on June 6, 2023, in the [Proceedings of the National Academy of Sciences](#).

In several different cell lines, including those derived from lung and brain tissue, the decoy shut down SARS-CoV-2 infection. Cells treated with the decoy before being exposed to the virus had levels of virus similar to those in uninfected cells.

The researchers next gave the decoy to mice by three different routes of administration: through the nose, by injection into a muscle, or injection into a vein. They then exposed the animals to the original SARS-CoV-2 virus three days later.

Both intranasal and intramuscular administration of the decoy provided strong protection against disease. Similar results were seen when mice were exposed to several different Omicron variants. Protection appeared to remain strong for at least two months after the mice received the decoy.

The decoy also worked as a treatment when given to mice shortly after infection. When mice were exposed to SARS-CoV-2, the decoy provided protection when given up to a day after infection.

In people, the timeline for progression from infection to disease is longer than in mice, suggesting that such a decoy could potentially protect people over the course of several days after an exposure.

AAV-based systems are already used to deliver gene therapies.

The researchers also tested a second decoy using a type of virus called a lentivirus. Decoys based on lentiviruses have the potential to last longer in the body than those based on AAV. The team saw similar levels of protection with this decoy. However, further safety studies would be needed before lentiviral-based decoys could be tested in people.

“Decoy-based prevention strategies have the potential to remain useful even as the SARS-CoV-2 virus continues to change, since they’re based on the protein every viral variant needs to infect cells,” Landau says.

This [research summary](#) was published by the National Institutes of Health on June 13 2023.