Newly developed inhaled vaccine delivers broad protection against SARS-CoV-2, variants

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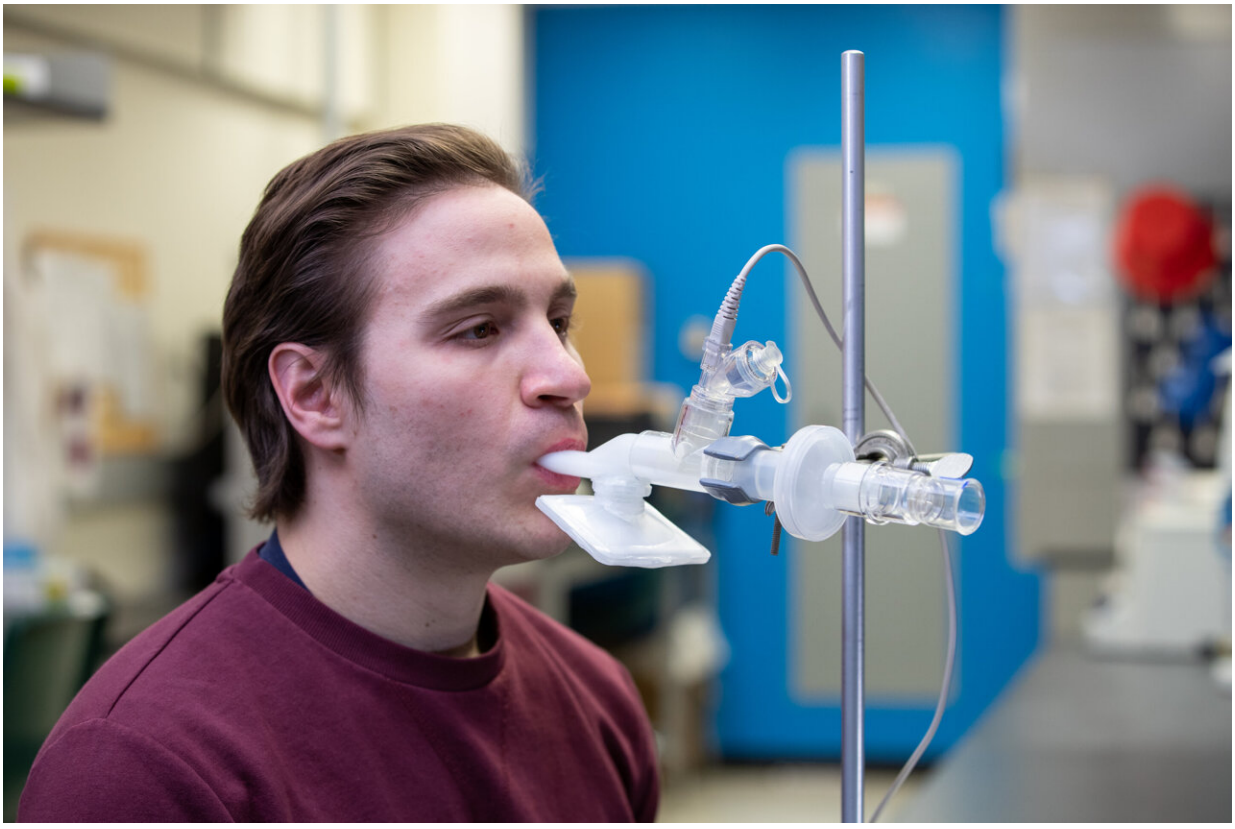

Michael D'Agostino demonstrates how a nebulizer would deliver an inhaled vaccine. A new study has found the McMaster-developed vaccine to be effective against variants of concern. Credit: McMaster University

Scientists at McMaster University who have developed an inhaled form of COVID vaccine have confirmed it can provide broad, long-lasting protection against the original strain of SARS-CoV-2 and variants of concern.

The research, recently published in the journal *Cell*, reveals the immune mechanisms and significant benefits of vaccines being delivered directly into the respiratory tract, rather than by traditional injection.

Because inhaled vaccines target the lungs and upper airways where respiratory viruses first enter the body, they are far more effective at inducing a protective immune response, the researchers report.

The reported preclinical study, which was conducted on animal models, has provided the critical proof of concept to enable a Phase 1 clinical trial that is currently under way to evaluate inhaled aerosol vaccines in healthy adults who had already received two doses of a COVID mRNA vaccine.

The tested COVID vaccine strategy was built upon a robust tuberculosis vaccine research program established by Zhou Xing, a co-lead author of the new study and a professor at the McMaster Immunology Research Centre and Department of Medicine.

"What we've discovered from many years' research is that the vaccine delivered into the lung induces all-around protective respiratory mucosal immunity, a property that the injected vaccine is lacking," Xing says.

Currently authorized COVID vaccines are all injected.

"We wanted, first and foremost, to design a vaccine that would work well against any variant," explains the study's co-lead author Matthew Miller, an associate professor at McMaster's Michael G. DeGroote

Institute for Infectious Disease Research.

The McMaster COVID vaccine represents one of only a handful developed in Canada. The urgent work is a critical mission of Canada's Global Nexus for Pandemics and Biological Threats, which is based at McMaster.

Researchers compared two types of adenovirus platforms for the vaccine. The viruses serve as vectors that can deliver vaccine directly to the lungs without causing illness themselves.

"We can remain ahead of the virus with our vaccine strategy," says Miller. "Current vaccines are limited because they will need to be updated and will always be chasing the virus."

Both types of the new McMaster vaccine are effective against highly transmissible variants because they are designed to target three parts of the virus, including two that are highly conserved among coronaviruses and do not mutate as quickly as spike. All COVID vaccines currently approved in Canada target only the spike protein, which has shown a remarkable ability to mutate.

"This vaccine might also provide pre-emptive protection against a future pandemic, and that's really important because as we've seen during this pandemic—and as we saw in 2009 with the swine flu—even when we are able to rapidly make a vaccine for a pandemic virus, it's already way too late. Millions of people died, even though we were able to make a vaccine in record time," says Miller.

"We have revealed in our report that besides neutralizing antibodies and T cell immunity, the vaccine delivered into the lungs stimulates a unique form of immunity known as trained innate immunity, which is able to provide very broad protection against many lung pathogens besides

SARS-CoV-2," Xing adds.

In additional to being needle and pain-free, an inhaled vaccine is so efficient at targeting the lungs and upper airways that it can achieve maximum protection with a small fraction of the dose of current vaccines—possibly as little as 1 percent—meaning a single batch of vaccine could go 100 times further, the researchers say.

"This pandemic has shown us that vaccine supply can be a huge challenge. Demonstrating that this alternative delivery method can significantly extend vaccine supply could be a game changer, particularly in a pandemic setting," says Brian Lichty, an associate professor in the Department of Medicine who co-led the preclinical study along with Miller, Xing and the senior trainees Sam Afkhami and Michael D'Agostino, who are the joint first authors of the study.

More information: Sam Afkhami et al, Respiratory mucosal delivery of next-generation COVID-19 vaccine provides robust protection against both ancestral and variant strains of SARS-CoV-2, *Cell* (2022). DOI: 10.1016/j.cell.2022.02.005

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