

Preclinical data for COVID-19 vaccine candidate show effectiveness and advantages

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A COVID-19 vaccine candidate that underwent extensive preclinical testing at the University of Alabama at Birmingham this spring and summer shows potent preclinical immune responses—including several

that distinguish it from other COVID-19 vaccine approaches—according to a preprint deposited in the BioRxiv repository this week.

Partial preclinical results had been announced in July and August by the Maryland-based Altimmune Inc., a clinical stage biopharmaceutical company. This week's expanded results show strong activation of both arms of the adaptive immune system following a single intranasal dose of Altimmune's AdCOVID, as tested at UAB in two strains of mice. The vaccine potently stimulated: 1) neutralizing antibodies in the blood plasma that can inactivate SARS-CoV-2, the virus that causes COVID-19 and has killed more than 213,000 people in the United States; 2) the immune system's T cells, priming them to attack virus-infected cells; and 3) importantly, the vaccine elicited mucosal antibody and T cell responses in the respiratory tract, including the lung and the nose, creating a possible barrier to infection and transmission at the viral point of entry.

The COVID-19 pandemic—with more than 1 million global deaths—has highlighted the urgent need for effective preventive vaccination to reduce the burden and spread of SARS-CoV-2 in humans. Intranasal vaccination is an attractive strategy as the [nasal mucosa](#) represents the first-line barrier to SARS-CoV-2 entry before viral spread to the lung. In contrast, current intramuscular formulated vaccine candidates elicit systemic immunity without conferring mucosal immunity.

In detail, the single intranasal dose of Altimmune's AdCOVID:

- Elicited a median serum neutralization titer against SARS-CoV-2 virus of up to 1:563 one month post-vaccination, as tested in a foci reduction assay. This neutralizing activity is at least threefold higher than the minimum titer recommended by the United States Food and Drug Administration for convalescent plasma used to treat COVID-19.

- Stimulated both CD4 and CD8 T cells, two types of the body's immune cells, with a focus in the lungs of the vaccinated mice and a bias toward CD8 T cells. A significant fraction of the CD8 T cells in the lung were resident memory T cells, a type that is important in fighting viral respiratory infections.
- Evoked nasal mucosal immunity, with a 29-fold increase in mucosal immunoglobulin A, or IgA, that was specific to the viral antigen in the vaccine, the receptor binding domain of the SARS-CoV-2 spike protein. This increase is well above the level associated with protection in clinical studies of mucosal influenza vaccines, where a two- to fourfold increase in IgA was found to be protective. Significantly, only an intranasal vaccine can activate this important type of immunity.

The observed IgA response, together with the lung-associated resident memory T cell response, provides an additional level of immune response, as compared to intramuscular vaccination, that may provide enhanced protection against COVID-19 disease and transmission.

The UAB preclinical testing was led by Fran Lund, Ph.D., chair of the UAB Department of Microbiology. Altimmune anticipates submitting an investigational new drug application to the FDA to begin a Phase 1 safety and immunogenicity trial for AdCOVID in the last quarter of 2020.

AdCOVID is based on Altimmune's adenovirus-based intranasal vaccine platform, and the [vaccine candidate](#) expresses the receptor binding domain of the SARS-CoV-2 spike protein. This domain is essential for viral infection, and the majority of neutralizing antibodies found in people who recovered from COVID-19 bind to this receptor binding domain, highlighting it as a target to control infection.

Altimmune expects AdCOVID will have an important advantage over

some other vaccine candidates that require freezers or ultra-low freezers during distribution. AdCOVID's expected stability at room temperature would allow distribution without refrigeration, followed by long-term storage in simple refrigerators at clinics or pharmacies. Also, an intranasal inoculation does not require syringes or needles.

"Our collaboration with UAB has been extremely productive, and the preclinical data for AdCOVID continues to show promising differentiation from other COVID-19 vaccine candidates," said Scot Roberts, Ph.D., chief scientific officer for Altimmune. "Intranasal vaccination represents an attractive strategy to prevent COVID-19 infection, as the nasal cavity comprises the first-line of defense against the SARS-CoV-2 virus prior to entry into the lungs. By stimulating mucosal antibody and T cell immunity, along with potent systemic neutralizing antibody titers, both arms of the immune system can work in concert to prevent and control infection."

Current first-generation COVID-19 vaccines, Roberts says, that are given by intramuscular injection, are unable to activate nasal mucosal immunity. Nasal mucosal immunity may be critical for mounting a comprehensive immune response, and it may also prevent further spread of the virus by blocking transmission.

Lund, who holds the Charles H. McCauley Chair of Microbiology at UAB, said, "We are delighted that our work has provided convincing data on the potential of AdCOVID to provide a broad and effective immune response. We look forward to continued collaboration with Altimmune on this important program."

Twenty-four researchers from six labs at UAB—all working under UAB COVID-19 safety protocols—and eight researchers at Altimmune tested the potential COVID-19 [vaccine](#) in a collaboration that was announced March 30. "The goal," Lund said at that time, "is to get the data to

Altimmune as rapidly as possible, so they will use the information gained from the preclinical study to design their clinical trial in people."

More information: Rodney G. King et al. Single-dose intranasal administration of AdCOVID elicits systemic and mucosal immunity against SARS-CoV-2 in mice, (2020). [DOI: 10.1101/2020.10.10.331348](https://doi.org/10.1101/2020.10.10.331348)

Provided by University of Alabama at Birmingham

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