COVID-19: An innovative candidate vaccine shows efficacy in preclinical models

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As the the COVID-19 vaccination campaign continues worldwide, research is ongoing to improve the vaccines available and develop new, effective, and innovative candidates to fight the pandemic and its

variants and protect as many people as possible. Researchers from Inserm and Université Paris-Est Créteil at the Vaccine Research Institute (VRI), along with their counterparts from CEA and Université Paris-Saclay, have developed a vaccine targeting key immune system cells called dendritic cells. It has been shown to be effective in preclinical models, inducing a protective immune response against the virus. To begin with, the researchers believe that this vaccine could be useful for convalescent or already vaccinated people whose immune response has started to decline, in order to "boost" their immunity. Clinical trials in humans are expected to begin in 2022. The findings of this research will be published on 1 September 2021 *Nature Communications*.

More than a year after the start of the COVID-19 pandemic, several vaccines have been authorized thanks to unprecedented worldwide research efforts. These first-generation vaccines bring great hope and are a mainstay in fighting the virus. However, questions persist regarding the duration of the immune response or the need for a booster. Also, controlling the pandemic means vaccinating billions of people. Yet manufacturing sufficient doses to protect the entire world population represents a considerable challenge. That is why vaccine research is still ongoing in order to develop additional candidate vaccines and to continue to meet these various challenges.

Researchers from the Vaccine Research Institute (VRI) (Inserm/Université Paris-Est Créteil), CEA and Université Paris-Saclay are working on the development of a vaccine comprised of a monoclonal antibody that targets immune cells circulating throughout the body: dendritic cells. These cells play a key role in stimulating the immune system through their ability to induce a robust and long-lasting antibody and cellular response, as demonstrated by the team in other models of infection. The monoclonal antibody is fused to a SARS-CoV-2 protein, which stimulates the dendritic cells.

In addition, this dendritic cell targeting vaccine technology is currently in phase I of a clinical trial evaluating the safety and immunogenicity of a preventive HIV vaccine.

Restimulate the production of neutralizing antibodies

In their study published in *Nature Communications*, the scientists began by studying the ability of their candidate vaccine to induce anti-COVID-19 "booster" responses in models using convalescent animals (having contracted SARS-CoV-2 six months earlier) .

They show that this vaccine is well tolerated and effective, inducing a strong increase in neutralizing antibodies. Faced with a new exposure to the virus, convalescent and vaccinated animals present an undetectable viral load or clear the virus in a shorter time (within three days) compared to unvaccinated convalescent animals or control animals free from any previous infection. A dose of this vaccine therefore provides better protection against reinfection than natural immunity. In addition, the vaccinated animals were protected from lung complications following infection.

Finally, the researchers have already adapted the candidate vaccine so that it is effective against the new variants identified in recent months. In the laboratory, the antibodies induced by the vaccine are capable of neutralizing very effectively the alpha variant (B.1.1.7) and also of neutralizing significantly the beta variant (B.1.351). Thus, the vaccine developed from the initial strain circulating in early 2020 is capable of inducing an antibody response that also neutralizes the new variants tested.

In conclusion, this study shows that a single administration of the candidate vaccine, with no adjuvant, restimulates the production of neutralizing antibodies capable of controlling the virus during

reinfection. This provides better protection against reinfection than natural immunity. This vaccine could therefore supplement the arsenal of existing COVID vaccines. The results presented in this study suggest that it could be particularly useful for people recovering or already vaccinated whose immune response has started to decline, in order to strengthen their immunity. Due to the good knowledge of subunit vaccine safety, this vaccine could also be useful for vulnerable people or for immunizing children.

Clinical trials are planned for 2022 with convalescent patients or people who have already received a first-generation vaccine. They will also be carried out in individuals who have never been exposed to either vaccination or the virus.

More information: Romain Marlin et al, Targeting SARS-CoV-2 receptor-binding domain to cells expressing CD40 improves protection to infection in convalescent macaques, *Nature Communications* (2021). DOI: 10.21203/rs.3.rs-244682/v1

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