

PRESS RELEASE

August, 2020

COVID-19: a lentiviral vaccine candidate for intranasal administration provides sterilizing protection in animal models

Scientists from the Institut Pasteur-TheraVectys Joint Laboratory recently published in *Cell Host & Microbe*¹ the results of tests, in two preclinical models, of a COVID-19 vaccine candidate using a lentiviral vector administered by nasal route. Their study demonstrates that the vaccine candidate induces antibody response with strong neutralizing activity against SARS-CoV-2, as well as substantial cell-mediated responses. Intranasal vaccination with this vector drastically reduces lung viral loads and prevents pathogenic pulmonary inflammation. This research proves the high vaccine efficacy and the fact that its intranasal administration attracts the effectors from the protective immune response into the upper respiratory tract through which the virus enters the body.

"In order to be effective, a coronavirus vaccine must provide protection at the site where the virus enters the body, namely the respiratory tract.

Neutralizing antibodies present in the blood only contribute partially to protection. The lentiviral vector is now emerging as a promising vaccine candidate for intranasal administration to induce mucosal immunity with an almost sterilizing effect in two highly sensitive preclinical animal models."

Pierre Charneau

Head of the Institut Pasteur Molecular Virology and Vaccinology Unit,
Chief Scientific Officer of TheraVectys,
Head of the two entities' Joint Lab.

Characteristics of the vaccine candidate

The vaccination strategy developed in this study is based on a lentiviral vaccine vector, which is a harmless, non-replicative viral vector. An initial injection of a vector induced expression of the SARS-CoV-2 Spike protein which triggered very high antibody titers in mouse serum with an *in vitro* neutralization capacity comparable to that of symptomatic human patients recovered from COVID-19. Cellular immunity, based on specific T cells, was also induced at a significant level in the vaccinated animals.

After intramuscular vaccination, despite the intense neutralizing activity measured in the blood, partial protection (lung viral loads reduced by a factor of 10) was observed following SARS-CoV-2 challenge. A parallel study² demonstrated that lung mucosal IgA antibodies were much more efficient in virus neutralization than serum IgG antibodies. Therefore, a prime and target vaccination regimen was applied, in which the immune response was initiated by a standard intramuscular vaccination, and then targeted into the respiratory tract through nasal instillation.

When this prime and target vaccination strategy was used, neutralizing activity measured in the blood did not increase substantially. However, a significant effect on protection was observed after challenge, with lung viral load reduced by a factor of >1,000, falling below the detection limit of an RT-PCR assay in most animals tested. In parallel to drastic viral load reduction, pulmonary inflammation, tissue injury and cytokine storm were also completely inhibited.

"This work introduces the important notion that neutralizing activity of antibodies measured in serum is probably not correlated to the level of protection, and that vaccine protection against SARS-CoV-2 requires mucosal immunity, and notably the presence of IgA antibodies at the site of virus entry, namely the upper respiratory tract," explains Dr. Laleh Majlessi, co-author of the study and head of research at the Institut Pasteur-TheraVectys Joint Lab.

These results generated in mice, in which expression of the human SARS-CoV-2 receptor (human ACE2) was induced artificially, were confirmed in the physiological hamster model that develops a severe pathology mirroring severe human COVID-19. These results are highly predictive of strong vaccine efficacy in humans. Once again, the prime and target vaccination strategy induced almost full protection with a major reduction in lung viral loads which fall below the detection limit, after SARS-CoV-2 challenge, as well as very significant inhibition of pulmonary inflammation, cytokine storm, and histopathological lung lesions.

Since the main target population for the SARS-CoV-2 vaccine is the elderly, convincing protection in preclinical models is essential for subsequent development. The duration of induced protection is a further important criterion. Although by definition, these ongoing tests take time, long-standing protection has already been demonstrated with the lentiviral vaccine platform in several vaccine candidates previously developed against SIV, Zika virus and West Nile viruses, as well as for immune therapy of tumors, in various animal models.

This COVID-19 vaccine candidate was developed in parallel with a sero-neutralization assay, namely "Lenti.S", by the same team from the Institut Pasteur-TheraVectys joint Lab under Dr. Pierre Charneau's³ scientific supervision.

Source

[1] Intranasal Vaccination with a Lentiviral Vector Protects against SARS-CoV-2 in Preclinical Animal Models, [Cell Host & Microbe](#), December 14, 2020

Min-Wen Ku^{1f}, Maryline Bourguin^{1,2f}, Pierre Authié^{1f}, Jodie Lopez¹, Kirill Nemirov¹, Fanny Moncoq¹, Amandine Noirat¹, Benjamin Vesin¹, Fabien Nevo¹, Catherine Blanc¹, Philippe Souque², Houda Tabbal³, Emeline Simon^{3,4}, David Hardy⁵, Marine Le Dudal⁶, Françoise Guinet⁷, Laurence Fiette⁶, Hugo Mouquet⁸, François Anna¹, Annette Martin³, Nicolas Escriou⁹, Laleh Majlessi^{1,5,#,*} and Pierre Charneau^{1,2,5*}

¹Institut Pasteur-TheraVectys Joint Lab, Virology Department, 28 rue du Dr. Roux, Paris F-75015, France

²Molecular Virology and Vaccinology Unit, Virology Department, Institut Pasteur

³Molecular Genetics of RNA Viruses Unit, Virology Department, Institut Pasteur, CNRS UMR3569, Université de Paris, Paris-F 75015, France

⁴Université de Paris, Paris F-75006, France

⁵Experimental Neuropathology Unit, Global Health Department, Institut Pasteur

⁶IMMR, 42 boulevard Jourdan, Paris F-75014, France

⁷Lymphocytes and Immunity Unit, Immunology Department, Institut Pasteur

⁸Laboratory of Humoral Immunology, Immunology Department, Institut Pasteur, INSERM U1222

⁹Innovation Lab, Vaccines, Virology Department, Institut Pasteur

^fThese authors contributed equally

§Senior authors

#Lead Contact

*Corresponding authors

[2] **IgA dominates the early neutralizing antibody response to SARS-CoV-2**, [Science Translational Medicine](#), December 7, 2020

Sterlin D, Mathian A, Miyara M, Mohr A, **Anna F**, Claër L, Quentric P, Fadlallah J, Devilliers H, Ghillani P, Gunn C, Hockett R, Mudumba S, Guihot A, Luyt CE, Mayaux J, Beurton A, Fourati S, Bruel T, Schwartz O, Lacorte JM, Yssel H, Parizot C, Dorgham K, **Charneau P**, Amoura Z, Gorochov G.

[3] **A comparison of four serological assays for detecting anti-SARS-CoV-2 antibodies in human serum samples from different populations**, [Science Translational Medicine](#), August 17, 2020