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The intranasal lentiviral vaccine candidate (Lenti-S) protects brain and lung in a pre-clinical animal model

The SARS-CoV-2 virus, responsible for the COVID-19 pandemic, primarily targets the respiratory tract, but its ability to infect cells of the nervous system has also been largely reported. Indeed, the expression of the receptor of this virus, the Angiotensin Converting Enzyme 2 (ACE2), by neuronal and glial cells makes the brain susceptible to SARS-CoV-2. Moreover, neurological manifestations are present in the majority of hospitalized COVID-19 patients. The development of new COVID-19 vaccine strategies, complementary to those currently implemented, should therefore contribute to the protection of the central nervous system against SARS-CoV-2. To this end, researchers from the Institut Pasteur-TheraVectys Joint Laboratory have demonstrated, in a preclinical animal model, the ability of an intranasal lentiviral vaccine candidate (Lenti-S) to protect not only the lungs but also the brain against the Gamma variant of SARS-CoV-2. These results were published in the *EMBO Molecular Medicine* journal on October 15, 2021.

COVID-19 is a viral infectious disease whose main symptoms are respiratory. However, neurological manifestations affect many COVID-19 patients. These symptoms may include loss of taste and smell, headache, syncope, but also other more serious conditions such as acute encephalopathy, stroke, epilepsy, meningitis and coma. These various manifestations, whose pathophysiological mechanisms are not yet fully understood, must be taken into account in the vaccine strategies currently in development.

In this context, researchers from the Institut Pasteur-Theravectys Joint Laboratory, headed by Pierre Charneau, have previously developed and established, in preclinical experiments, the efficacy of a lentiviral vector (LV)[1] when used for primary vaccination by the muscular route, followed by a boost by the nasal route. This vaccine candidate not only induces in animals long lasting immunity based on neutralizing antibodies but also a strong durable cellular immunity linked to T-cells.

In a new study, researchers from the Institut Pasteur-Theravectys Joint Laboratory have demonstrated, in an animal model[2], the ability of the Lenti-S vaccine candidate to induce protection not only of the lungs but also of the central nervous system against SARS-CoV-2 infection. In all animals immunized with the vaccine candidate, viral replication is absent or largely reduced in the brain. Immunization also eliminates the infection-mediated inflammatory phenomena in the brain. The researchers established that the booster injection of Lenti-S by nasal route is necessary in the protection of the brain.

"*Intranasal vaccination allows immune defenses to be directed straight into the upper respiratory tract and therefore act immediately at the site of entry of the virus into the body. The protective capacity of the respiratory and nervous systems of Lenti-S extends with the same efficacy to the Gamma variant of SARS-CoV-2 as to the ancestral strain*" explains Laleh Majlessi, director of research at the Institut Pasteur-TheraVectys Joint Laboratory, and co-last author of this study.

[1] The lentiviral vector is devoid of all viral genes in order to be harmless to humans and produces the Spike protein. This protein, which forms spicules around the virus, is the key to entry of the virus into human cells.

[2] In the animal model used in this study, expression of the human SARS-CoV-2 receptor (human ACE2) has been artificially induced in the organs including the brain to mimic the neurological effects of COVID-19.

Beyond the induction of potent neutralizing antibodies, the mechanism responsible for this broad spectrum of protection involves protective immunity based on T cells, whose efficacy remains intact against the Gamma variant of the SARS-CoV-2, despite accumulated mutations in their Spike protein. These data must now be confirmed in human clinical trials.

Source

Brain Cross-Protection against SARS-CoV-2 Variants by a Lentiviral Vaccine in New Transgenic Mice, EMBO Molecular Medicine, 15 October 2021

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About Institut Pasteur

The Institut Pasteur, a non-profit foundation with recognized charitable status set up by Louis Pasteur in 1887, is today an internationally renowned center for biomedical research. In the pursuit of its mission to tackle diseases in France and throughout the world, the Institut Pasteur operates in four main areas: research, public health, training, and development of research applications. The Institut Pasteur is a globally recognized leader in infectious diseases, microbiology, and immunology, with research focusing on the biology of living systems. Among its areas of investigation are emerging infectious diseases, antimicrobial resistance, certain cancers, neurodegenerative diseases, and brain connectivity disorders. The Institut Pasteur's outstanding research is facilitated by the development of a technological environment of the highest standard, with core facilities for nanoimaging, computational biology and artificial intelligence. Since its inception, 10 Institut Pasteur scientists have been awarded the Nobel Prize for Medicine, including two in 2008 for the 1983 discovery of the human immunodeficiency virus (HIV) that causes AIDS.

The Institut Pasteur is part of the Pasteur Network a worldwide network of 33 members on five continents, united by Pasteurian values, that contribute to global health.

About TheraVectys

The French immunotherapy biotech TheraVectys is the result of more than 20 years of research on lentiviral vectors and is bringing a dramatic paradigm shift in the field of vaccinology. The research work is conducted under the scientific direction of Pierre Charneau, inventor and pioneer of the lentiviral technology, in the Pasteur-TheraVectys Joint Laboratory.
Christian Bréchot, former CEO of Institut Pasteur and INSERM, is the Medical Director of TheraVectys.
The biotech's work is based on a proprietary platform to deliver remarkably safe and highly effective T-cell vaccines in response to critical unmet medical needs. The TheraVectys' technology and its worldwide license area have an almost unlimited number of applications in infectious diseases, cancers and viral cancers, and is driving a silent revolution in the field of vaccination, the impact of which could rival the discovery of the rabies vaccine by Louis Pasteur.

Our goal: To profoundly improve global health.
Our approach: Strategic industry partnerships to take our vaccine candidates from proof of concept to clinical trials and commercialization.