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February 14, 2022

PRESS RELEASE

INNOVATION

An intranasal boost with a Lenti-COVID vaccine candidate is more immunogenic than a third dose of messenger RNA vaccine in a preclinical model

Scientists at the Institut Pasteur-TheraVectys Joint Laboratory have demonstrated, in preclinical animal studies, the ability of their lentiviral candidate vaccine "Lenti-COVID", administered as an intranasal booster dose six months after primary vaccination with a messenger RNA vaccine, to induce protective mucosal immunity. This approach paves the way for an innovative vaccine strategy to reduce the viral transmission chain. These results have been published on the BioRxiv pre-print website. https://www.biorxiv.org/content/10.1101/2022.01.30.478159v1

As the COVID-19 pandemic continues and new SARS-CoV-2 variants of concern emerge, the adaptive immunity initially induced by the first generation COVID-19 vaccines weakens and needs to be reinforced. In this context, the development of a vaccine that would block the transmission of the virus in the long term and maintain this capacity against various emerging variants appears relevant.

Nasal vaccination induces antibodies and cellular immunity, based on cytotoxic T cells, in the respiratory mucosa at the point of entry of SARS-CoV-2 into the host organism in animal models. In addition, cellular immunity targets conserved regions among the variants and thereby provides broad-spectrum and long-term memory protective immunity against the SARS-CoV-2 variants. This mucosal immunity has been shown to be the most effective in reducing SARS-CoV-2 transmission in numerous studies [1].

The lentiviral vaccine vector is particularly well suited to the nasal immunization route. In previous preclinical studies, the Institut Pasteur-TheraVectys Joint Laboratory has demonstrated the high performance of this vaccine strategy against SARS-CoV-2 in animal models, when used as an intramuscular immunization followed by an intranasal booster. In these studies, the lentiviral vaccine vector is well tolerated, does not induce an inflammatory response, and does not multiply in the vaccinated host. The intranasal booster with this candidate vaccine, called "Lenti-COVID", protects not only the respiratory pathways but also the central nervous system [2,4].

In the work now available online, scientists from the Institut Pasteur-TheraVectys Joint Laboratory compared the immune responses of mice following a booster vaccination with either the intranasal Lenti-COVID vaccine candidate or a third dose of intramuscular messenger RNA vaccine. The mice were initially immunized in a prime-boost protocol with a messenger RNA vaccine and their primary humoral immunity had decreased four months after this vaccination.

Whether the booster dose is performed with the intranasal Lenti-COVID vaccine candidate or with an intramuscular messenger RNA vaccine, IgG antibody responses in the blood are enhanced in both cases. In contrast, only the intranasal Lenti-COVID vaccine candidate induces major players of mucosal immunity in the airways: (i) mucosal anti-Spike IgA, and (ii) lung resident memory B cells, able to locally produce antibodies, and (iii) lung resident memory T cells, able to kill infected cells.

Induction of these major players of mucosal immunity by the Lenti-COVID vaccine candidate leads to complete pulmonary protection against the Delta variant of SARS-CoV-2, demonstrating the suitability of the Lenti-COVID vaccine candidate as an intranasal booster against COVID-19 [5].
A clinical phase will have to be initiated to confirm the effectiveness of this approach in humans.

About TheraVectys

The French immunotherapy biotech, TheraVectys, is based on more than 20 years of research on lentiviral vectors and brings innovative technology to the field of vaccinology.

The research is conducted under the scientific direction of **Pierre CHARNEAU**, inventor and pioneer of the lentiviral technology, and **Laleh MAJLESSI**, research director in immunology, within the Institut Pasteur-TheraVectys Joint Laboratory.
Christian BRECHOT, former General Director of Institut Pasteur and INSERM, is Medical Director of TheraVectys.
The biotech's work is based on a proprietary platform to deliver T-cell vaccines in response to critical unmet medical needs.
TheraVectys holds an exclusive worldwide license on this technology from Institut Pasteur in the field of vaccines against infectious diseases, cancers and virus-induced cancers.

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.

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