Research team discovers a novel vaccine strategy to prevent SARS-CoV-2 nasal infection

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Researchers at the Department of Microbiology and State Key Laboratory of Emerging Infectious Diseases, LKS Faculty of Medicine of The University of Hong Kong (HKUMed) have conducted a comprehensive study for identifying an effective vaccine regimen in

preventing SARS-CoV-2 nasal infection. The study demonstrated that a combination of intramuscular PD1-based receptor-binding domain (RBD) DNA vaccine (PD1-RBD-DNA) prime and intranasal live attenuated influenza-based vaccine (LAIV-HK68-RBD) boost vaccination regimen induced the strongest mucosal broadly neutralizing antibodies and lung resident memory CD8 T cells, which prevented live SARS-CoV-2 nasal challenges in two animal models. The full research article is now online in the journal of *EBioMedicine*, published by *The Lancet*.

Background

The COVID-19 pandemic has resulted in over 275 million of infections with nearly 5.36 million deaths by now, yet few vaccines approved for emergency use can induce sufficient mucosal protection for preventing robust SARS-CoV-2 nasal infection. Although the current vaccination reduced rates of hospitalization, severity, and death significantly, these vaccines are much less effective in preventing SARS-CoV-2 respiratory transmission, which has posted great challenges for the pandemic control. With continuous emergence of SARS-CoV-2 variants of concerns including the rapidly spreading of immune escape Omicron strain, it is urgent to discover a more effective vaccine strategy to block or reduce nasal transmission of SARS-CoV-2.

Research methods and findings

In this HKUMed study, substantially higher systemic and mucosal antibodies IgA/IgG and lung resident polyfunctional memory CD8 T cells were induced mainly by the heterologous combination regimen as compared with current COVID-19 vaccination regimens. When two vaccinated mouse models were challenged at the memory phase, 35 days after the second vaccination, prevention of robust SARS-CoV-2

infection in nasal turbinate was achieved primarily by the heterologous combination regimen besides consistent protection in lungs. The new regimen-induced antibodies also cross-neutralized many pandemic variants of concern tested, including Alpha, Beta and Delta. The findings provided the proof-of-concept that vaccine-induced robust mucosal immunity is necessary for preventing SARS-CoV-2 nasal infection, which has significant implication for ending the ongoing COVID-19 pandemic.

Significance of the study

"The findings suggested that the clinical development of our two HKU vaccines remains a top priority for eliminating the uncontrolled spread of COVID-19 pandemic. We are currently testing the influenza-based nasal spray vaccine and the DNA vaccine in humans," remarked Professor Yuen Kwok-yung, Henry Fok Professor in Infectious Diseases and Chair of Infectious Diseases, Department of Microbiology, HKUMed, who is currently leading the clinical trials of these two vaccines in Hong Kong.

"The biggest challenge for our COVID-19 vaccine development is that we do not have a vaccine manufacturing plant in Hong Kong, which has delayed the translation of scientific discovery into clinical use. Now, we face the same challenge after we have already made the Omicron-targeted DNA vaccine for timely clinical development," said Professor Chen Zhiwei, Director of the AIDS Institute, Professor of Department of Microbiology, HKUMed, who co-led the research.

"We believe that using nasal spray vaccination to build up protection in the upper respiratory tract is the key strategy to reduce transmission of SARS-CoV-2 and important for the ultimate control of COVID-19 pandemic," said Professor Chen Honglin, Professor of Department of Microbiology, HKUMed, who co-led the research.

More information: Runhong Zhou et al, Nasal prevention of SARS-CoV-2 infection by intranasal influenza-based boost vaccination in mouse models, *EBioMedicine* (2021). DOI: 10.1016/j.ebiom.2021.103762

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