New research provides clues to developing better intranasal vaccines for COVID-19 and flu

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While gut microbiota play a critical role in the induction of adaptive immune responses to influenza virus infection, the role of nasal bacteria in the induction of virus-specific adaptive immunity is less clear. New research published this week in *mBio*, an open-access journal of the American Society for Microbiology, explores the role of nasal bacteria and provides clues to developing better intranasal vaccines for flu and COVID-19.

"Our study shows that both integrity and amounts of nasal bacteria may be critical for effective intranasal vaccine," said study principal investigator Takeshi Ichinohe, Ph.D., an associate professor in the Division of Viral Infection, Department of Infectious Disease Control, International Research Center for Infectious Diseases, Institute of Medical Science, the University of Tokyo, Minato-ku, Tokyo, Japan. "We showed that oral bacteria-combined intranasal vaccine protects from influenza virus and SARS-CoV-2 infection."

In the new study, to determine the effects of nasal bacteria in the induction of mucosal immune responses to influenza virus infection, Dr. Ichniohe and colleagues treated mice intranasally with an antibiotic cocktail to kill the nasal bacteria before influenza virus infection.

The researchers found that disruption of nasal bacteria by antibiotics before influenza virus infection enhanced the virus-specific antibody responses. "We found that intranasal application of antibiotics (to kill nasal bacteria) could release bacterial pathogen-associated molecular patterns (PAMP), which are bacterial components that stimulate innate immunity that act as mucosal adjuvants for influenza virus-specific antibodies response," said Dr. Ichniohe.

Innate immunity, which is not specific to a particular pathogen, is the first line of defense against non-self pathogens such as bacteria and virus. The main purpose of the innate immune response is to immediately prevent the spread and movement of foreign pathogens throughout the body. The innate immune responses play an essential role for inducing the pathogen-specific adaptive immune responses. Adjuvants are substances that increase or modulate the immune response to a vaccine and stimulate the innate immune system.

The researchers also found that while the upper respiratory tract contained commensal bacteria, relative amounts of culturable commensal bacteria in nasal mucosal surface were significantly lower than that in the oral cavity. The researchers tested whether intranasal supplementation of cultured oral bacteria enhances antibody responses to intranasally administered vaccine and found that oral bacteria combined with intranasal vaccine increased antibody responses to intranasally administered vaccine.

Dr. Ichniohe said the findings provide clues to developing better intranasal vaccines. "We wish to develop effective intranasal vaccines for influenza and COVID-19 in the near future," said Dr. Ichniohe.

More information: Minami Nagai et al, Oral Bacteria Combined with an Intranasal Vaccine Protect from Influenza A Virus and SARS-CoV-2 Infection, *mBio* (2021). DOI: 10.1128/mBio.01598-21

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