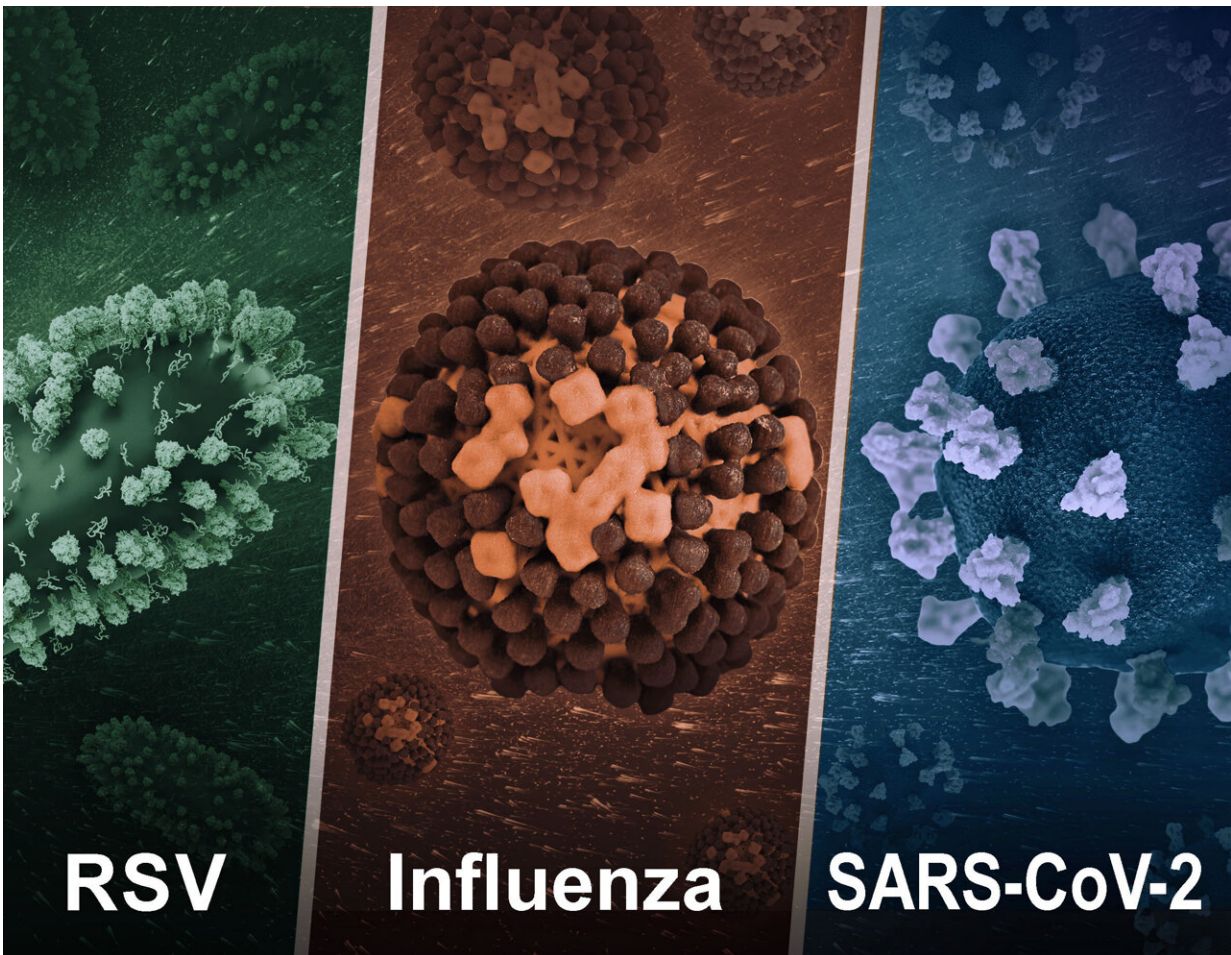


Developing mucosal vaccines for respiratory viruses

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3D renditions of three dangerous respiratory viruses. Credit: NIAID

Vaccines that provide long-lasting protection against influenza,

coronaviruses and respiratory syncytial virus (RSV) have proved exceptionally difficult to develop. In a new review article in *Cell Host & Microbe*, researchers from the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, explore the challenges and outline approaches to improved vaccines. Anthony S. Fauci, M.D., former NIAID director, is an author along with Jeffery K. Taubenberger, M.D., Ph.D., and David M. Morens, M.D.

Unlike the [respiratory viruses](#) that cause measles, mumps and rubella—for which vaccination or recovery from illness provides decades-long protection against future infection—flu, RSV, SARS-CoV-2 and "common cold" coronaviruses share several characteristics that enable them to cause repeated re-infections. These include very short incubation periods, rapid host-to-host transmission and replication in the [nasal mucosa](#) rather than throughout the body. This last feature—non-systemic replication—means these viruses do not stimulate the full force of the adaptive immune response, which typically takes a week or more to mount.

A next generation of improved vaccines for mucosa-replicating viruses will require advances in understanding on several fronts, the authors say. For instance, more must be learned about interactions between flu viruses, coronaviruses and RSV and the components of the immune response that operate largely or exclusively in the upper respiratory system.

Over time, these interactions have evolved and led to "immune tolerance," wherein the human host tolerates transient, limited infections by viruses that are generally non-lethal to avoid the destructive consequences of an all-out immune system attack.

The authors note that mucosal immunization appears to be an optimal route of vaccination for the viruses of interest, when feasible. However,

to develop useful mucosal vaccines, significant knowledge gaps must be filled including finding ideal vaccine formulations; determining dosage size, frequency and timing; and developing techniques for overcoming immune tolerance.

The NIAID authors urge fellow researchers to "think outside the box" to make strides toward vaccines that can elicit durable protection against these viruses of considerable public health impact. They conclude, "we are excited and invigorated that many investigators...are rethinking, from the ground up, all of our past assumptions and approaches to preventing important respiratory viral diseases and working to find bold new paths forward."

More information: David M. Morens et al, Rethinking next-generation vaccines for coronaviruses, influenzaviruses, and other respiratory viruses, *Cell Host & Microbe* (2023). [DOI: 10.1016/j.chom.2022.11.016](https://doi.org/10.1016/j.chom.2022.11.016)

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