Researchers identify flu-fighting pathways and genes essential for influenza a immune defense

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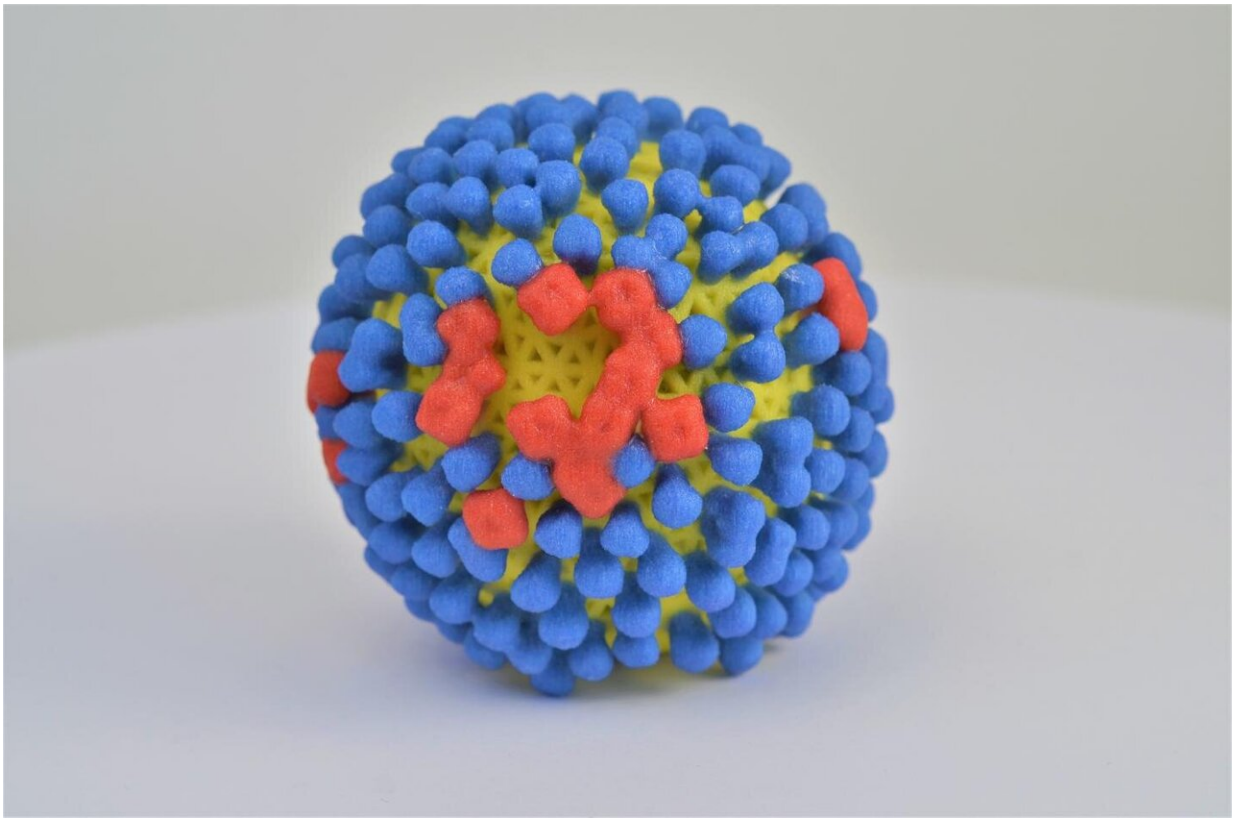

Influenza viruses, like the model shown here, display several kinds of surface proteins on their exteriors. Credit: NIAID

Researchers have identified the gene TDRD7 as a key regulator against

influenza A virus (IAV), which causes respiratory tract infections in 5 to 20 percent of the human population. These findings could facilitate the development of novel therapeutic interventions against influenza virus infection. The study, led by the Icahn School of Medicine at Mount Sinai in collaboration with other institutions, was published in *Science Advances* on October 5.

IAV is responsible for 250,000-500,000 deaths per year worldwide. When IAV infects its host, an immunological response composed of a series of molecular processes begins. IAV can infect several different species, and physiological and genetic differences among these species can contribute to different host responses, although some responses are shared.

"Identifying key defense processes and key regulators in multiple species can facilitate the development of treatments for IAV in humans," said Bin Zhang, Ph.D., Director of the Center for Transformative Disease Modeling, Willard T.C. Johnson Research Professor of Neurogenetics, and Professor of Genetics and Genomic Sciences at Icahn Mount Sinai, who led the study.

The study used RNA sequencing to analyze gene expression over time in cells and tissues collected from IAV-infected humans, ferrets, and mice, identifying multiple key defense processes specific to tissues and species. One gene found to play a key role in immunological defense mechanisms against IAV across all species was TDRD7, which encodes a Tudor domain-containing protein, a type of protein shown to be involved in epigenetic regulation. In light of this discovery, the researchers conducted subsequent experiments inhibiting the function of TDRD7, resulting in an increase of virus replication in IAV-infected models.

"Identifying both common and species-specific responses to influenza is

essential in developing effective therapies for the flu and can help inform future research of other respiratory infections, such as COVID-19," said Christian Forst, Ph.D., Assistant Professor of Genetics and Genomic Sciences, and Microbiology, at Icahn Mount Sinai and a first author of the study.

More information: Christian V. Forst et al, Common and species-specific molecular signatures, networks, and regulators of influenza virus infection in mice, ferrets, and humans, *Science Advances* (2022). DOI: 10.1126/sciadv.abm5859

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