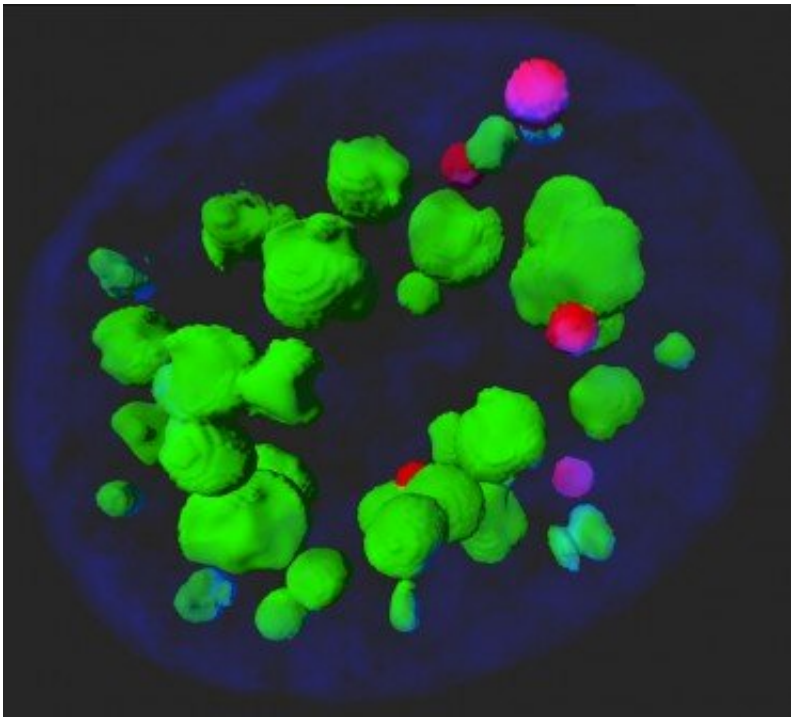
Scientists identify a protein key to inhibiting replication of the flu virus

June 20 2022



Nuclear speckles (green) shown inside a host cell nucleus. Protein complexes (red/pink) regulate its assembly and function. Credit: UT Southwestern Medical Center

A collaborative study from UT Southwestern scientists has identified a new function for a protein called TAO2 that appears to be key to inhibiting replication of the influenza virus, which sickens millions of individuals worldwide each year and kills hundreds of thousands. The

findings were published in *PNAS*.

"These results uncover new strategies for interfering with influenza virus replication, providing a potential avenue for the development of new antivirals against influenza," said Beatriz Fontoura, Ph.D., Professor of Cell Biology at UT Southwestern, whose lab studies the interplay between RNA viruses, such as influenza A virus, with their hosts. The study was led by Dr. Fontoura, together with first author and postdoctoral fellow Shengyan Gao, Ph.D., and Melanie H. Cobb, Ph.D., Professor of Pharmacology.

To replicate, influenza virus takes over parts of the host cell nucleus known as nuclear speckles, which then provide the virus an environment to express its genes. Dr. Fontoura and her colleagues, including experts in cell biology, molecular biology, and pharmacology, identified a novel role in regulating nuclear speckle assembly and function for the TAO2 kinase—a protein involved in transferring phosphate groups to other proteins.

"We found that TAO2 is needed to maintain the physical integrity and function of nuclear speckles. Among the functions of nuclear speckles is regulation of key steps in gene expression, which are usurped by influenza virus at these compartments to support viral replication. Consequently, by down-regulating TAO2 levels—or its kinase activity—we were able to inhibit influenza virus replication without causing major toxic effects to the host cell," said Dr. Fontoura.

Other UTSW researchers who contributed to this study include Matthew Esparza, Ishmael Dehghan, Ke Zhang, Kimberly Batten, Tolga Cagatay, Jerry W. Shay, Elizabeth J. Goldsmith, and Zhijian "James" Chen.

More information: Shengyan Gao et al, Nuclear speckle integrity and function require TAO2 kinase, *Proceedings of the National Academy of*

Sciences (2022). DOI: 10.1073/pnas.2206046119

Provided by UT Southwestern Medical Center