

Healthcare industry BW

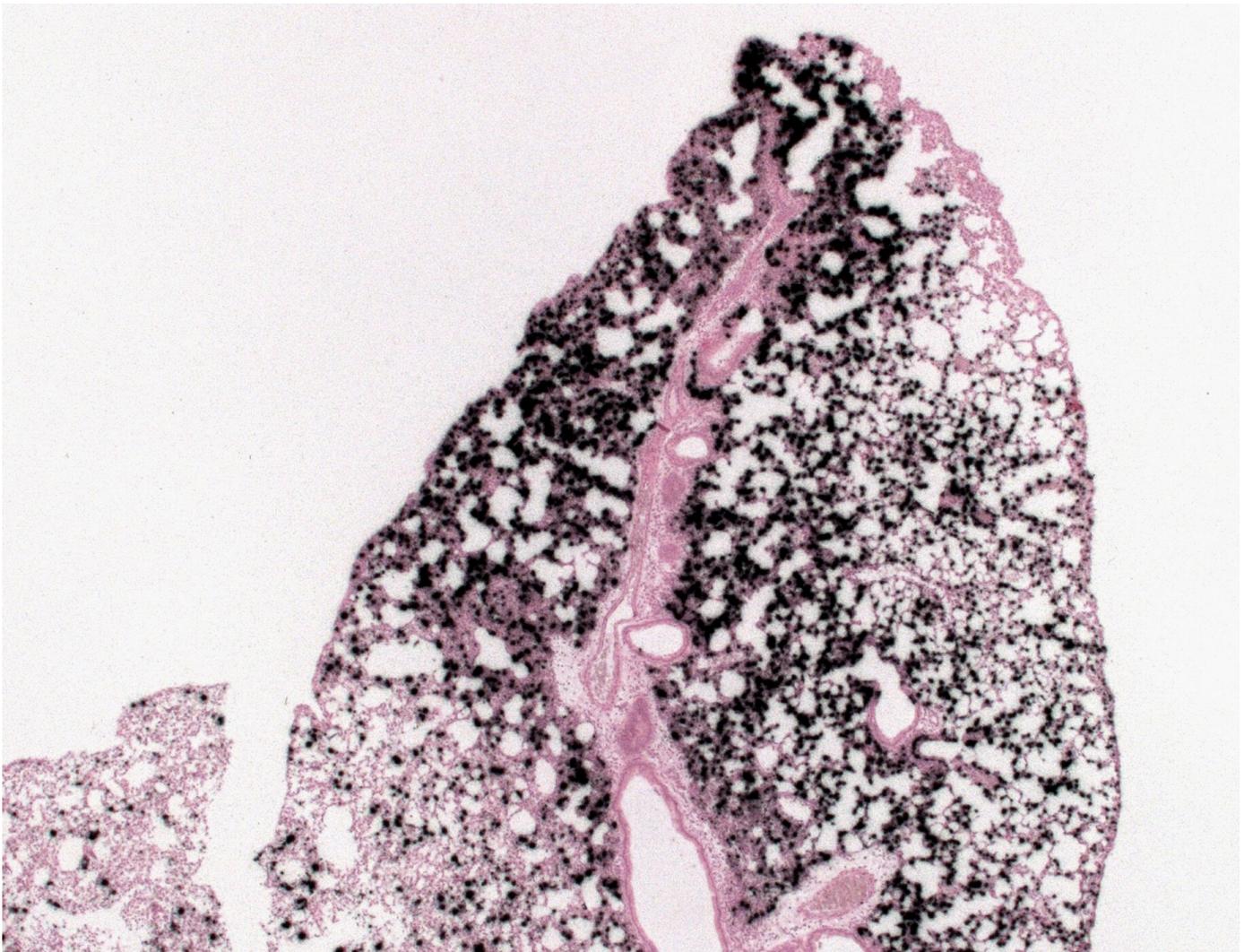
Door opener for influenza viruses

An international group of researchers, including scientists from the University of Tübingen, has deciphered mechanisms that enable the initiation and also the inhibition of influenza virus infections. The importin alpha-7 variant plays a crucial role in the ability of influenza A viruses to infect humans.

Influenza A viruses pose a particular threat to human health. A number of different influenza A variants can cross species barriers. In the last few years, these viruses have on occasions been transmitted from pigs or birds to humans. In order for type A influenza viruses to replicate and lead to the spread of infection, the viruses need to enter the nuclei of the cells of an infected host. They have to find a way to adapt to specific proteins that mediate their entry into the cell nucleus. These proteins are variants of proteins called importin alpha. A team of researchers, including two researchers from the University Hospital of Tübingen, has now shown that the importin alpha-7 variant plays a crucial role in the ability of influenza A viruses to infect humans. The researchers believe that this finding might have major therapeutic potential. They think it is likely that the temporary suppression of importin alpha-7 in patients suffering from an influenza A infection might help prevent the spread of the infection.

Cell nuclei are protected by a membrane (nuclear envelope) that separates their contents from the cellular cytoplasm. The membrane is impermeable to most molecules, except small ones. Larger molecules and viruses are imported into the cell nucleus by proteins known as importin alpha and beta. The role of the six known importin alpha isoforms had long been unknown. A new study, published on 18th January 2011 in the journal "Nature Communications" by a group of German and British virologists, immunologists, biologists and molecular pathologists, has now shed light on the important role that importin alpha proteins play in the course of influenza A infections in cell cultures and mice. The scientists selectively suppressed or switched off importin alpha protein variants of several viruses, including the H5N1 influenza A variant (avian flu) and the new H1N1v variant which was observed for the first time in pigs in 2009.

The paper is co-authored by Prof. Dr. med Karin Klingel, who is deputy head of the Department of Molecular Pathology at the Institute of Pathology at the University Hospital Tübingen. She is supported in her work by her colleague Dr. med. vet. Martina Sauter. Karin Klingel commented on their findings: "Our work shows that viral proteins react highly specifically to different importin alpha variants. We also found that these differences determine which hosts are likely to be infected by the viruses."



Acute viral infection of the lungs of a mouse infected with influenza A/H5N1 virus ("bird flu virus"). Radioactive in situ hybridisation reveals black areas that are characterised by massive virus replication.

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Literature:

Gülsah Gabriel, Karin Klingel, Anna Otte, Swantje Thiele, Ben Hudjetz, Gökhan Arman-Kalcek, Martina Sauter, Tatiana Schmidt, Franziska Rother, Sigrid Baumgarte, Björn Keiner, Enno Hartmann, Michael Bader, George G Brownlee, Ervin Fodor and Hans-Dieter Klenk: Differential use of importin- α isoforms governs cell tropism and host adaptation of influenza virus. *Nature Communications*, 18th January 2011, DOI: 10.1038/ncomms1158

Further information:

Prof. Dr. Karin Klingel
University Hospital Tübingen
Institute of Pathology
Deputy Head of the Dept. of Molecular Pathology
Liebermeisterstraße 8
72076 Tübingen
Tel.: + 49 7071 29-84925
Fax: + 49 7071 29-5334
E-mail: Karin.Klingel[at]med.uni-tuebingen.de

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