Press Release

April 21, 2020

Immune response in influenza infections: Importin-α3 identified as "immune sensor"

"Cell Reports" publication: Importin-α3 key factor in the immune defense against influenza infections

Hamburg. A scientific team from the Research Department "Viral Zoonoses - One Health" of the Heinrich Pette Institute, Leibniz Institute for Experimental Virology (HPI) and the University of Veterinary Medicine Hannover (TiHo) has identified importin-α3 as an "immune sensing protein" of the lung, which controls the induction of a number of antiviral gene expressions. Highly pathogenic avian influenza viruses inhibit the transcription of the importin-α3 gene in the lung through the massive release of inflammatory cytokines. This characteristic correlates with pneumonia and a severe course of infection. The study has now been published in the renowned journal "Cell Reports".

Importin-α proteins belong to the most important nuclear transport factors of the cell, are highly conserved evolutionarily and have the task of transporting cargo proteins from the cytoplasm to the nucleus. Disturbances in these highly sensitive regulatory processes can lead to an imbalance of cellular and nuclear proteins and eventually cause diseases. However, little is known about the expression profiles of importin-α isoforms in the individual organs. Researchers of the HPI Research Department "Viral Zoonoses - One Health", headed by Prof. Gülsah Gabriel, have now investigated this in more detail: Using primary human lung models, genome-wide transcription analyses and transgenic mouse models, they investigated the anatomical expression profile of the importin-α isoforms in the lungs of mammals and humans as well as the influence on influenza virus-induced pneumonia.

The new publication provides important new insights into the dynamic role of the protein importin-α3 as an "immune sensor" of viral infections in the lung: It is shown that importin-α3 is the most abundant importin-α isoform in the respiratory tract of mammals, including humans. Importin-α3 is one of the major transporters of the transcription factor NF-κB into the cell nucleus, which is responsible for the expression of a large number of antiviral genes. However, highly pathogenic avian influenza viruses can inhibit the NF-κB-mediated transcription of the importin-α3 gene by inducing a cytokine storm. This leads to a bottleneck in the availability of importin-α3 in the lungs. As a consequence, important antiviral NF-κB mediated gene expressions cannot be induced and severe pneumonia occurs in the animal model. These data shed new light on the pathomechanisms of the often-fatal avian influenza in humans.

"These results could form an important basis for the development of new antiviral strategies against respiratory infections," explains Prof. Gülsah Gabriel, head of the HPI Research Department "Viral Zoonoses - One Health" and professor at the University of Veterinary Medicine Hannover.

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Publication

Cellular importin-α3 expression dynamics in the lung regulate antiviral response pathways against influenza A virus infection.
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The results have been published in the journal "Cell Reports":

Swantje Thiele, Stephanie Stanelle-Bertram, Sebastian Beck, Nancy Mounogou Kouassi, Martin Zickler, Martin Müller, Berfin Tuku, Patricia Resa-Infante, Debby van Riel, Malik Alawi, Thomas Günther, Franziska Rother, Stefanie Hügel, Susanne Reimering, Alice McHardy, Adam Grundhoff, Wolfram Brune, Albert Osterhaus, Michael Bader, Enno Hartmann, Gülsah Gabriel (2020). **Cellular importin-α3 expression dynamics in the lung regulate antiviral response pathways against influenza A virus infection.** Cell Reports, 2020 April 21.

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Heinrich Pette Institute, Leibniz Institute for Experimental Virology

The Heinrich Pette Institute, Leibniz Institute for Experimental Virology (HPI) investigates the biology of human pathogenic viruses with the aim of unraveling the molecular mechanisms that control viral life cycles and virus induced pathogenesis. The institute applies basic experimental research to develop new approaches for contemporary treatments of viral infections such as AIDS, influenza and hepatitis but also of emerging viral diseases.

The HPI was established by the philanthropist Philipp F. Reemtsma and the neurologist Heinrich Pette in 1948. The institute is a non-profit, independent research foundation that is part of the Leibniz Association.

Further information: www.hpi-hamburg.de