

PRESS RELEASE

Millions in funding for development of influenza drugs
Open Philanthropy funds Bonn research with around 2.2 million US dollars

Bonn, October 09 – How can the propagation of influenza viruses be stopped? For a new approach in the therapy of influenza infections, Prof. Hiroki Kato from the Institute of Cardiovascular Immunology at the University Hospital Bonn (UKB) and the Cluster of Excellence ImmunoSensation2 of the University of Bonn receives an Open Philanthropy grant of 2.2 million US dollars. Together with his team, he found a compound that inhibits the body's own methyltransferase MTr1 and thus prevents the replication of influenza viruses. The funded project now aims to identify further MTr1 inhibitors with influenza-inhibiting activity that could be considered for clinical trials in the near future.

When a virus enters our body, it binds to the host cell and introduces its genetic information in form of ribonucleic acid (RNA). Using these blueprints, the host cell is now forced to produce numerous new viruses. "This is because viruses have evolved various mechanisms, including modifications of the viral genetic material, to successfully replicate in the host," explains Prof. Hiroki Kato from the Institute of Cardiovascular Immunology at UKB, who is a member of the ImmunoSensation2 cluster of excellence at the University of Bonn.

One of these mechanisms is so-called "cap snatching," which avoids recognition by the innate immune system and thus enables efficient viral replication. To be able to distinguish foreign from its own genetic information, the human cell marks, for example, its own RNA for the immune system with a molecular cap at the end of the RNA chain. RNA without this cap is recognized and combated by the immune system. To avoid this, viruses steal this molecular cap from the cellular RNA during a process called "cap snatching".

RNA methyltransferases are the key to flu therapy

The enzyme methyltransferase MTr1 provides the cap structure of cellular RNA. Prof. Kato's team found out how much influenza viruses depend on the activity of this enzyme for their replication and have already described this in a publication in the journal Science. This is because, unlike other viruses such as SARS-CoV-2, they are not able to cap their RNA molecules independently. Therefore, they rely on "cap snatching". If the function of MTr1 is disturbed, however, there are no molecular caps that could be transferred to the viral RNA. The researchers in Bonn want to exploit this relationship for the therapy of influenza infections and are looking for inhibitors that specifically inhibit MTr1. So far, they have been able to find a candidate in the form of a derivative of the natural product, trifluoromethyl tubercidin (TFMT), which is produced by bacteria of the streptomycin genus.

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"Thanks to the excellent collaboration within the University Hospital Bonn and the University of Bonn, as well as with external universities, I am very pleased that we have been given the opportunity to pursue the preclinical aspect of MTr1 inhibitors," said Prof. Kato. "We will continue to search for superior agents and investigate the extent to which MTr1 inhibitors can suppress the emergence of drug-resistant mutant viruses through combination therapy with existing drugs."

Information on Open Philanthropy:

<https://www.openphilanthropy.org/>
<https://padinitiative.com/>

Publication

Yuta Tsukamoto et. al: Inhibition of cellular RNA methyltransferase abrogates influenza virus capping and replication, DOI: <https://www.science.org/doi/10.1126/science.add0875>

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Visuals:



Caption: For a new approach in the therapy of influenza, Prof. Hiroki Kato of the University Hospital Bonn (UKB) and the Cluster of Excellence ImmunoSensation2 of the University of Bonn receives a grant of 2.2 million US dollars from Open Philanthropy.

Picture credits: University Hospital Bonn (UKB)

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About the University Hospital Bonn: The UKB cares for about 500,000 patients per year, employs about 9,000 people and has a balance sheet total of 1.6 billion euros. In addition to the more than 3,300 medical and dental students, a further 585 people are trained in numerous healthcare professions each year. The UKB is ranked number 1 among university hospitals (UK) in NRW in the Science Ranking as well as in the Focus Clinic List and has the third highest case mix index (case severity index) in Germany. In 2022 and 2023, the F.A.Z. Institute named UKB Germany's most sought-after employer and training champion among public hospitals in Germany.