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## Immunoprotein impairs Sars-Cov-2

**An international team with researchers of the Institute of Virology and Immunology (IVI) of the University of Bern and the Swiss Federal Food Safety and Veterinary Office (FSVO) showed that an endogenous protein prevents the virus from fusing with host cells. This raises hopes for new therapeutic approaches.**

A protein produced by the human immune system can strongly inhibit corona viruses, including Sars-Cov-2, the pathogen causing Covid-19. An international team from Germany, Switzerland and the USA successfully showed that the so-called LY6E-Protein prevents coronaviruses from causing an infection. "This finding might lead to the development of new therapeutic approaches against coronaviruses," says Professor Stephanie Pfänder from the Department for Molecular and Medical Virology at Ruhr-Universität Bochum (RUB), co-lead author of the study, which started at the Institute of Virology and Immunology (IVI) in Bern. "We wanted to find out which factors prevent corona viruses from spreading from animals to humans," says corresponding author Prof. Volker Thiel from the IVI. "Now we have succeeded in finding the needle in the haystack, so to speak". The study was published in the journal Nature Microbiology.

### **Strengthening influenza viruses, impairing corona viruses**

The LY6E protein plays a role in various diseases: US researchers Professor John Schoggins and Professor Charles Rice discovered that the protein enhances the infectivity of influenza viruses. In contrast, coronaviruses are inhibited by LY6E.

Funded by a Marie Curie Individual Fellowship of the European Union, Stephanie Pfänder, who was then working at the Institute of Virology and Immunology in Bern, visited Professor Charles Rice's lab at Rockefeller University in New York in 2017, in order to continue her search for genes that prevent coronavirus infections. In order to identify proteins in the human body that inhibit the spread of corona viruses, Pfänder carried out genetic screening of several hundred so-called interferon-stimulated genes (ISGs). Among other things, ISGs produce antiviral proteins and protect against pathogens. The protein LY6E showed the strongest inhibitory effect on all corona viruses tested, including the pathogens causing SARS and MERS as well as SARS-CoV-2 which causes COVID-19. "This now led to the discovery that LY6E has the opposite effect on coronaviruses compared to influenza viruses: it prevents their spreading," explains the researcher.

### **Viruses unable to fuse**

Tests with different cell cultures showed that LY6E affects the ability of the virus to fuse with the host cells. “If the virus is unable to fuse with these cells, it can’t cause infection,” explains Volker Thiel.

The validation in an animal model succeeded thanks to a collaboration with the laboratory of Professor John Schoggins at the Southwestern Medical Center of the University of Texas. The experiments conducted there by co-lead author Dr. Katrina Mar led to the discovery that the mouse variant of the protein called LY6E is crucial for the protection of immune cells against infections. In the absence of LY6E, immune cells such as dendritic cells and B-cells become more susceptible to infection and their numbers decrease dramatically. Mice lacking LY6E in immune cells are highly susceptible to a normally non-lethal mouse coronavirus and succumb to infection.

### **Understanding basic concepts**

The researchers point out that the mouse coronavirus used in the experiment differs significantly from the pathogen causing the current COVID-19 outbreak – for example, it causes hepatitis rather than respiratory disease. Nevertheless, it is widely accepted as a model for understanding the basic concepts of coronavirus replication and immune responses in a living animal.

“Our study provides new insights into how important these antiviral genes are for the control of viral infection and for an adequate immune response against the virus,” says Thiel. Since LY6E is a naturally occurring human protein, the researchers hope that this knowledge will aid the development of therapies that may one day be used to treat coronavirus infections. A therapeutic approach that mimics the mechanism of action of LY6E may provide a first line of defence against novel coronavirus infections.

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