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Weak Points in the Human Immune System Max Planck Researchers Investigate the Attack Strategies of Viruses

For viruses to spread, they must enter host cells to replicate, assemble and propagate. Scientists of the Max Planck Institute (MPI) of Biochemistry in Martinsried near Munich and the Research Center for Molecular Medicine (CeMM) of the Austrian Academy of Sciences in Vienna have for the first time performed a comprehensive survey of the antiviral defense strategies of human cells. They were able to identify vulnerable points in the immune system that viruses modulate for their own purposes. In the survey the researchers compared the attack strategies of 30 well-known viruses. The insights gained from the study may advance the development of new antiviral therapies in the future. The findings have now been published in *Nature*.

Viruses are not independent organisms. In order to spread, they must invade and hijack cells for their own purposes. They insert their own genetic information into the host cell and exploit its molecular machinery in order to replicate. While doing so, they face host immune defense mechanisms that they have to overturn. One strategy is to use camouflage: Some viruses disguise and mask themselves to avoid being recognized. Another tactic is to manipulate the signaling pathways within the host cell, thus preventing the immune defense from raising an alarm.

In earlier studies, other researchers focused on the strategies of individual viruses. In this study, Andreas Pichlmair, research group leader at the MPI of Biochemistry, examined 30 different viruses simultaneously to obtain insight into the overall system of immune defense in human cells. Giulio Superti-Furga, director of the Center for Molecular Medicine (CeMM) in Vienna, who also participated in the study, described the work as follows: "Figuratively speaking, we allowed the enemy to invade the kingdom in order to pinpoint the weak points in the immune system's defense. Thus, we identified the most important control points of the cell's security strategy."

The researchers discovered that the various viruses usually follow one of two different strategies during their attack: Some try to block cellular communication pathways and prevent the coordination of the cell. Others try to control specific processes. The comparison of the different virus families also showed that some related viruses tend to pursue similar attack strategies. However, even distantly related viruses like influenza viruses, hepatitis C and herpes viruses intervene with similar cellular processes, highlighting the importance of certain cellular mechanisms for antiviral immunity. In the future, based on the findings of this survey, it may be possible to distinguish viruses by the strategies and target molecules they utilize and thus to develop new target-specific treatment approaches.



Original publication:

A. Pichlmair, K. Kandasamy, G. Alvisi, O. Mulhern, R. Sacco, M. Habjan, M. Binder, A. Stefanovic, C.-A. Eberle, A. Goncalves, T. Bürckstümmer, A. Müller, A. Fauster, C. Holze, K. Lindsten, S. Goodbourn, G. Kochs, F. Weber, R. Bartenschlager, A.G. Bowie, K.L. Bennett, J. Colinge and G. Superti-Furga: Viral immune modulators perturb the human molecular network by common and unique strategies. *Nature*, July 18, 2012
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