

How immune cells defend themselves against HIV

October 2 2012

A team of scientists led by virologists Prof. Oliver T. Fackler and Prof. Oliver T. Keppler from Heidelberg University Hospital have decoded a mechanism used by the human immune system to protect itself from HIV viruses. A protein stops the replication of the virus in resting immune cells, referred to as T helper cells, by preventing the transcription of the viral genome into one that can be read by the cell. The ground-breaking results provide new insights into the molecular background of the immunodeficiency syndrome AIDS and could open up starting points for new treatments. The study has now been published – ahead of print online – in the international journal *Nature Medicine*.

Human immunodeficiency viruses attack different cells of the [human immune system](#), most frequently, "T helper cells". These lymphocytes play a key role in [immune defense](#), since they activate other immune cells upon contact with pathogens and set off subsequent immune responses. In the course of the HIV infection, they are continuously depleted until the immune system ultimately fails, culminating in AIDS with various infections.

In healthy people, the vast majority of T helper cells in the blood are in a resting state. They are not activated until they contact the pathogens against which they are specialized in defending. In the activated state, the cells are susceptible to HIV infection. "In contrast, resting T helper cells are immune to HIV: While the virus docks, and delivers its [genetic information](#) to the cell, the infection does not progress further. We have investigated why this is the case," explained Prof. Fackler, head of the

working group at the Department of Infectious Diseases, Virology. Even if the T helper cells are activated later on, the virus does not replicate, because the genetic information of the virus is degraded during this period.

HIV genome cannot be transcribed into cell-compatible version

The team is headed by Prof. Fackler and Prof. Keppler, who moved from Heidelberg to the University Hospital in Frankfurt in April 2012 and now heads the Institute of Medical Virology there. The researchers discovered that the cellular protein SAMHD1 significantly contributes to protecting the resting immune cells. The protein is present in both resting and activated T helper cells and depletes nucleotides, the building blocks of genetic information. In the active phase the cells double their genetic information and divide, a process that depends on the continuous production of nucleotides. In the resting state, the cell does not require any nucleotides and stops their production, and SAMHD1 degrades the remaining nucleotides. "As a result, the HIV viruses most likely also lack the material they need to transcribe their genetic information into a version that can be used for the cell and to allow it to replicate," Fackler explained.

In the experiment, if SAMHD1 expression was silenced, resting T helper cells became susceptible to [HIV infection](#). The same was true for [immune cells](#) of a patient who is unable to produce SAMHD1 due to a hereditary condition. "This shows that HIV can only replicate in lymphocytes if the effect of the protective protein SAMHD1 is eliminated," Keppler said. In addition, the researchers discovered that this early protective measure must be followed by other barriers to HIV replication. Even without SAMHD1, no new viruses were released from resting T [helper cells](#). Now that they have described the protective

function of SAMHD1 and are able block it, the scientists can for the first time also investigate the downstream mechanisms. "We hope that we will be able to use these findings to develop new strategies in the fight against HIV," the virologist said.

More information: Baldauf, H-M., et al. (2012). The deoxynucleoside triphosphate triphosphohydrolase SAMHD1 restricts HIV-1 infection in resting CD4+ T cells. *Nature Medicine*, published online ahead of print September 12, [doi:10.1038/nm.2964](https://doi.org/10.1038/nm.2964)

Provided by University Hospital of Heidelberg

Citation: How immune cells defend themselves against HIV (2012, October 2) retrieved 4 May 2024 from <https://medicalxpress.com/news/2012-10-immune-cells-defend-hiv.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--