

How TRIM5 fights HIV

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Thanks to a certain protein, rhesus monkeys are resistant to HIV. Known as TRIM5, the protein prevents the HI virus from multiplying once it has entered the cell. Researchers from the universities of Geneva and Zurich have now discovered the protein's mechanism, as they report in *Nature*. This also opens up new prospects for fighting HIV in humans.

Unlike people, certain monkey species, such as rhesus or night monkeys, are resistant to <u>HIV</u> thanks to TRIM5, a cellular protein: In the case of an <u>HIV infection</u>, the protein intercepts the virus as soon as it enters the cell and prevents it from multiplying. We have known about TRIM5 for over six years. However, the mechanism TRIM5 uses to prevent the HI virus from multiplying was still largely unknown.

The majority of the key aspects of TRIM5's defense mechanism against HIV was discovered by the Swiss research teams of Prof. Jeremy Luban, University of Geneva, and Prof. Markus Grütter, University of Zurich, in collaboration with teams from the USA and France. They demonstrated that TRIM5 immediately triggers an immune response if infected with HIV. Consequently, TRIM5 is an HIV sensor in the innate immune system. Unlike the adaptive immune system, which only develops when confronted with a pathogen, the innate immune system is already able to eliminate pathogens as soon as it comes into contact with them.

The HI virus, which penetrates the cell during an infection, has a shell, the components of which are arranged in a lattice, similar to the pattern on a soccer ball. TRIM5 recognizes this lattice structure and specifically



attaches itself to it. This stimulates the protein to produce signal molecules known as polyubiquitin chains in the cell. These chains immediately trigger an anti-viral reaction. The "alerted" cell can then start eliminating cells infected with HIV by releasing messenger substances (cytokines).

Humans also have a TRIM5 protein, but it is less effective in fending off HIV. However, the findings in resistant monkeys have opened up new possibilities and ways of fighting HIV in humans. 33 million people are currently infected with HIV worldwide; two million die of AIDS each year. And with 2.7 million people becoming infected every year, HIV remains a major problem.

Provided by University of Zurich

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