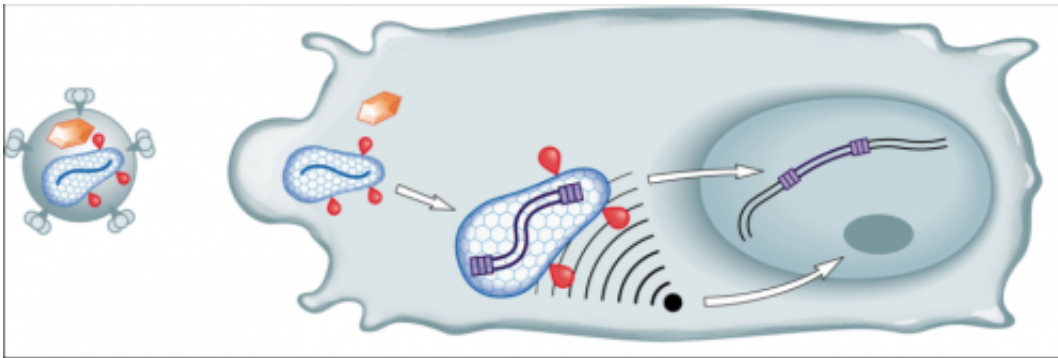


# Scientists find the invisibility cloak that shields HIV-1 from the immune system

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The image depicts an HIV-2 virus (left) getting in contact with a dendritic cell (right). When the virus enters the dendritic cell, the capsid shell (cone) containing a viral RNA (line) can get efficiently reverse-transcribed into DNA through activity of the Vpx protein (orange) that degrades SAMHD1 (not shown). The resulting cDNA (double line) has two different fates, which are determined by the sequence of the capsid and its interaction with Cyclophilin A proteins (red drops). In HIV-2 and capsid-mutated viruses described in the paper, the cDNA gets sensed by the cytosolic sensor cGAS (radar) leading to induction of antiviral and immune response gene expression. In HIV-1, the capsid allows the virus to escape sensing of its viral cDNA, leading to productive infection of the cell (integrated cDNA in the nucleus). Credit: Nicolas Manel

Of the two major types of HIV, only one, HIV-1, typically causes AIDS in infected people who don't receive treatment. A study published by Cell Press November 21st in the journal *Immunity* reveals how HIV-1 escapes detection by essentially becoming invisible to a patient's immune

system, whereas HIV-2 triggers protective immune responses in patients. This understanding of how HIV-1's "invisibility cloak" works could lead to the development of effective vaccines against HIV-1.

"Our study shows for the first time exactly how [immune cells](#) sense the virus and how the virus uses one of its proteins to tune its stealthiness and infectivity," says senior study author Nicolas Manel of the Institut Curie. "We also show how to modify the virus so that it is properly recognized and leads to a beneficial immune response."

Individuals who are infected with both HIV-1 and HIV-2 do better than those infected with HIV-1 alone, suggesting that the [immune response](#) against HIV-2 protects against the effects of HIV-1 infection. While searching for an explanation in previous studies, Manel and his collaborators found that HIV-2, but not HIV-1, naturally infects and activates [dendritic cells](#), which play a major role in triggering protective immune responses. But until now, it was not known how HIV is detected in dendritic cells.

In the new study, Manel and his team focused on the capsid—the protein shell of a virus that encloses its genetic material. By mutating HIV-1 and HIV-2 capsids, they discovered that these viral proteins control the ability of dendritic cells to sense the viruses and activate immune responses.

The researchers found that the HIV-1 capsid allows the virus to escape detection by dendritic cells under normal conditions. But when they mutated the HIV-1 and HIV-2 capsids, the dendritic cells produced immune responses without getting infected by the viruses. These cells relied on a protein called cyclic GMP-AMP synthase (cGAS) to sense the viral DNA in the cytosol before the foreign DNA became integrated into the host genome.

These findings open new avenues for the development of effective treatments against HIV-1. "By modifying the capsid of a virus, we could engineer a [virus](#) that is both better recognized by the [immune system](#) and that has also lost its ability to infect cells," Manel says. "Beyond capsid-mutated viruses, our results suggest that activating the cGAS pathway in dendritic cells could induce immunity against HIV-1."

**More information:** *Immunity*, Lahaye et al.: "The capsids of HIV-1 and HIV-2 determine immune detection of the viral cDNA by the innate sensor cGAS in dendritic cells."

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