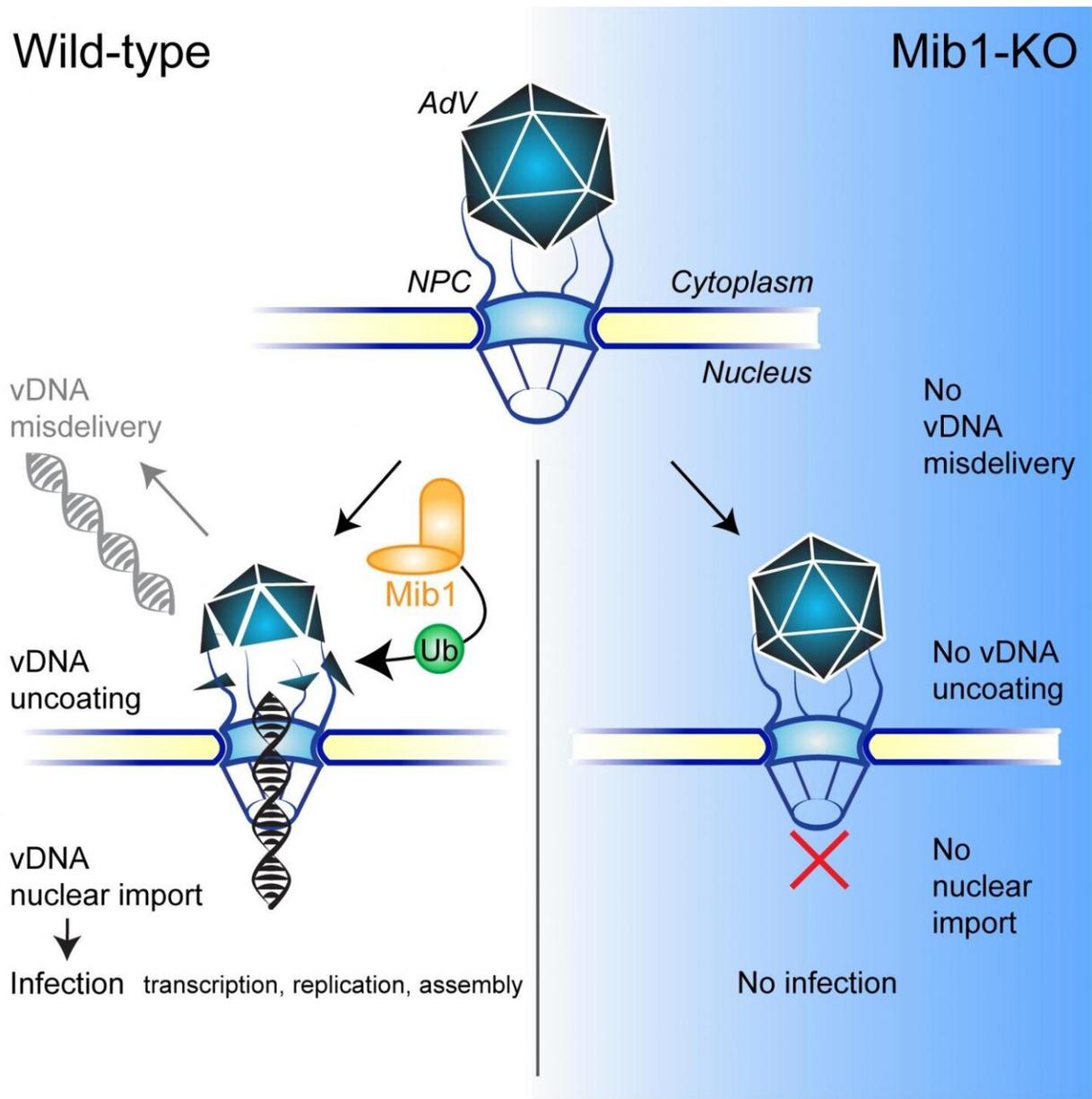


Newly discovered protein gives signal for virus infection

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In human cells of the lung epithelium where the gene for Mib1 is knocked out, the uncoating of the viral DNA is blocked and the adenoviruses remained stuck at the pore structures outside of the nucleus, which prevents viral infection.

Credit: University of Zurich

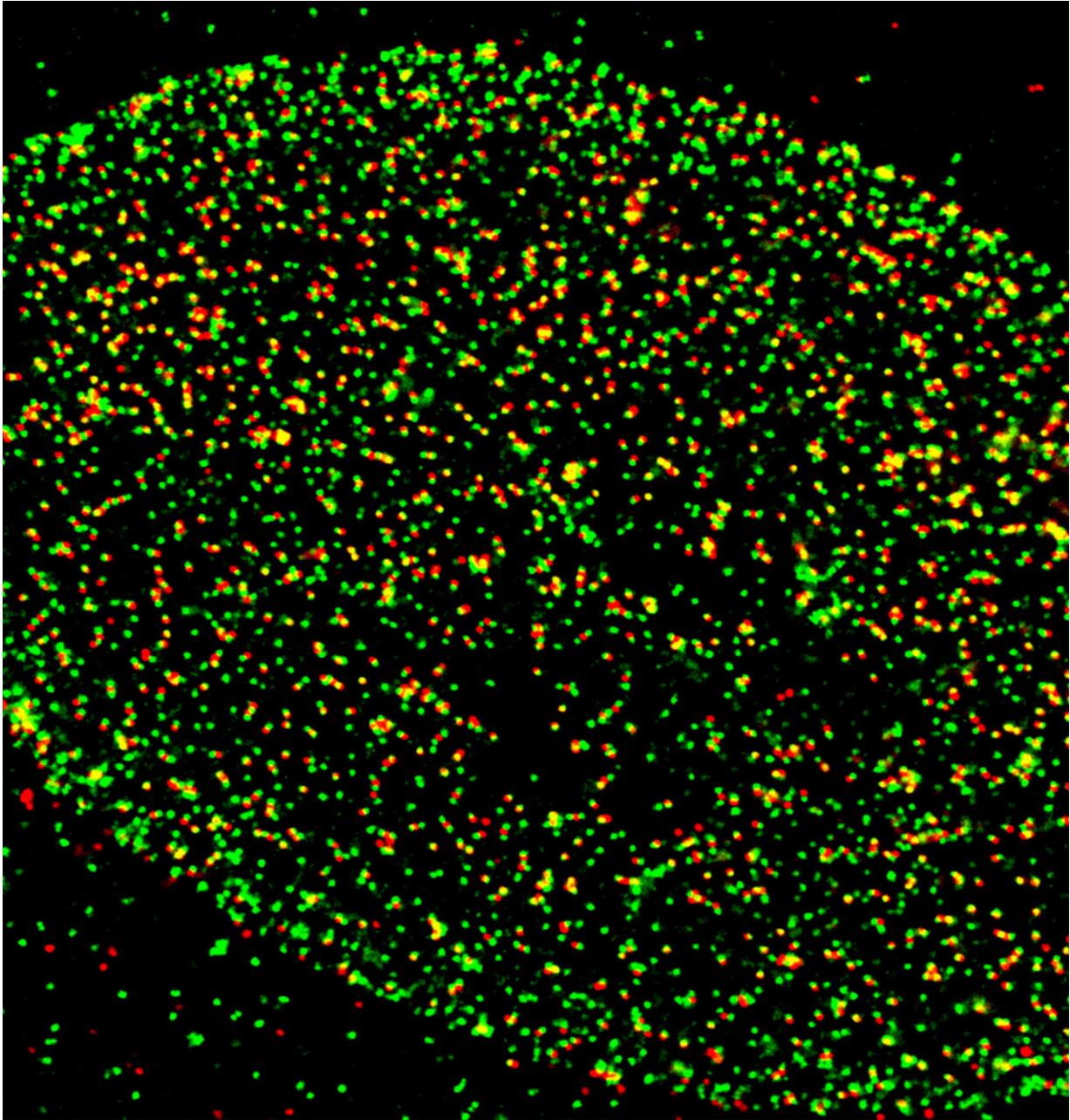
Viruses have been part of animals and humans for eons. When viruses invade a cell, they can infiltrate the nucleus with their genome and become part of the genome of the infected organism. Viruses transfer their genes between various organisms, as well as between tissues containing well-differentiated cells inside a living creature. But how they uncoat their well-packed genes and release them to cause infection is largely unknown.

Mib1 protein systematically controls virus infection

The research group of Urs Greber, professor at the Institute of Molecular Life Sciences of the University of Zurich (UZH), has now for the first time identified a protein in [human cells](#) that is key for successful viral DNA uncoating: the ubiquitin-ligase Mind bomb 1 (Mib1). "The protein enables adenoviruses to uncoat their DNA and discharge it into the nucleus—which is necessary for successful infection," says Greber. If the protein is not produced or fails to work properly, the [viruses](#) can penetrate into the cell and reach the nuclear membrane, but they remain stuck on the porous structures of the nuclear envelope. "This finding opens up a new possibility for developing anti-viral therapies that block Mib1 in well differentiated [cells](#)," says Greber. At present, there are no effective drugs to combat these widespread viruses.

Looking for door handle at nucleus entrance

Researchers found the protein by switching off most of the genes in human cells of the lung epithelium using RNA interference one by one, and then testing whether adenoviruses could infect the cells. "When we inhibited the gene for Mib1 or knocked it out using CRISPR-Cas technology, the virus infection rate declined drastically. Practically all adenoviruses remained stuck at the pore structures outside of the nucleus," says Greber. As soon as these cells, after genetic interventions, produced small amounts of Mib1 again, the Mib1 reached the viruses at the nuclear pores, and the viruses uncoated their genes and infected the cells.



Without the signal to uncoat their DNA, the adenoviruses (red) are stopped at the nuclear pore complexes of the human cell (green). Credit: Michael Bauer, University of Zurich

Adenoviruses: Life-threatening for people with weakened immune

systems

Adenoviruses are widespread in humans and many animals. In humans, they can cause infections in the respiratory system and the [gastrointestinal tract](#), as well as the kidney, liver, eyes and blood cells. For healthy people, the viruses are not life-threatening—the viruses simply settle in [immune cells](#), where they remain for months without damaging the cells or tissue. In a person with a weakened [immune system](#), however—for example stem-cell or organ transplant recipients—adenoviruses can easily spread to other cells and become life-threatening.

More information: Michael Bauer et al, The E3 Ubiquitin Ligase Mind Bomb 1 Controls Adenovirus Genome Release at the Nuclear Pore Complex, *Cell Reports* (2019). [DOI: 10.1016/j.celrep.2019.11.064](https://doi.org/10.1016/j.celrep.2019.11.064)

Provided by University of Zurich

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