

Genome editing method targets AIDS virus

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By destroying the regulatory genes of the AIDS virus HIV-1 using the genome editing system CRISPR/Cas9, a Japanese research group has succeeded in blocking the production of HIV-1 by infected cells.

Human immunodeficiency virus-1 (HIV-1) infection is a chronic disease affecting more than 35 million people worldwide. The infection can be controlled by antiretroviral therapy (ART), but there is still no complete cure. It is hard to eradicate [cells](#) latently infected with HIV-1 in a patient's body because when the virus proliferates, the viral gene is inserted into the chromosomes in the infected cells.

Genome editing methods cut specific parts of [genes](#), allowing us to remove or add sections of the DNA sequence. The recently developed CRISPR/Cas9 system is a promising tool for deactivating the HIV-1 genes that have been incorporated into the chromosomes of infected individuals.

This study targeted two genes that regulate the proliferation of HIV-1, known as *tat* and *rev*. Based on genetic information from six major HIV-1 subtypes, the team designed six types of guide RNA (gRNA) that enable specific [genome editing](#)

using the CRISPR/Cas9 system. They created a lentiviral vector that expresses Cas9 and gRNA. When they introduced this vector to cultured cells that expressed the regulatory gene products *Tat* and *Rev*, they succeeded in significantly lowering the expression and functions of both *Tat* and *Rev*. The team found no off-target mutations (non-specific genome editing that unintentionally targets the host cell genes), and the expression of Cas9 and gRNA did not affect the survival rate of the cultured cells.

By introducing gRNA and Cas9 to cultured cells with a latent or persistent HIV-1 infection, they were able to markedly suppress cytokine-dependent HIV-1 reactivation in latently infected cells and HIV-1 replication from persistently infected cells. Furthermore, by introducing all six types of gRNA at the same time, they managed to almost completely block virus production from the infected cells.

The research team was led by Associate Professor Masanori Kameoka, Assistant Professor Tomohiro Kotaki (Kobe University Graduate School of Health Sciences) and Youdiil Ophinni (Kobe University Graduate School of Medicine). The findings were published on May 17 in *Scientific Reports*.

"These results show that the CRISPR/Cas9 system, by targeting the regulatory genes of HIV-1, *tat* and *rev*, is a promising method for treating HIV infection" comments Associate Professor Kameoka.

"We now need to investigate how we can selectively introduce a CRISPR/Cas9 system that targets HIV-1 genes into the [infected cells](#) of patients. In order to safely and effectively introduce the CRISPR/Cas9 system the vectors must be improved. We hope this research will provide us with useful information in developing a treatment method that can completely cure the HIV-1 infection."

More information: Youdiil Ophinni et al. CRISPR/Cas9 system targeting regulatory genes of

HIV-1 inhibits viral replication in infected T-cell cultures, *Scientific Reports* (2018). DOI: [10.1038/s41598-018-26190-1](https://doi.org/10.1038/s41598-018-26190-1)

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