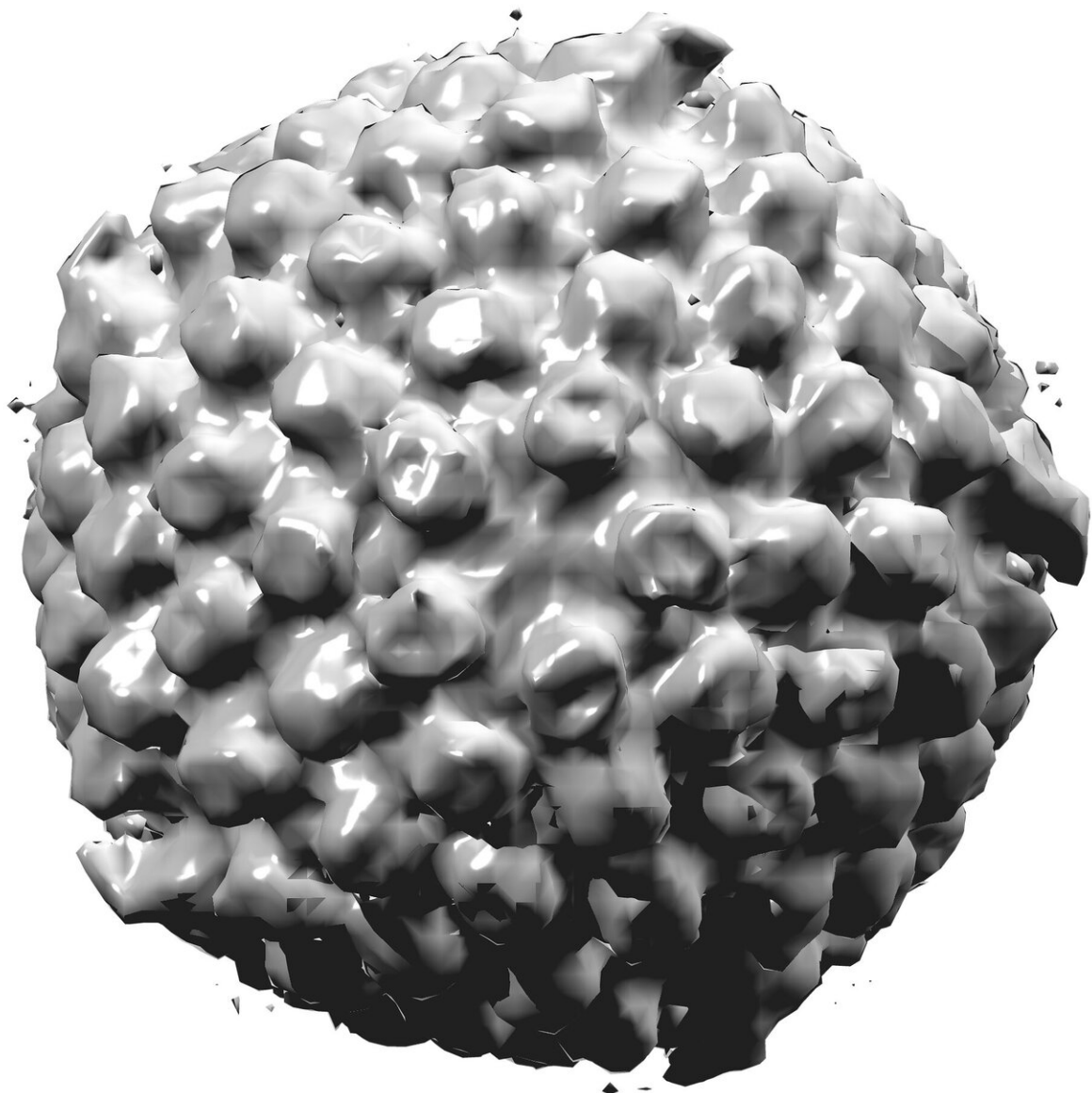


New gene therapy approach eliminates at least 90% latent herpes simplex virus 1

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Infectious disease researchers at Fred Hutchinson Cancer Research Center have used a gene editing approach to remove latent herpes simplex virus 1, or HSV-1, also known as oral herpes. In animal models, the findings show at least a 90 percent decrease in the latent virus, enough researchers expect that it will keep the infection from coming back.

The study, published August 18 in *Nature Communications*, used two sets of genetic scissors to damage the [virus](#)'s DNA, fine-tuned the delivery vehicle to the infected [cells](#), and targeted the nerve pathways that connect the neck with the face and reach the tissue where the virus lies dormant in individuals with the [infection](#).

"This is the first time that scientists have been able to go in and actually eliminate most of the herpes in a body," said senior author Dr. Keith Jerome, professor in the Vaccine and Infectious Disease Division at Fred Hutch. "We are targeting the root cause of the infection: the infected cells where the virus lies dormant and are the seeds that give rise to repeat infections."

Most research on herpes has focused on suppressing the recurrence of painful symptoms, and Jerome said that his team is taking a completely different approach by focusing on how to cure the disease.

"The big jump here is from doing this in test tubes to doing this in an animal," said Jerome, who also leads the Virology Division at UW Medicine. "I hope this study changes the dialog around herpes research and opens up the idea that we can start thinking about cure, rather than just control of the virus."

Two-thirds of the world population under the age of 50 have HSV-1, according to the World Health Organization. The infection primarily causes cold sores and is lifelong.

In the study, the researchers used two types of genetic scissors to cut the DNA of the herpes virus. They found that when using just one pair of the scissors the virus DNA can be repaired in the [infected cell](#). But by combining two scissors—two sets of gene-cutting proteins called meganucleases that zero in on and cut a segment of herpes DNA—the virus fell apart.

"We use a dual meganuclease that targets two sites on the virus DNA," said first author Martine Aubert, a senior staff scientist at Fred Hutch. "When there are two cuts, the cells seem to say that the virus DNA is too damaged to be repaired and other molecular players come in to remove it from the cell body."

The dual genetic scissors are introduced into the [target cells](#) by delivering the gene coding for the gene-cutting proteins with a vector, which is a harmless deactivated virus that can slip into infected cells. The researchers injected the delivery vector into a mouse model of HSV-1 infection, and it finds its way to the target cells after entering the nerve pathways.

The researchers found a 92% reduction in the virus DNA present in the superior cervical ganglia, the nerve tissue where the virus lies dormant. The reductions remained for at least a month after the treatment and is enough the researchers say to keep the virus from reactivating.

The team did other comparisons to fine-tune the gene editing approach:

- Gene cuts with meganucleases were more efficient than with CRISPR/Cas9.

- Refining the vector delivery mechanism, they found the adeno-associated virus (AAV) vector that was the most efficient at getting the gene edits to cells infected with the virus.

The researchers are pursuing a similar strategy for herpes simplex 2, which causes genital herpes. They expect it to take at least 3 years to move toward clinical trials.

"This is a curative approach for both oral and genital HSV infection," Aubert said. "I see it going into clinical trials in the near future."

More information: Martine Aubert et al, Gene editing and elimination of latent herpes simplex virus in vivo, *Nature Communications* (2020). DOI: [10.1038/s41467-020-17936-5](https://doi.org/10.1038/s41467-020-17936-5)

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