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One Edit Closer to a Cure for HIV: CRISPR and CCR5 mutants

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CRISPR and CCR5 mutants

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One of the most notable incurable diseases of the past century is Acquired Immunodeficiency Syndrome (AIDS). However, in the past five years, there have been some notable advances in treatment for HIV-AIDS. In September 2019, Chinese scientists demonstrated the use of clustered regularly-interspaced short palindromic repeats (CRISPR)-edited donor stem cells to treat an HIV-positive man with leukemia for approximately nineteen months without serious side effects, though the number of edited cells was not enough to cure the man's HIV. While similar experiments were carried out in 2007 and 2014, this study demonstrates more clearly how gene-editing can play an important and successful role in treating a seemingly incurable disease like HIV.

HIV has a shorter history than most other viruses, such as tuberculosis, polio, and influenza, whose histories date back centuries. Researchers first discovered the virus in the blood of a man from the Democratic Republic of the Congo in the early 1900s and believe the virus was spread from chimpanzees to humans sometime before 1931 from hunting encounters. HIV was first discovered in the United States Midwest in 1968. It is not clear how the virus got to the U.S. because the first infected man had no history with unsanitary blood transfusions or unprotected sexual activities. When the epidemic began in the 1980s, HIV was heavily stigmatized through its association with gay men; the CDC even called it gay-related immunodeficiency syndrome (GRIDS). People falsely believed that only men who have sex with other men could contract HIV.

During the past four decades, HIV expertise has increased throughout the world, with treatments more widely available. Doctors are now able to treat HIV more effectively than ever before. The virus' life cycle is exhaustively documented. Medications, like pre-exposure prophylaxis (PrEP), a preventative contraction process; antiretroviral drugs, like Combivir; and over twenty other FDA approved drugs, are making the virus more treatable, and mortality rates are down 80% since 1995.

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The goal of HIV research today is to create new ways to kill the virus in the long term. Antiretroviral drugs are becoming less invasive, from an injection, to a handful of pills, to a single pill. Researchers are working on vaccines to prevent the spread of the virus. Meanwhile, HIV-positive individuals now experience a better quality of life than in any other decade, with viral loads of HIV infected cells nearing zero in those with high compliance to medication. However, scientists have still not found a cure. So, how are they going about finding one?

The first clue may lie within our genes. In 2007, a man in Berlin was the first person to be cured of HIV. Timothy Ray Brown underwent a bone marrow transplant to treat his leukemia. The bone marrow contained a version of the CCR5 gene that encodes immunity to HIV and is what caused Brown to become HIV free. While only about 1% of those with European descent have this mutation of their CCR5 gene, it is virtually nonexistent in all other ethnic groups, so it is difficult to find donors with this curable mutation. In March of 2019, another person underwent a similar procedure to Brown and appears to have no trace of the virus. Knowing that mutated CCR5 has the potential for a cure, researchers Xu et al. decided to use CRISPR, the new leading gene-editing technology, to create these CCR5 mutants from donor stem cells themselves. The subject was a 27-year-old HIV-positive Chinese man with leukemia who received a bone marrow transplant as Brown had in 2007. Researchers described the process as being very tough, and eventually, they were able to edit only 17.8% of the donor's stem cells. Their study, published in September of 2019 in the New England Journal of Medicine, has the potential to make a cure more accessible because of its use of donor stem cells.

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The researchers found that after 19 months, the CRISPR-edited stem cells did persist, although they comprised only 5–8% of the recipient's total stem cells. This means that a little over one-half of the edited cells died in the man's body after they were transplanted. And although the man's leukemia is in remission, he is still infected with HIV. This result is clearly not the ultimate goal, but the researchers believe it is an important first step in treating HIV using CRISPR gene-editing technology. Greater therapeutic benefits in future trials may come when CRISPR-edited cells make at least 5-8% of the recipient's total stem cells moving forward.

CRISPR is still a new technology with massive unexplored potential. Every research study comes closer to unlocking the solution to killing HIV. If researchers keep putting their time and effort into studies like Xu and their colleagues, HIV-positive individuals living today could see a cure in their lifetime. • • •