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HIV overcomes CRISPR gene-editing attack

-Ravi Mandla

HIV has long been a global epidemic that has taken the lives of millions of people. However, with further advances in technology and molecular biology, scientists hope to apply new breakthroughs in their quest to cure HIV.

Also known as human immunodeficiency virus, HIV is a type of virus that infects a person's T cells, or their immune system. HIV works by attaching itself to one of these cells, merging its RNA with the DNA of the host cell, and then using this cell's own resources to mass produce more HIV to infect other cells. Eventually, this drains the T cells and kills them. Having no more T helper cells, a person is no longer able to fight infections by themselves and are classified as having AIDS, or acquired immune deficiency syndrome.

This disease has long eluded a cure due to its incredibly fast rate of mutation. The HIV virus is constantly changing, and this makes any attempts at prevention and alleviation of infection very difficult. Recently, scientists tried directly cutting the genes of HIV to try and render the virus innate.

This process was made possible through the use of the CRISPR/Cas9 system, a method by which a Cas9 enzyme cuts out a specific region of a genome, rendering that section useless. Cas9 is accompanied by a guiding RNA segment, which helps specify which sections of the genome that Cas9 should cut. The scientists essentially "armed" the helper T-cells with Cas9 and the appropriate guiding RNA segment so that these cells can specifically cut out any HIV virus inserted inside of themselves, essentially killing the virus.

T-cells with the Cas9 enzymes were cultured in vitro, or outside of the body, and then exposed to the HIV virus. Unfortunately, HIV continued to replicate itself within the cultures, signifying that the Cas9 method failed. Upon examination of the HIV viruses created, they found signs of mutations occurring around the regions where its genome was supposed to be cut by the Cas9. This has prompted two theories:

1. In the process of translating its RNA to DNA, the HIV virus created so many errors that Cas9 no longer could recognize and cut this DNA out of the infected host cell.
2. The mutations occurred after being cut. Usually, when Cas9 cuts out a region of a genome, the cell tries to repair those regions. However, most of the time these attempts only render that area innate. However, it is possible that the repairing of the HIV DNA segment actually worked, and created a new sequence of nucleic acids that still function as HIV.

Regardless of which scenario is true, now that the HIV viruses have mutated, this same approach can no longer work. This is because the mutations of the HIV DNA were extensive enough so that now the Cas9 cannot detect the viral DNA because of these immense changes.

Even with our advances in technology, viruses and infections continue to plague society. But although this method of prevention failed, scientists believe that cutting out multiple essential genes, or combining Cas9 with other HIV-attacking drugs might produce more promising results. Many are also

trying to make T cells resistant to HIV insertion in the first place. Though currently hindered, a genetic approach to stopping HIV may not be that far away.

References:

Article: http://www.nature.com/news/hiv-overcomes-crispr-gene-editing-attack-1.19712

Paper: http://www.cell.com/cell-reports/abstract/S2211-1247(16)30298-4