The promise of genetic therapy for HIV

As early as 1988, researchers published their ideas about using genetic therapy to try to cure HIV infection. However, it is only in the last several years that diverse approaches to genetic therapy are being pursued.

The VIRxSYS Corporation (Gaithersburg, Maryland, U.S.) has developed a gene therapy for helping CD4+ T cells resist the destructive effects of HIV infection. This experimental therapy is called VRX496, or Lexgenleucel.

The therapy works by infecting cells with the genetic material for incorrectly making HIV-related proteins. Cells treated with VRX496 and infected with HIV produce copies of HIV that are defective.

In a clinical trial, five HIV-positive participants whose ART was failing received a single intravenous infusion of VRX496-treated CD4+ T cells. Researchers found that as a result of this, participants’ CD4+ counts temporarily rose and in one participant viral load fell by as much as 100-fold. Importantly, this genetic therapy was found to be safe.

Based on these promising results, researchers proposed that multiple infusions of gene-therapy-treated CD4+ cells would likely be more effective.

The latest study

The most recent report of VRX496 involved 17 HIV-positive participants, all of whom were taking ART. Therapy with VRX496 was generally safe. When ART was interrupted, viral load rose and then fell modestly. Side effects related to the infusion of T cells included temporary fever and chills.

For the most part, the infused T cells disappeared from the body within weeks. However, in some participants the genetically fortified T cells were still present, albeit in very small amounts, up to five years after their infusion. The reason for their disappearance is not known.

Making the cells last

Giving participants more than three infusions of these treated cells did not make the cells last any longer in the body. The research team involved with this study suggests that “conditioning agents” may be a remedy for helping the body to retain the modified T cells. Conditioning agents is coded language for intensive chemotherapy and radiation. However, such therapies would be accompanied by greatly increased toxicity. Long before researchers can consider this approach much more potent and sophisticated gene therapy would be required.

Hitting several spots at once

Led by France’s premier scientific research agency, the ANRS (Agence nationale de recherches sur le sida et les hépatites virales), researchers in France, Austria, Germany, Italy and the U.S. are planning to conduct clinical trials of a gene therapy that has the potential to interfere with key HIV proteins (called Tat, Rev and Vif) and to also block the CCR5 receptor of cells. Such a multifaceted approach carries the possibility of not only protecting cells from the entry of HIV but also helping the immune system overcome the toxic effect of HIV’s proteins.

—Sean R. Hosein

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