MedicalXpress

Genetically modified T cell therapy shown to be safe, lasting in decade-long study of HIV patients

May 2 2012

HIV patients treated with genetically modified T cells remain healthy up to 11 years after initial therapy, researchers from the Perelman School of Medicine at the University of Pennsylvania report in the new issue of *Science Translational Medicine*. The results provide a framework for the use of this type of gene therapy as a powerful weapon in the treatment of HIV, cancer, and a wide variety of other diseases.

"We have 43 patients and they are all healthy," says senior author Carl June, MD, a professor of Pathology and Laboratory Medicine at Penn Medicine. "And out of those, 41 patients show long term persistence of the modified T cells in their bodies."

Early gene therapy studies raised concern that gene transfer to cells via retroviruses might lead to leukemia in a substantial proportion of patients, due to mutations that may arise in genes when new DNA is inserted. The new long-term data, however, allay that concern in T cells, further buoying the hope generated by work June's team published in 2011 showing the eradication of tumors in patients with chronic lymphocytic leukemia using a similar strategy.

"If you have a safe way to modify cells in patients with HIV, you can potentially develop curative approaches," June says. "Patients now have to take medicine for their whole lives to keep their virus under control, but there are a number of gene therapy approaches that might be

curative." A lifetime of anti-HIV drug therapy, by contrast, is expensive and can be accompanied by significant side effects.

They also note that the approach the Penn Medicine team studied may allow patients with cancers and other diseases to avoid the complications and mortality risks associated with more conventional treatments, since patients treated with the modified T cells did not require drugs to weaken their own immune systems in order for the modified cells to proliferate in their bodies after infusion, as is customary for cancer patients who receive stem cell transplants.

To demonstrate the long-term safety of genetically modified T cells, June and colleagues have followed HIV-positive patients who enrolled in three trials between 1998 and 2002. Each patient received one or more infusions of their own T cells that had been genetically modified in the laboratory using a retroviral vector. The vector encoded a chimeric antigen receptor that recognizes the HIV envelope protein and directs the modified T cell to kill any HIV-infected cells it encounters.

As is standard for any trial, the researchers carefully monitored patients for any serious adverse events immediately after infusion -- none of which were seen. Additionally, because of the earlier concerns about long-term side effects, the U.S. Food and Drug Administration also asked the team to follow the patients for up to 15 years to ensure that the modified T cells were not causing blood cancers or other late effects. Therefore, each patient underwent an exam and provided blood samples during each of the subsequent years.

Now, with more than 500 years of combined patient safety data, June and colleagues are confident that the retroviral vector system is safe for modifying T cells. By contrast, June notes, the earlier, worrying side effects were seen when viral vectors were used to modify blood stem cells. The new results show that the target cell for gene modification

plays an important role in long-term safety for patients treated. "T cells appear to be a safe haven for gene modification," June says.

The multi-year blood samples also show that the gene-modified T cell population persists in the patients' blood for more than a decade. In fact, models suggest that more than half of the T cells or their progeny are still alive 16 years after infusion, which means one treatment might be able to kill off HIV-infected cells for decades. The prolonged safety data means that it might be possible to test T cell-based gene therapy for the treatment of non-life threatening diseases, like arthritis.

"Until now, we've focused on cancer and HIV-infection, but these data provide a rationale for starting to focus on other disease types," June says. "What we have demonstrated in this study and recent studies is that gene transfer to T cells can endow these cells with enhanced and novel functions. We view this as a personalized medicine platform to target disease using a patient's own cells."

Provided by University of Pennsylvania School of Medicine

Citation: Genetically modified T cell therapy shown to be safe, lasting in decade-long study of HIV patients (2012, May 2) retrieved 24 April 2024 from https://medicalxpress.com/news/2012-05-genetically-cell-therapy-shown-safe.html