Biotech Innovations

Case Study: Engineered T Cells Shrank Pancreatic Cancer Tumors

Metastatic pancreatic cancer tumors shrank by nearly three-quarters 6 months after a patient received a single infusion of engineered autologous T cells targeting a common *KRAS* gene variant, according to a case study published in the *New England Journal of Medicine*.

The therapy centered on genetically modifying the patient's own T cells to express 2 T-cell receptors (TCRs) targeting the *KRAS* G12D variant expressed by the tumors. The study authors noted that autologous tumor-infiltrating lymphocyte therapy targeting the same *KRAS* variant in a patient with colorectal cancer had led to metastatic tumor regression, suggesting the T-cell therapy could help patients with pancreatic ductal adenocarcinoma, which frequently expresses *KRAS* G12D.

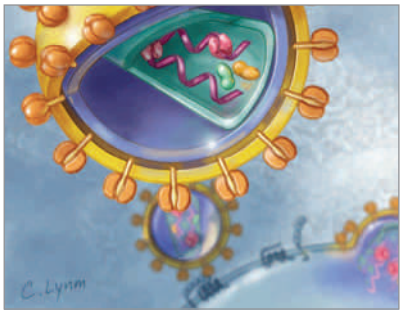
Before receiving the engineered T cells, the patient's cancer had progressed despite chemotherapy, surgery, chemoradiotherapy, radiotherapy, autologous lymphocyte therapy, and interleukin 2 therapy. One month after the infusion, lung metastases had regressed by 62%. At 6 months, overall partial response reached 72% and engineered cells represented about 2.4% of circulating T cells.

According to an accompanying editorial, about 41% of patients with pancreatic ductal adenocarcinoma have the *KRAS* G12D variant, which drives cancer proliferation. However, the editorial noted that only about 11% of Black people and 8% of White people in the US have the HLA antigen allele needed to present G12D on the cell surface so the engineered T cells can detect it. This limits the studied treatment's potential, although similar therapies may be possible for other mutations and HLA antigen alleles.

The study authors noted that although the durability of their patient's clinical response hasn't been determined, the case report shows that TCR gene therapy targeting the *KRAS* G12D variant facilitated metastatic pancreatic cancer regression.

Dual Anti-HIV Antibodies Provide Long-term Viral Suppression

Treatment with 2 monoclonal antibodies completely suppressed HIV for about 40 weeks in patients who participated in a small phase 1 trial. The findings, reported in *Nature*, suggest that future antibody therapies may offer effective HIV treatment for extended periods without antiretroviral therapy (ART).



In the first trial component, 14 patients taking ART randomly received a combination of 2 broadly neutralizing anti-HIV antibodies or placebo up to 8 times in 24 weeks. ART was stopped shortly after their first infusions. None of the 7 patients receiving antibodies had to restart ART within 28 weeks after the last infusion, compared with 6 of the 7 in the placebo group. Median time off of ART was 39.6 weeks in the antibody group and 9.4 weeks in the placebo group.

In the second trial component, 5 patients with a low HIV viral load who never took ART received the antibodies. Two of the 5 maintained complete viral suppression, lasting an average of 41.7 weeks after infusion. No safety issues occurred in the study, and infusions were well tolerated.

The antibody combination was ineffective in patients with HIV that was resistant to 1 or both antibodies. However, future antibodies with greater potency and durability, possibly supplemented with injectable long-term antiretroviral drugs, "could lead to ART-free HIV suppression for extended periods (years)," the authors wrote.

Dissolving "Smart" Pacemaker Design for Temporary Heart Pacing

An implantable, dissolving "smart" cardiac pacemaker has been designed for patients who need temporary pacing after cardiovascular surgery, according to a report in *Science*. The device could eliminate prolonged hospitalizations and infection risks associated with temporary pacemakers that keep patients tethered to external monitors and power packs with percutaneous lead wires.

Consisting of a stretchable, battery-free implanted cardiac pacemaker and 4 flexible external modules that adhere to the skin, the implant has been tested in vivo on rat and canine hearts and ex vivo on a human heart. The device provides pacing on demand and dissolves slowly and harmlessly when it's no longer needed. It releases an anti-inflammatory drug to prevent foreign-body reactions.

The 4 soft modules track physiological functions including heart rhythm, blood oxygen level, and respirations. A module placed on the chest can record real-time electrocardiograms. The modules also communicate with the patient using vibrations indicating malfunctions, heart rate, and low batteries in the external modules.

Communicating wirelessly as a closed-loop system, the pacemaker and modules decide when and how to stimulate the heart based on algorithms without external inputs. The components interface with a smartphone or tablet, which acts as a control module and allows physicians to monitor patients remotely.

"It introduces an interesting concept," Jim Cheung, MD, professor of medicine at Weill Cornell Medicine and chair of the Electrophysiology Section Leadership Council at the American College of Cardiology, said in an interview. However, the design is preliminary and more testing in animals and ultimately patients is needed. "It does appear to be potentially useful for temporary pacing after valve or bypass surgery," said Cheung, who isn't involved with the research. **– Howard D. Larkin**

Note: Source references are available through embedded hyperlinks in the article text online.