

USING THE IMMUNE SYSTEM TO BATTLE CANCER

Researchers are now developing tumor-specific vaccines that present the body's own immune cells with tumor-associated antigens in order to elicit an immune response that specifically targets cancerous cells. There is currently one such vaccine on the market—Sipuleucel-T (below, left), which is made by Seattle-based cancer research company Dendreon and was approved in 2010 as a last-resort treatment for metastatic prostate cancer. Similar treatments for some other cancers are now in late-stage clinical trials.

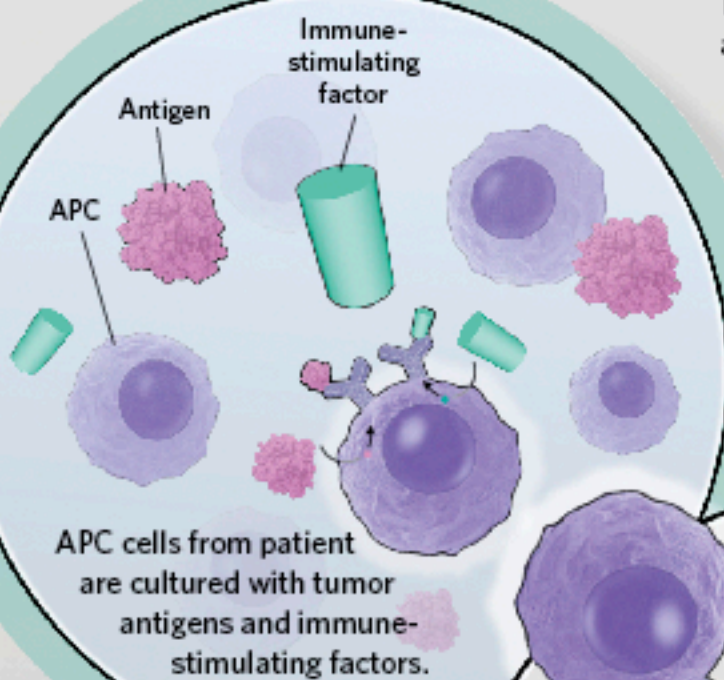
Other strategies aim to maintain T cells in an active state so they can continue the fight against cancer. One approach is to block the inhibitory pathways known as immune checkpoints that halt the immune response using drugs that block these inhibitory signals (box, right). The FDA approved the humanized monoclonal antibody ipilimumab (marketed by Bristol-Myers Squibb as Yervoy) for the treatment of advanced melanoma in 2011, and researchers are now testing the drug in patients with other cancers, as well as developing similar immune checkpoint blockade therapies.

A third immunotherapy currently under development is known as adoptive T-cell transfer. This treatment involves isolating T cells from a patient; expanding them in the lab, where they can be trained to more effectively target the cancer; then reinfusing them into the body. To increase the efficacy of the method, researchers are genetically engineering patients' T cells to express receptors specific for the tumor (below right).

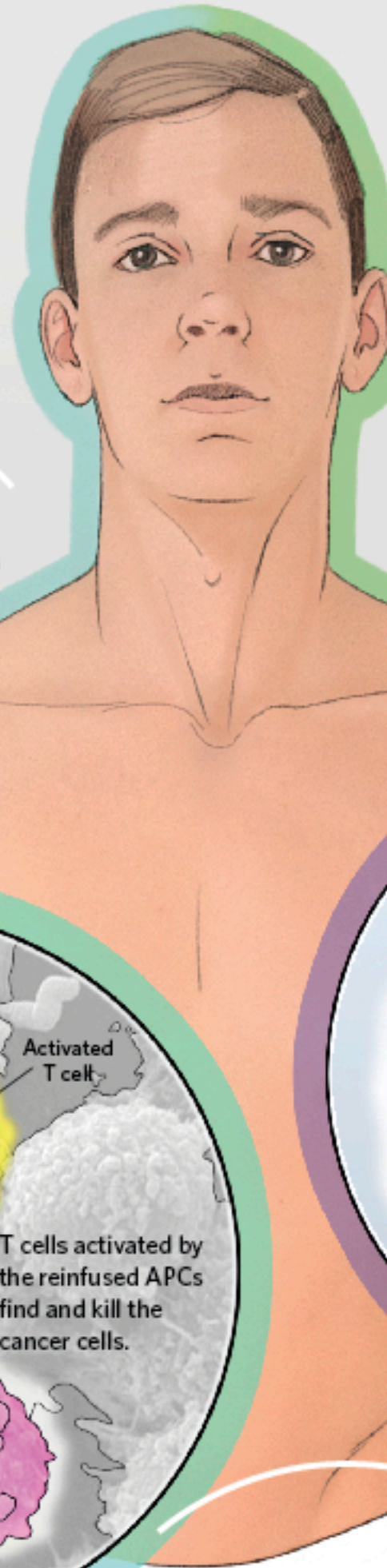
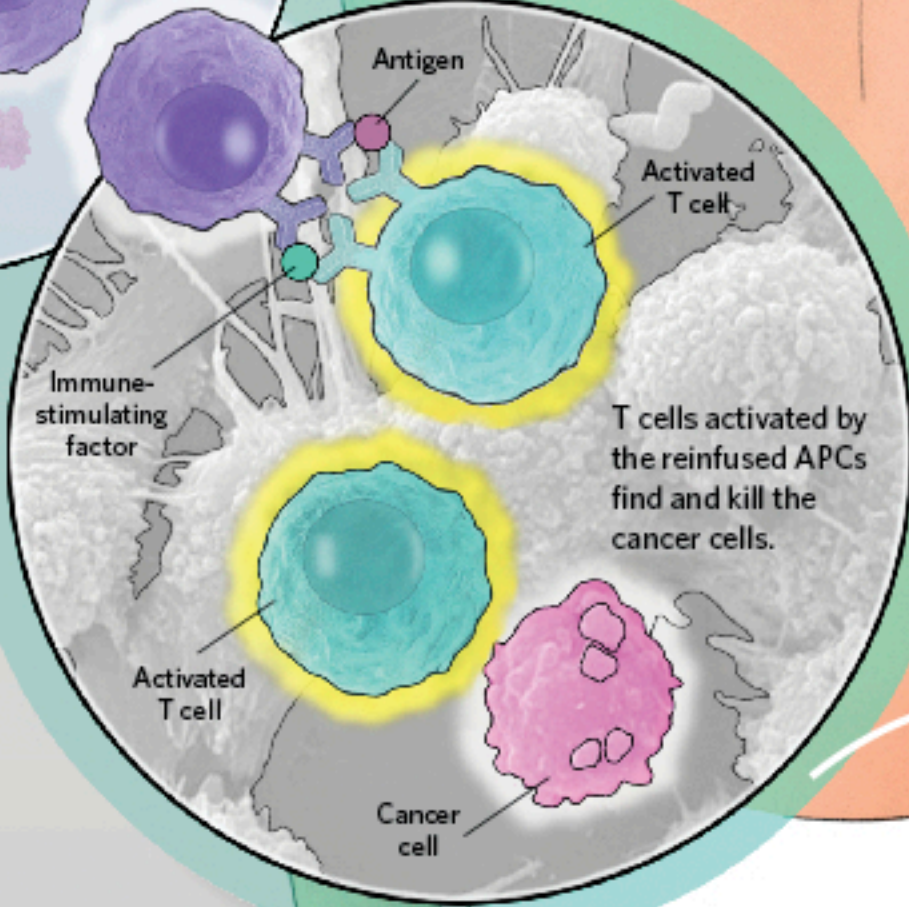
VACCINATING CANCER

Most cancer vaccines in development involve an injection containing a component of a tumor-specific antigen, with the goal of increasing the immune system's tumor-specific activity. Others, such as Sipuleucel-T, involve the extraction of a patient's antigen-presenting cells (APCs), which are cultured with tumor antigens along with immune-stimulating factors to prime the APCs to activate T cells in the body.

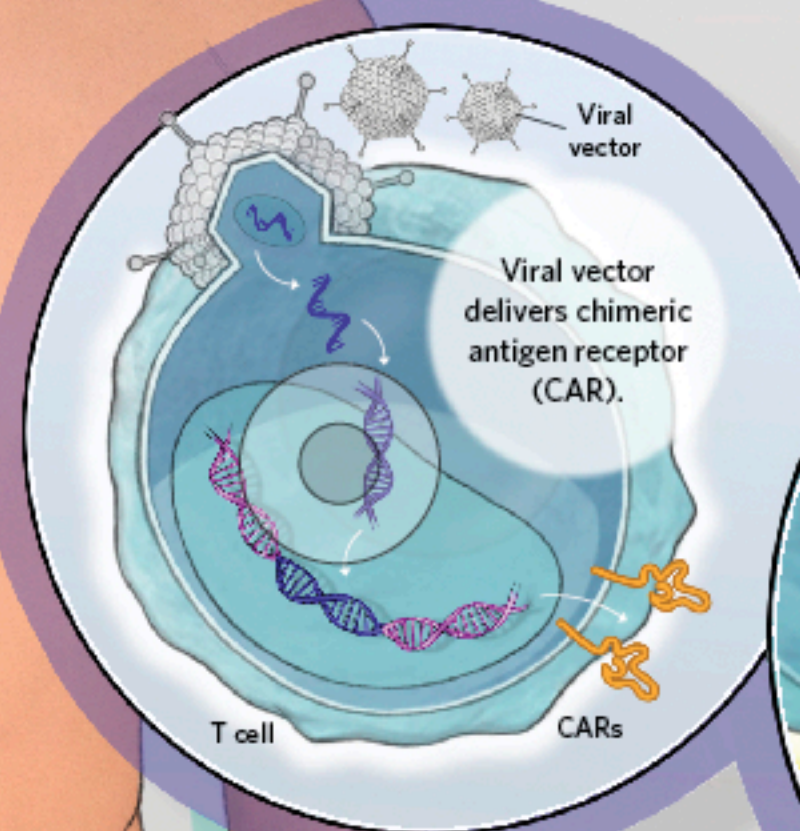
Extraction of a patient's antigen-presenting cells (APCs)



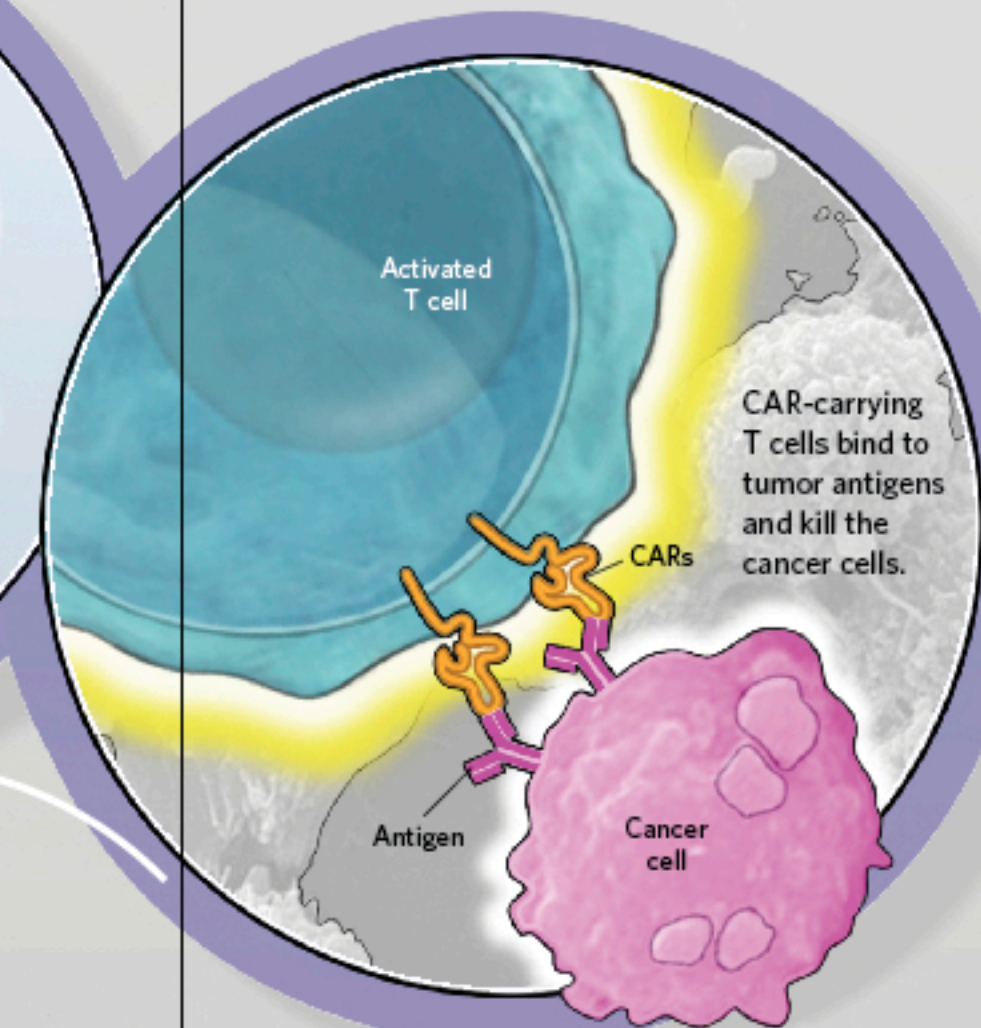
APC cells from patient are cultured with tumor antigens and immune-stimulating factors.



Extraction of a patient's T cells



Cells infused back into patient



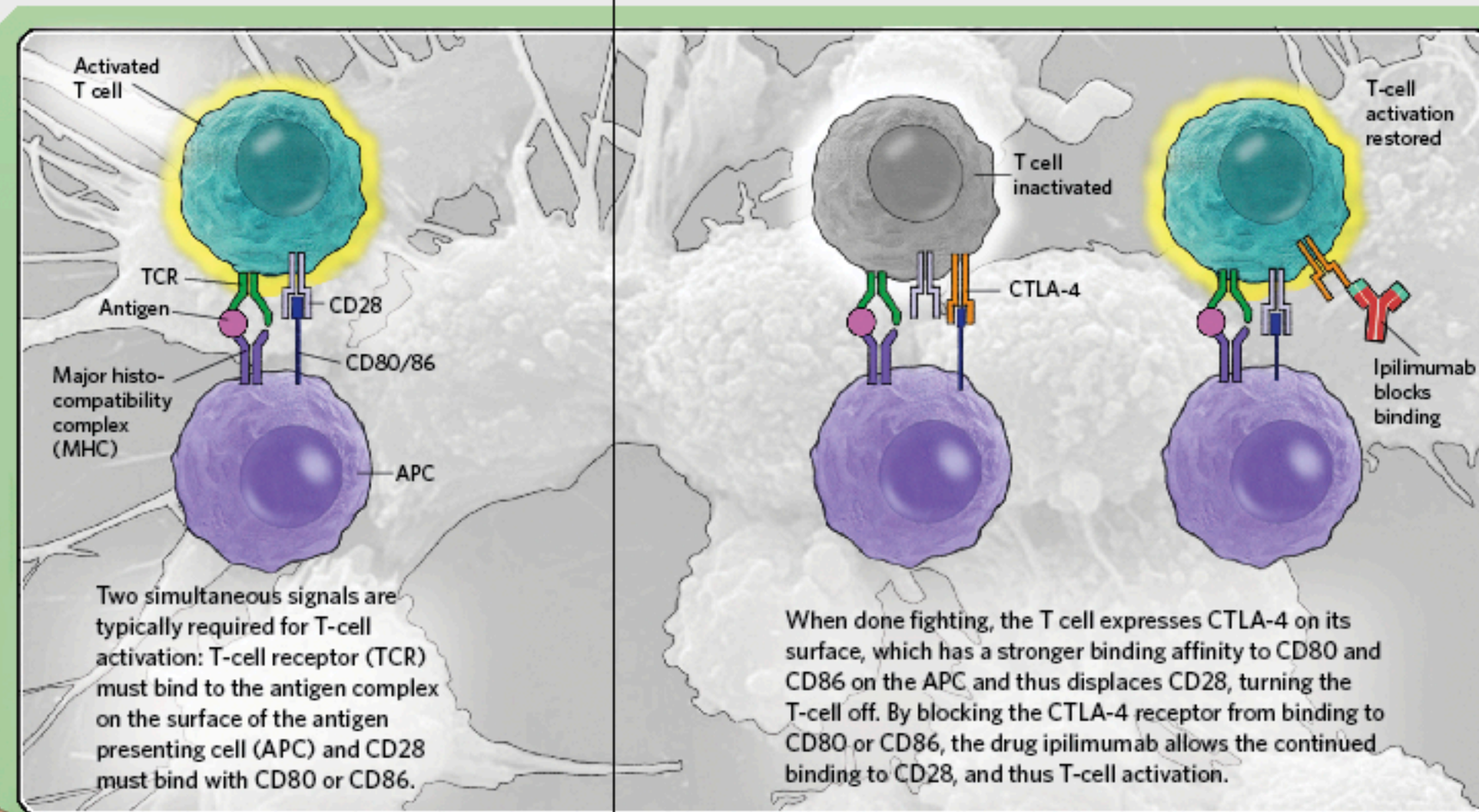
CAR-carrying T cells bind to tumor antigens and kill the cancer cells.

T-CELLS TO THE RESCUE

In adoptive T-cell transfer, T cells isolated from a patient's blood or tumor are transfected with a virus to express cancer-targeting chimeric antigen receptors (CARs), arming the cells to attack the cancer once reinfused into the patient.

DON'T STOP FIGHTING

Immune checkpoint blockade therapies work by preventing the immune response from turning off when it normally would. By blocking these immune checkpoints using molecules that bind T-cell surface proteins such as cytotoxic T-lymphocyte antigen 4 (CTLA-4) or programmed death-1 receptor (PD-1), which are expressed on activated T-cells and normally dampen the immune response, the treatments are able to maintain an active immune attack.



Two simultaneous signals are typically required for T-cell activation: T-cell receptor (TCR) must bind to the antigen complex on the surface of the antigen presenting cell (APC) and CD28 must bind with CD80 or CD86.

When done fighting, the T cell expresses CTLA-4 on its surface, which has a stronger binding affinity to CD80 and CD86 on the APC and thus displaces CD28, turning the T-cell off. By blocking the CTLA-4 receptor from binding to CD80 or CD86, the drug ipilimumab allows the continued binding to CD28, and thus T-cell activation.