HOW TO HARNESS THE IMMUNE SYSTEM

Chimeric antigen receptor T cells (CARTs) are made by reprogramming a patient’s own immune cells to home in on cancer.

1. Extracting T cells: A patient is hooked up to a machine akin to a centrifuge that separates out white blood cells, including T cells, and returns red cells and platelets to the patient. The resulting pink bag of cells is sent to the manufacturing facility for reprogramming.

2. Reprogramming: At the manufacturing facility, a viral vector inserts into T cells the genes carrying the instructions for a chimeric antigen receptor, or CAR. The CAR consists of an antibody domain that can recognize specific cancer cells; a hinge and transmembrane domain that tethers the antibody to the cell; and costimulatory and essential activity domains, which together signal the cell to divide.

3. Manufacturing: To elicit a powerful response in the patient, oncologists need to return many more of the reprogrammed T cells than they drew out. Reprogrammed T cells are “expanded” in a bioreactor with the help of magnetic beads coated with two antibodies, anti-CD3 and anti-CD28, that signal the T cells to proliferate. After the expansion, which takes about 10 days, the magnetic beads are washed out.

4. Patient preparation: The patient is given chemotherapy to lower his or her white blood cell count, thus increasing the chance that the immune system will accept the modified T cells.

5. Treatment: The reprogrammed T cells are infused back into the patient’s blood. Once in circulation, they search for and destroy cancer cells expressing the antigen targeted by the CAR.

SOURCES: C&EN, Novartis, U of Pennsylvania, Kite Pharma