Immunotherapy as a Universal Cancer Treatment

A universal cancer treatment might seem unattainable since there exist a multitude of cancers that respond differently to various treatments and treatments for the same cancer are not always effective among different patients (1). At the cutting edge of cancer treatment are two types of immunotherapy in which T-cells are genetically modified to target and kill cancer cells. There is a class of T-cells that kills cells infected with bacteria or viruses in order to contain an infection. With advances in immune therapy, T-cells can be modified to target cancer cells. While CAR-T, and TCR-T therapies are the two most promising immune-therapy techniques, both of these therapies have side effects and technical challenges. As shown in Figure A (2), CAR-T Therapy (Chimeric Antigen Receptor T-cell) therapy uses T-cells typically isolated from a patient’s peripheral blood and then inserted with genetically modified chimeric antigen receptors (CARs) (3). These CARs are modified to match specific antigens, or recognizable parts, of cancer cells. After being injected back into the patient, the CARs bind to the cancer cells causing an immune response that kills the cancer cells. There are a number of limitations to CAR-T therapy including: it does not work on solid tumors that are the most common form of cancer, the therapy targets a specific-person’s cancer cells and must be redesigned for each patient, and it can cause a common, possibly deadly, side effect called a T-cell storm where the T-cells attack normal tissue and can lead to organ failure and death (3).

Figure A. An overview of CAR-T therapy. T-cells are removed from the patient, genetically modified to recognize cancer cells, grown in the lab, and then put back into the patient where they can attack the cancer.
While attempting to discover a type of T-cell that would recognize a multitude of different bacteria, a team of researchers at Cardiff University found a T-cell that could kill many types of cancers. As shown in Figure B, these T-cells utilize a T-cell receptor (TCR), which detects a protein present on the membrane of nearly all cancer cells (4, 5).

In an attempt to gain a more complete understanding of how the TCR detects these cells, the researchers used CRISPR-Cas 9 gene editing to systematically delete specific surface proteins of the target cancer cells. After deleting a protein called MR-1, the T-cells no longer killed the cancer cells, indicating they had found the protein targeted by the TCRs. Because MR-1 is present on the surface of many healthy cells as well, it had not been identified previously as a possible cancer treatment. Miraculously, the TCR of this specific T-cell was able to differentiate between the MR-1 proteins of cancer cells and those found on healthy cells (6).

This method has not yet been tested in human subjects but, in mice, T-cells killed all the cancer cells of many different types of cancer. Unlike traditional CAR-T cell therapy, the TCR did not have to be tailored for each individual because MR-1 does not differ from patient to patient, so the same receptors work universally. TCR therapy also shows greater promise in treating solid tumors than CAR-T cell therapy (7). A potential hazard of this new therapy is that the researchers do not yet understand how the TCR differentiates between healthy and cancerous cells. Without a complete understanding of how these cells differentiate, there is no guarantee that the T-cells will not attack healthy cells, even if they haven’t in early non-human trials (5).

The research team from Cardiff University has teamed up with Ervaxx, a UK biotechnology company that specializes in developing immunotherapy technology. The treatment is currently undergoing safety testing, in preparation for its first human trials. This immunotherapy could prove to be a universal cancer treatment, so long as it does not target healthy cells and cause an autoimmune side effect similar to the one that plagues CAR-T therapy (7).

A universal cancer treatment would be a major treatment to the second leading cause of death in the United States. Nearly everyone knows someone who has died from cancer. This discovery opens the possibility for a world where we could prevent many more cancer-related deaths.
Works cited: