



## Cancer Immunotherapy: Break through or deja vu, all over again?

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Cancer immunotherapy, also known as immuno-oncology, is a form of cancer treatment that uses the power of the body's own immune system to prevent, control, and eliminate cancer. Cancer immunotherapy comes in a variety of forms, including targeted antibodies, cancer vaccines, adoptive cell transfer, tumor-infecting viruses, checkpoint inhibitors, cytokines, and adjuvants. Immunotherapies are a form of biotherapy (also called biologic therapy or biological response modifier (BRM) therapy) because they use materials from living organisms to fight disease. Some immunotherapy treatments use genetic engineering to enhance immune cells' cancer-fighting capabilities and may be referred to as gene therapies. Many immunotherapy treatments for preventing, managing, or treating different cancers can also be used in combination with surgery, chemotherapy, radiation, or targeted therapies to improve their effectiveness. Immunotherapy is treatment that uses certain parts of a person's immune system to fight diseases such as cancer. This can be done in a couple of ways: Stimulating, or boosting, the natural defenses of your immune system so it works harder or smarter to find and attack cancer cells. Making substances in a lab that are just like immune system components and using them to help restore or improve how your immune system works to find and attack cancer cells. In the last few decades immunotherapy has become an important part of treating some types of cancer. New immunotherapy treatments are being tested and approved, and new ways of working with the immune system are being discovered at a very fast pace. Immunotherapy works better for some types of cancer than for others. It's used by itself for some of these cancers, but for others it seems to work better when used with other types of treatment. Immune system is a collection of organs, special cells, and substances that help protect you from infections and some other diseases. Immune cells and the substances they make travel through your body to protect it from germs that cause infections. They also help protect you from cancer in some ways. The immune system keeps track of all of the substances normally found in the body. Any new substance that the immune system doesn't recognize raises an alarm, causing the immune system to attack it. For example, germs contain substances such as certain proteins that are not normally found in the human body. The immune system sees these as "foreign" and attacks them. The immune response can destroy anything containing the foreign substance, such as germs or cancer cells.

The immune system has a tougher time targeting cancer cells, though. This is because cancer starts when normal, healthy cells become changed or altered and start to grow out of control. Because cancer cells actually start in normal cells, the immune system doesn't always recognize them as foreign. Clearly there are limits on the immune system's ability to fight cancer on its own, because many people with healthy immune systems still develop cancer: Sometimes the immune system doesn't see the cancer cells as foreign because the cells aren't different enough from normal cells. Sometimes the immune system recognizes the cancer cells, but the response might not be strong enough to destroy the cancer. Cancer cells themselves can also give off substances that keep the immune system from finding and attacking them. To overcome this, researchers have found ways to help the immune system recognize cancer cells and strengthen its response so that it will destroy them. In this way, your own body is actually getting rid of the cancer, with some help from science. Immune checkpoint inhibitors, which are drugs that block immune checkpoints. These checkpoints are a normal part of the immune system and keep immune responses from being too strong. By blocking them, these drugs allow immune cells to respond more strongly to cancer. T-cell transfer therapy, which is a treatment that boosts the natural ability of your T cells to fight cancer. In this treatment, immune cells are taken from your tumor. Those that are most active against your cancer are selected or changed in the lab to better attack your cancer cells, grown in large batches, and put back into your body through a needle in a vein. T-cell transfer therapy may also be called adoptive cell therapy, adoptive immunotherapy, or immune cell therapy. Researchers are focusing on several major areas to improve immunotherapy, including: Researchers are testing combinations of immune checkpoint inhibitors and other types of immunotherapy, targeted therapy, and radiation therapy to overcome resistance to immunotherapy. Only a small portion of people who receive immunotherapy will respond to the treatment. Finding ways to predict which people will respond to treatment is a major area of research. A better understanding of how cancer cells get around the immune system could lead to the development of new drugs that block those processes.

The idea of exploiting the host's immune system to treat cancer dates back decades and relies on the insight that the immune system can eliminate malignant cells during initial

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transformation in a process termed immune surveillance . Individual human tumors arise through a combination of genetic and epigenetic changes that facilitate immortality, but at the same time create foreign antigens, the so-called neo-antigens, which should render neoplastic cells detectable by the immune system and target them for destruction. Nevertheless, although the immune system is capable of noticing differences in protein structure at the atomic level, cancer cells manage to escape immune recognition and subsequent destruction. To achieve this, tumors develop multiple resistance mechanisms, including local immune evasion, induction of tolerance, and systemic disruption of T cell signaling. Moreover, in a process termed immune editing, immune recognition of malignant cells imposes a selective pressure on developing neoplasms, resulting in the outgrowth of less immunogenic and more apoptosis-resistant neoplastic cells

From the application of Coley's toxin in the early 1900s to the present clinical trials using immune checkpoint regulatory inhibitors, the history of cancer immunotherapy has consisted of extremely high levels of enthusiasm after anecdotal case reports of enormous success, followed by decreasing levels of enthusiasm as the results of controlled clinical trials are available. In this review, this pattern will be documented for the various immunotherapeutic approaches over the years. The sole exception being vaccination against cancer causing viruses, which were already, prevented thousands of cancers. We can only hope that the present high level of enthusiasm for the use of immune stimulation by removal of blocks to cancer immunity will be more productive than the incremental improvements using previous immunotherapies.