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Dendritic Cell Therapy in Cancer Immunotherapy

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Opinion Article

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DESCRIPTION

Cancer immunotherapy (also known as immune-oncology) is the use of immune system stimulation to treat cancer, enhancing the immune system's natural ability to combat the disease. It is a growing subspecialty of oncology and an application of fundamental research in cancer immunology. Cancer immunotherapy takes advantage of the fact that cancer cells frequently have tumour antigens, molecules on their surface that immune system antibody proteins can detect and bind to. Proteins or other macromolecules are frequently used as tumour antigens (e.g., carbohydrates). Normal antibodies bind to pathogens, but immunotherapy antibodies bind to tumour antigens, marking and identifying cancer cells for the immune system to inhibit or kill.

Clinical success of cancer immunotherapy varies greatly between different types of cancer; for example, certain subtypes of gastric cancer respond well to the approach, whereas immunotherapy is ineffective for other subtypes. In 2018, American immunologist James P. Allison and Japanese immunologist Tasuku Honjo were awarded the Nobel Prize in Physiology or Medicine for their discovery of cancer therapy through inhibition of negative immune regulation. During the 17th and 18th centuries, various forms of immunotherapy in cancer became widely used. In the 18th and 19th centuries, septic dressings enclosing ulcerative tumors were used to treat cancer. Surgical wounds were intentionally left open to allow infection to spread, and purulent sores were deliberately created.

One of the most well-known effects of microorganisms on cancer was reported in 1891, when an American surgeon named William Coley inoculated inoperable tumor patients with. Coley thoroughly reviewed the available literature at the time and discovered 38 cases of cancer patients with accidental or iatrogenic feverish erysipelas. The sarcoma or carcinoma had completely disappeared in 12 patients, while the others had significantly improved.

Coley decided to try iatrogenic erysipelas as a treatment. Coley created a toxin containing heat-killed bacteria. This treatment was used to treat sarcomas until 1963.

Dendritic cell therapy

Dendritic cell therapy induces anti-tumor responses by causing dendritic cells to present tumor antigens to lymphocytes, which activates them and primes them to kill other cells that present the antigen. Dendritic cells are Antigen-Presenting Cells (APCs) in the mammalian immune system. They aid in cancer antigen targeting. The only approved cellular cancer therapy based on dendritic cells is Sipuleucel-T. Vaccination with autologous tumor lysates or short peptides is one method of inducing dendritic cells to present tumor antigens (small parts of protein that correspond to the protein antigens on cancer cells). These peptides are frequently given in conjunction with adjuvants (highly immunogenic substances) to boost immune and anti-tumor responses.

Proteins or other chemicals that attract and/or activate dendritic cells, such as granulocyte macrophage colony-stimulating factor, are examples of adjuvants (GM-CSF). Whole tumor lysate, CMV antigen RNA, and tumor associated peptides such as EGFR VIII were the most common sources of antigens used for dendritic cell vaccine in Glioblastoma (GBM), an aggressive brain tumor. Dendritic cells can also be activated *in vivo* by expressing GM-CSF in tumor cells. This can be accomplished by genetically modifying tumor cells to produce GM-CSF or infecting tumor cells with an oncolytic virus that expresses GM-CSF. Another approach is to remove dendritic cells from a patient's blood and activate them outside the body.

Dendritic cells respond to tumor antigens, which can be a single tumor-specific peptide/protein or a tumor cell lysate (a solution of broken down tumor cells). These cells are infused (along with optional adjuvants) and cause an immune response. Antibodies that bind to receptors on the surface of dendritic cells are used in dendritic cell therapies. Antigens can be added to antibodies to induce dendritic cell maturation and provide tumor immunity. TLR3, TLR7, TLR8, and CD40 are dendritic cell receptors that have been used as antibody targets. The dendritic cell-NK cell interface is also important in immunotherapy. NK cell-stimulating potency should be considered when developing new dendritic cell-based vaccination strategies. Monitoring NK cells as an outcome in antitumor DC-based clinical trials is critical.