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Effectiveness of Cancer Treatment Vaccines

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Immunotherapy is a treatment designed using the patient's immune system to attack cancer in the body. It can manipulate the immune system and allow it to identify cancer cells and initiate immune responses to kill them. Cancer treatment vaccines are an emerging topic in immunotherapy treatments. By injecting a cancer vaccine, the immune system is able to combat cancer, causing tumors to shrink. The use of vaccines also allows for immunity to the cancer cells with the use of memory T cells, meaning the tumor will be unable to continue growing after most treatments. Multiple variations of cancer treatment vaccines have been studied in clinical trials. (American Society of Clinical Oncology 2019) The stimulation of anti-tumor cells has been studied with the use of cell, peptide, virus, or nucleic acid-based vaccines. These vaccines are used as an aid for the immune system when cancer cells are present; they are not a preventative measure.

Introduction

Cancer treatment vaccines are necessary to treat cancers that have already developed. The goal is to be able to impede or halt cancer cell growth and deteriorate tumors. These vaccines are effective at eliminating cancer cells that have survived other forms of cancer treatment. Additionally, cancer treatment vaccines can forestall infections. These vaccines are effective because they boost the body's immune system to fight antigens. Unlike other invasive cancer treatments, vaccines have been shown to leave the patient with mild flu-like symptoms that are extremely manageable. Two cancer treatment vaccines approved in the United States: these being the Sipuleucel– T (provenge) vaccine and the Talimogene Laherparepvec (T-Vec) vaccine.

Sipuleucel – T (Provenge) Vaccine

The Provenge Vaccine treats prostate cancer that continues to spread throughout the body. Often, prostate cancer patients present little to no symptoms. This vaccine is given to patients that fail to respond to treatments that lower testosterone. The vaccine is made by taking the patient's immune cells after they have been treated with Granulocyte-Macrophage-Colony-Stimulating Factor (GM-CSF). This allows greater white blood cell production, granulocyte growth, and macrophage

development and boosts the development of cells that will become platelets. (Antoni, et al. 2003) Provenge is a dendritic cell vaccine. Dendritic cells are responsible for T cell response, allowing for the patient's immune system to directly terminate tumor cells.

Talimogene Laherparepvec (T – Vec) Vaccine

T-VEC is used to treat advanced melanoma skin cancer. This form of vaccine therapy is oncolytic virus therapy. The injection that is given to the patient contains the genetically modified virus that infects and kills cancer cells while avoiding healthy cells. This modification includes the addition of the GM-CSF protein. (Chen, Ke-Jun, et al. 2021) After the vaccine is injected directly into the tumor it begins destroying cancer cells. With the use of tumor antigens, the immune system can quickly recognize the cancer cells throughout the patient's body. After recognition the GM-CSF protein activates immune cells, allowing them to begin attacking cancer cells. T-VEC is most effective when it comes to treating non-surgical and rapidly forming melanoma cancer in the skin and lymph nodes.

How Cancer Vaccines Are Modified

We can further understand how viruses interact with the host in oncolytic immunotherapy by using virus biology and viral genes. Scientists can use non-replicating viruses as vectors affecting tumor antigens. Oncolytic vaccines attack and kill cancer cells by activating dendritic cells then process through antigen material, alerting the T cells of any abnormality. The cytotoxic T cell begins to destroy the infected antigen-presenting cell. With the use of these vaccines T cells can develop immunity towards pathogens. (Ryding, Sara. 2023)

Antigen selection cancer vaccines maintain the ability to trigger the immune system to attack the cancer cells by identifying antigens. Antigens reside on the surface of cancer cells. This allows the immune system to attack only the cancer-presenting cells. Scientists do this in the lab by introducing the antigens expressed on the cancer cell to the vaccine.

Genetic modification involves the ability to modify cancer cells to be more identifiable to the immune system. Ultimately, the immune response will be stronger and more accurate thanks to the magnification of the cancer cells.

When adjuvants are added to vaccines the immune response becomes enhanced. This can possibly lead to a personalized cancer vaccine. The vaccine will then become effective to a specific patient's cancer by using their own genetic material to help build immunity and fight cancer cells.

Four Types of Cancer Vaccines

The type of preparation method it takes to create the cancer vaccine determines how it will perform. Cancer vaccines are divided into four separate categories: cell based, virus based, peptide based, and nucleic acid based. These vaccines show a promising future when it comes to immunotherapy.

Cell Based Vaccine

Cell based cancer vaccines use the patient's immune cells as antigen carriers. Multiple cellular antigens and tumor antigens will be introduced to the immune system. This leads to the large army of dendritic cells weakening and killing tumor antigens. Cell based vaccines are personalized to the patient's individual tumor allowing for a higher rate of success. ("Cell Based Vaccine." 2017) Cell based vaccines ultimately stimulate the patient's immune system to only attack cancer cells, leaving healthy cells unscathed unlike other forms of cancer treatment. This allows the patient to have fewer side effects. The use of these vaccines is still being researched;

however, they have shown promising results when it comes to the treatment of breast, prostate, and melanoma cancers. (Ribas, Antoni, et al. 2003)

Peptide Based Vaccine

Peptide based vaccines contain a combination of adjuvants to strengthen the body's immune response. The vaccine creates anti-drug antibodies that play a role by binding to therapeutic protein products. The antigen can provoke the patient's immune response. This is to train the immune system to attack and kill cancer cells. The patient is injected with peptides that include important immune defenders called dendritic cells. After the injection the dendritic cells signal to T -Cells. The T- cells then can register and invade the cancer cells. Peptide based vaccines are currently still being studied and are not yet available to the United States. This vaccine shows promising results when it comes to preventing metastasis and recurrence. (Zhang, Lu, et al. 2019)

Viral Based Vaccine

The viral based vaccine uses a virus to provide cancer attacking antigens. Using these virus-based vaccines the immune response is able to target cancer cells. This is done by modifying the virus to contain antigens. This makes the virus infect cancer cells allowing the immune system to be able to recognize and attack the cancer. (Guo, Zong Sheng, et al. 2019) Scientists also have the ability to use a virus like adenovirus that naturally targets cancer cells. The virus infects the cancer cell allowing for immune recognition. The viral based vaccines attack healthy cells, allowing for less symptoms than other immunotherapies. These vaccines are still being studied in clinical trials due to being such an emerging part of cancer research.

Nucleic Acid-Based Vaccine

Nucleic acid-based vaccines use DNA or RNA to activate the immune system response to cancer cells. This form of immunotherapy takes fragments of DNA or RNA. Then the vaccine is reintroduced to the body resulting in the activation of anti-cancer specific antigens. After the DNA vaccination is given the antigen is encoded, which results in the making of cancer-specific antigens. (Yang, Benjamin, et al. 2014) After the vaccination has been given to the patient the foreign nucleic acid transfects the cell. The antigen-presenting cells activate T cells resulting in an immune response. (S, Nawrocki, et al. 1999)

RNA based nucleic vaccines differ in the way that they utilize messenger RNA to encode an antigen. With the use of liposomes and nanoparticles, mRNA is then transferred by the target cells to an infectious protein antigen. The immune system then responds and attacks the cancer cells. (Nierengarten, MB 2022)

Both choices of nucleic acid-based cancer vaccines demonstrate the ability to attack cancer antigens. This results in a less toxic form of immunotherapy, especially when compared to chemotherapy. Ongoing research is being performed and shows a promising future for long lasting immune attacks against cancer antigens. As scientists increasingly research immune response, they approach more effective cancer treatments.

Recent Progress with Heat Shock Proteins

Heat shock proteins (HSP) and keyhole limpet hemocyanin (KLH) help aid the body's immunity to the melanoma antigen when using peptide-based vaccinations. (Chen, Ke-Jun, et al. 2021) Heat shock proteins aid in immunity by having the ability to fold, unfold, or translocate proteins along with having the ability to create and destroy protein complexes. HSPs are activated as cells are exposed to hotter

temperatures or stressful conditions. Activating the heat shock factor increases the transcription of heat shock genes. Meanwhile exposure can be lethal by activating apoptosis. However, heat shock proteins work to provide healthy cells with thermal stability and the ability to restore their natural structures. These proteins are used in cancer treatments to enhance the immune response while protecting healthy cells from these stressful conditions. The HSPs bind to tumor-associated antigens (TAAs). By doing this, the antigen tricks the immune system to believe it is foreign. This then triggers the immune response needed to attack the cancer cells. (Das, Jugal Kishore, et al. 2019)

KLH is an outside protein that is transported from the blood of a mollusk. It consists of a carrier protein that is immunogenic when paired with tumor-associated antigens. After the KLH adjuvant vaccine is injected, the immune response recognizes it as foreign, allowing for a swift attack on cancer cells. These variations of peptide vaccines are effective when it comes to the treatment and riddance of melanoma.

Recent Progress with TVEC

Talimogene Laherparepvec (TVEC) is a form of immunotherapy derived from a strain of the herpesvirus, HSV-1, that is then modified in a laboratory. After undergoing modification, the virus then can break down cancer cells. This leaves the healthy cells secure allowing for a stronger immune system. The virus that is injected directly into tumors and lymph nodes is unable to duplicate in healthy cells but able to infect and replicate inside of cancer cells. This causes the cell to combust resulting in the release of tumor-specific antigens and tumor-associated antigens triggering an immune response leading to the attack of cancer cells. After many years of clinical studies and research the TVEC vaccine was approved on October 27, 2015, in the United States to treat metastatic melanoma.

Recent Progress with Cytokines as Adjuvants

Cytokines are chemical messenger proteins released by macrophages and lymph nodes. These messenger proteins signal immune cells and tell them to produce more cytokines to effectively kill any infection present in the body. Cytokines play a part in controlling growth of blood cells and cells that correlate in immune and inflammatory response, like T cells and antigen presenting cells (APCs). By exaggerating cancer cells with a cancer vaccine and boosting cytokine signals cancer cells are more heavily attacked. Leading to healthier normal cells while the cancer cells die.

The use of cytokines as adjuvants for cancer vaccines would be able to assist in treating tumors that haven't shown affects to conventional cytotoxic therapies. However, cytokines combined with vaccines can result in vaccine toxicity. This is a result to the addition of interleukin 2. However, vaccines containing interleukins 7, 21, and 15 can show major improvement when it comes to anti-tumor immunity. (Capitini, Christian M, et al. 2009) To prevent major relapse, gamma(C) cytokines must be added to the vaccine. All of the cytokines previously listed contain the correct gamma chain that affects T cells and natural killer (NK) cells, allowing for a stronger anti-tumor immune response with the help of gamma(C) cytokines.

Disadvantages of using Treatment vaccines

These vaccines show effective results when it comes to immunotherapy, however, advanced tumors are difficult to get rid of solely with a cancer vaccine. If the patient has a weak immune system, then they may be unable to support the actions the vaccines case. Dendritic cell vaccines work by making a stronger presentation of tumor associated antigens to T cells. A faulty antigen becoming present could lead to tumor progression within the patient. (Body, B, et al.) Aside from these side effects

when paired with an existing immunotherapy they show up to a 75% success rate. (Kenney, Skylar. 2021)

Discussion

Overall, cancer vaccines are used to boost the ability to remove cancer antigens in the tumor it is injected into. However, there is the risk of relapse and autoimmunity. Anti-tumor activity has been proven in many clinical trials, with more effective use when paired with other immunotherapies. With the use of vaccines scientists can boost the body's natural defense against cancer. The immune system is supported by the vaccine, it does this by effectively helping the immune system identify cancer cells. The vaccine disrupts the cancer cells, leaving healthy cells untouched. This is a remarkable achievement when it comes to immunotherapies. The patient will only experience mild flu like symptoms.

The objective is to stop cancer cells from growing while working to shrink the tumor and keep it localized. The vaccine is not a prevention, it can only be injected into tumors and lymph nodes to fight cancer cells. The purpose of cancer vaccines is to halt cancer growth while shrinking the tumor. By signaling TAAs, T cells, APCs, gamma(c) cytokines, HSPs, etc… the vaccine becomes effective. Cancer vaccines are a relatively new concept when it comes to immunotherapies. They have resulted in scientific breakthroughs in the treatment of solid tumors. (Ribas, Antoni, et al. 2003) The tumor resistance that is a result of the vaccine has shown clinical efficacy when combined with other therapies.

By advancing immunology and DNA sequencing, personalized cancer vaccines have potential to become a promising method of cancer treatment in the near future. (Liu, Jian, et al. 2022) Moving forward scientists are focusing on improving target antigen identification and delivery system. Further research and advancement of personalized treatment vaccines and the way they activate immune response shows to be a promising step going forward. Due to the advancements in tumor specific antigen treatments, we will be able to target specific tumors. Multiple studies showed that after vaccination T cells accumulate at sites where melanoma had previously been reoccurring. (Melssen, Marit M., et al. 2021) By gaining the ability to better direct tumor associated antigens scientists will be able to combat more cancers effectively with the use of cancer treatment vaccines.

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