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Cancer Immune System: A focus on clinical trails of Cancer Vaccines

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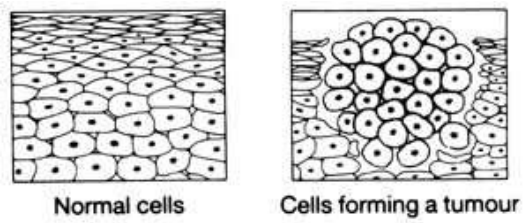
Cancer became a big question for scientific community as no existing treatments could solve the problems related to this dreadful disease. Research is in well progress since half century but it failed to give a right solution to fight against it. However the developments in science and technology facilitated scientists to develop new methods of treatment. One such mile stone treatment for cancer that is giving good hope to the people is cancer vaccines. The aim of cancer vaccines is to stimulate the immune system to be able to recognise cancer cells as abnormal and destroy them. Majorly, cancer vaccine research is in progress to develop universal as well as specific cancer vaccines. In the present paper the developments in cancer thearapy especially by empahising vaccine development against cancer was discussed.

Key words: Cancer Vaccines, Clinical Trials, Immune System, DNA Vaccines.

The human body is made up of tiny building blocks called cells. Cells look and function differently throughout the body, but reproduce and repair themselves in the same way. This process normally happens in an organised and controlled manner. If cells become cancerous they start to divide in an uncontrolled way.



Normal cells Cells forming a tumour

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The immune system sometimes has difficulty recognising cancer cells, and does not destroy them. The cancer cells then continue to grow.

The Role of Immune system

The immune system protects the body against infections by bacteria, viruses and other parasites. The cancer can weaken the immune system by invading the bone marrow where the cells that help to fight infection are made, which happens mostly in leukaemia or lymphoma.

Chemotherapy and radiotherapy can weaken immunity by causing a drop in the number of white blood cells made in the bone marrow. Some cells of the immune system can recognise cancer cells as abnormal and kill them. Unfortunately, this is not enough to get rid of a cancer altogether. But some new treatments aim to use the immune system to fight cancer.

Vaccines

Vaccines have been used for many years as a way of preventing certain infectious illnesses: for example, 'flu, tuberculosis (TB), measles, mumps, typhoid and German measles. Vaccines stimulate the body's immune system to recognise and fight abnormal 'foreign' cells in the body, such as viruses and bacteria.

The aim of cancer vaccines

The aim of cancer vaccines is to stimulate the immune system to be able to recognise cancer cells as abnormal and destroy them.Some vaccines for particular cancers have been developed and are being tested to see whether they can treat a cancer, or help to stop it from coming back after cancer treatment.

Types of cancer vaccines

Probably the most promising form of cancer treatment is immunotherapy, where scientists are developing several experimental cancer vaccines that could lead to the eradication of cancer in this century. There are two major categories that cancer vaccines fit into,

Specific cancer vaccine

Universal cancer vaccine

As the name suggests, specific cancer vaccines are designed to treat specific types of cancers. In other words, a vaccine could be developed for lung cancer, another vaccine could be used to treat colon cancer, and yet another vaccine could treat skin cancer, and so on. A more appealing cancer vaccine would be one that could fight cancer cells regardless of cancer type. This type of vaccine is called a universal cancer vaccine.

In these two categories, there are more specific types of cancer vaccines. Each type of cancer vaccine works on the same basic idea that the vaccine, which contains tumor cells or antigens, stimulates the patient's immune system, which produces special cells that kill cancer cells and prevent relapses of the cancer. Unlike vaccines for other disease that prevent the occurrence of the disease, there isn't a vaccine in development that can prevent the onset of cancer. Cancer vaccines are used only as a treatment after the cancer has been found in a patient. Here is a list of five kinds of cancer vaccines being developed,

1) Antigen vaccines
2) Anti-idiotype vaccines
3) Dendritic cell vaccines
4) DNA vaccines
5) Tumor cell vaccines

Antigen vaccines

These use tumor-specific antigens - proteins displayed on a tumor cell - to stimulate the immune system. By injecting these antigens into the cancerous area of the patient, the immune system will produce an increased amount of antibodies or cytotoxic T lymphocytes, also known as killer T cells, to attack cancer cells that carry that specific antigen. Multiple antigens can be used in this type of vaccine to vary the immune system response.

Anti-idiotype vaccines

In some instances, some antibodies, called idiotype antibodies, act as antigens, triggering an immune response similar to that described above. In this case, the immune system will produce anti-idiotype antibodies to attack the idiotypes. Anti-idiotype antibodies can be mass-produced to produce a vaccine that can be injected to treat cancer.

Dendritic cell vaccines

Dendritic cells break the antigens on the cancer cell surfaces into smaller pieces. The dendritic cells then act as most-wanted posters for the immune system, displaying those antigen pieces to the killer T cells. In order to make dendritic cell vaccines some of the patient's dendritic cells are extracted and immune cell stimulants are used to reproduce large amounts of dendritic cells in the lab. These dendritic cells are then exposed to antigens from the patient's cancer cells. This combination of dendritic cells and antigens is then injected into the patient, and the dendritic cells work to program the T cells.

Tumor Cell Vaccines (Autologous /Allogeneic Tumor Cells)

Autologous and allogeneic tumor cells were one of the first types of tumor vaccines to be used. Theoretically, the main advantage of tumor cell vaccines is that they have all the relevant tumor antigens needed by the immune system to mount an effective antitumor response. This is particularly true if autologous tumor cells are used instead of allogeneic tumor cells. A second advantage is that tumor cell-based immunization allows the development of cancer vaccines without knowing the specific antigens.

The advantages of tumor cell-based

cancer vaccines must be balanced against two major disadvantages: the potential for autoimmunity and the potential for increasing the anergic status of the T cells due to the lack of functional co stimulatory molecules on tumor cells. Initial attempts to immunize cancer patients with tumor cells were disappointing and temporarily decreased interest in the field.

Tumor-APC Hybrids

A novel development in cancer vaccines is the use of tumor-APC fusion technology. The vaccines produced by exposing tumor cells and APCs to polyethylene glycol (PEG) or electrical fields, which results in the generation of a tumor-APC hybrid. The rationale behind this approach is that the resulting hybrid will have the appropriate TAA derived from the tumor and the unparalleled co stimulatory capabilities of the APCs. Preclinical studies have provided the rationale for the use of cell hybrids in the cancer vaccine setting. More importantly, the tumor-APC strategy already has been associated with major clinical responses in patients with metastatic renal carcinoma.

DNA Vaccines

With recent DNA (deoxyribonucleic acid) research, scientists are finding ways to use the genetic code of proteins produced in cells to aid the immune systems fight against cancer. Bits of DNA from the patient's cells are injected into the patient, which instructs the other cells to continuously produce certain antigens. This DNA vaccine increases production of antigens, which forces the immune system to respond by producing more T cells.

Cancer Vaccine Preparation

Cancer vaccines are made from the person's own cancer cells or from cells that are grown in a laboratory. The cancer cells are treated with heat or radiation, then they become inactive and can be used for vaccine prepartion. Certain proteins may then be taken from the cancer cells and used to make a cancer vaccine. These include antigens (the proteins on the cell surface which can stimulate an immune response), in some cases, whole cells may be used to make the vaccine.Often a cancer vaccine will also contain substances that are already known to boost the immune system, such as BCG (the vaccine that protects against tuberculosis). As the cancer vaccine contains similar proteins to the cancer cells, it is hoped that the immune system will be stimulated to start to attack and destroy them.

Cancer Vaccines which are currently under clinical trials

1. Onyvax (a monoclonal antibody 105AD7 anti-idiotype vaccine) is used for the treatment of advanced colorectal adenocarcinoma. The vaccine is administered endemic together with the BCG vaccine or intramuscularly together with the alum adjuvant
2. Cancer VAX (a polyvalent melanoma vaccine) is being used together with the surgical treatment in the treatment of melanoma III stage. In order to increase the cellular immune response, this vaccine is given together with the BCG-vaccine
3. An autologous tumor cell vaccine is under clinical tests for the patients with II and III stage adenocarcinoma of colon to prevent relapses after surgical treatments.
4. NY-ESO-1 peptide vaccine is used endermic in the treatment of II-IV stage sarcoma of soft tissues expressing NY-ESO-1, LAGE antigen NY-ESO-1 or LAGE antigen. Granulocyte-macrophage colony stimulating factor (GM-CSF) is to be injected, subcutaneous, in additional to this vaccine.
5. A monoclonal antibody 11D10 anti-idiotype vaccine and monoclonal antibody 3H1 anti-idiotype vaccine are being used in the treatment of the patients with stage II or IIIA non-small cell lung cancer (T1-3, N1-2, M0) which is administered starting from the 14-45 days after operation.
6. A vaccinotherapy using Tyrosinase, gp100, and MART-1 peptides together with the alum adjuvant is being used for the treatment of the patients with IIB, IIC, III, or IV cutaneous melanoma OR stage III or IV ocular or mucosal melanoma. Interleukin-12 and the granulocyte-macrophage colony-stimulating factor (GM-CSF) are also used beside the vaccine.
7. ALVAC-CEA/B7.1, a deactivated strain of a virus, is being tested for the treatment of metastatic colorectal cancer. Virus antigens are identical to the antigens exhibited by colorectal tumors. Unlike its predecessors, this vaccine is being administered immediately upon diagnosis along with chemotherapy.
8. VG-1000 Vaccine is a specialized vaccine, which undermines the cancer cells defense mechanisms. This vaccine is most beneficial in treating carcinomas and melanomas. Patients subjected to chemotherapy or radiation respond more slowly to VG-1000 as they have a depressed immune system, however, patients who have

had neither radiation nor chemotherapy respond favorably indicating it as first-line treatment for persons with recently diagnosed cancers, as well as to help prevent recurrence.

9. The name "Tricom" shorthand for a combination of three powerful co-stimulatory molecules - B7-1, ICAM, and LFA-3 enhance T-cell response.
10. The vaccine, called HSPPC-96, or Oncophage®, is a heat-shock protein, a class of compounds that has shown activity as autologous therapy, which means that the therapeutic agent is derived from and tailored to the tumors of individual patients. The HSPPC-96 vaccine contains antigens extracted from melanoma. Some of these antigens, like MART-1 and gp100, are unique to melanoma; others are found in many types of cancer.

CONCLUSION

The vaccine development for Cancer is an exemplary approach of researchers to fight the most dread full disease around the globe. The various types of cancer vaccines and their clinical trails are most satisfactory and giving energy to the scientific community to concentrate more in this area. Future progress and development in this area surely provide the human kind beautiful weapons to fight with all kinds of cancer. In the present paper we highlighted the progress in cancer vaccine development and future perspective; it may be useful for researchers and student community to refresh their technical knowledge.

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