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Research Status of Tumor Therapy Based on Immunotherapy

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Abstract: *Cancer is the "top killer" of human health. Traditional cancer treatment methods include surgery, radiotherapy and chemotherapy, but all of them are carried out by directly killing cancer cells, which is difficult to completely remove cancer cells and cause serious damage to normal cells and tissues. Different from traditional treatments, immunotherapy destroys tumors by regulating the body's immune defense mechanism without damaging normal cells and tissues. This paper first introduces the characteristics of immunotherapy, and expounds the research status of tumor therapy based on immunotherapy from two aspects of active immunotherapy and passive immunotherapy, aiming to provide theoretical reference for tumor drug research and promote tumor immunotherapy to achieve greater breakthroughs.*

Keywords: *Immunotherapy; Treatment of Tumors; Research*

1. Introduction

Traditional treatment means of tumor has certain therapeutic effect in clinic, with the progress of medical technology, traditional treatments are constantly progress, effectively relieve the pain of cancer patients, patients won more survival practice are also making continuous progress, effectively alleviating the pain of cancer patients and winning more survival practice for patients. However, it is difficult to completely cure tumors by relying on traditional methods, and there are great limitations in the treatment of many cancers [1]. Take surgery as an example, this means of relying on surgical resection can only be effective in the early stage of cancer, but it is difficult to detect cancer in the early stage, and the effect of surgical resection in the middle and late stage is very poor, which will cause the metastasis of cancer cells and harm the body function at the same time. Chemotherapy and radiation can also damage normal cells, causing many adverse reactions in patients, so efforts have been made to find new treatments that can effectively destroy cancer cells without damaging normal cells. The treatment of cancer based on immunotherapy is to eliminate cancer cells completely by enhancing the ability of the human immune system to recognize tumor-specific antigens.

2. Characteristics of immunotherapy

The so-called immunotherapy refers to the concept of using the immune system to treat diseases, belonging to a large treatment system [2]. Cancer treatment has always been an important problem faced by the medical community. In recent years, tumor immunotherapy has made a lot of progress. Tumor therapy based on immunotherapy is to explain the response effect to cancer cells by improving the immune capacity of the body. The body's immune system consists of white blood cells and organs and tissues of the lymphatic system. Its main function is to help the body resist disease and keep the body healthy [3-4]. Immunity is divided into the innate immune system and adaptive immune system. The innate immune system can produce macrophages, dendritic cells and other immune cells, which can effectively protect the body. The adaptive immune system uses antigen-specific lymphocytes to resist specific threats. When using immunotherapy for tumor treatment, the body's immune system can effectively eliminate cancer cells when they reappear, forming immune memory and helping the body to remain cancer-free for a long time [5-6]. Tumors destroy the immune system by affecting the antigen presentation process, destroying the pathway of T cell, recruiting immunosuppressive cells, releasing immunosuppressive active factors, and at the same time regulate the immune system into a mode conducive to the survival of cancer cells. Compared with traditional tumor treatment methods, these immunodrugs have the advantages of fewer side effects on the body, longer duration, and stronger specificity, which can greatly reduce the recurrence rate of cancer.

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3. Active immunotherapy

Active tumor immunotherapy refers to the effective stimulation of the immune system by inputting antigenic vaccines into the body to promote its tumor immunity, so as to achieve the purpose of tumor treatment. In recent years, with the continuous development of molecular biology and medical technology, active immunotherapy has also made remarkable achievements. And a large number of vaccines have been developed, which play a great role in tumor treatment. Currently, the following types of vaccines are being imported.

3.1 Whole tumor lysate vaccine

In the actual treatment, it can be found that some tumor patients can only express partial antigen proteins, which unable to fully active the immune cell. Some experts [7-8] study the whole tumor lysate or embryonic stem cells as vaccines. Taking tumor bearing rats as the research object, H22 or S180 cancer cell lysate was given to them. It was found that the lysate could effectively activate CD4 + and CD8 + T lymphocytes. Whole tumor lysates strengthen immune effects when used in combination with dendritic cells or other adjuvants.

3.2 Polypeptide vaccines

Polypeptide vaccine is a vaccine prepared according to the whole or part of the amino acid sequence of the known antigen epitope of the pathogen. It can achieve the purpose of tumor treatment by activating the acquired immune system. At present, many tumor vaccines on the market are polypeptide vaccines [9]. In recent years, great progress has been made in the development of polypeptide vaccines. AE37, E75 and other vaccines have entered the clinical stage. AE37 is effective in controlling cancer cells by promoting the synthesis of immune cell and secretion of IFN and IL-2. E75 has also achieved grand results in the treatment of early breast cancer. Research shows that many patients have significantly reduced the recurrence rate after receiving E75 vaccine treatment [10-11].

3.3 DNA vaccine

DNA vaccine is a new research field derived and developed in gene therapy research in recent years, also known as "naked" DNA vaccine, gene vaccine or nucleic acid vaccine. It refers to the injection of recombinant eukaryotic expression vector encoding a certain protein antigen into the host body, so that foreign genes can be expressed in the body, and antigens can be generated to activate the immune system of the body, thus inducing specific humoral immunity and immune response. The basic function of DNA vaccine is to enter the animal body through a certain way, be absorbed by host cells transcription and translation expression of antigen protein, this antigen protein stimulates the body to produce two kinds of non-specific and specific immune response, promote the activation and proliferation of CD8+T cells, so as to achieve the effect of killing tumor cells. At present, the research reports on DNA vaccine show that the DNA vaccine for the treatment of prostate has entered the phase I clinical trial stage and has obvious therapeutic effect [12].

4. Passive immunotherapy

Passive immunotherapy is a kind of tumor immunotherapy that can exert antitumor effect by injecting exogenous immune substances into the body, causing immune response, inhibiting signal pathway and delivering drugs to the focus. Such as monoclonal antibodies, conjugate monoclonal antibodies, tumor adoptive immunotherapy.

4.1 Monoclonal antibody and bispecific antibody

Monoclonal antibody is mediated by ADCC(antibody-dependent cell-mediated cytotoxicity) CDC(complement dependent cytoxicity), and ADCP(antibody-dependent cellular phagocytosis) target tumor cell surface antigens or specific receptors, thereby blocking tumor growth factor signaling pathways, further killing tumor cells[13]. The second generation of monoclonal antibodies, represented by Bispecific Antibody (bsAb), have gradually entered the market. Bispecific antibodies possess two different antigen-binding sites and can bind to two target antigens or two different epitopes of one antigen at the same time to better exert anti-tumor effects [14].

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4.2 monoclonal antibody conjugate [15]

By connecting monoclonal antibody conjugates with drugs, radionuclides and mycin with monoclonal antibodies, chemical immune conjugates, radioimmuno conjugates and immunomycin can be formed to promote the therapeutic effect of antibodies and improve the therapeutic effect of drugs.

4.3 Tumor adoptive immunotherapy

Tumor adoptive cell therapy (ACT) mainly refers to the input of immune cells or cytokines into the body. Adoptive cellular immunotherapy is mainly used. Its principle is to first extract immune effector cells from the patient's body, expand the extracted immune effector cells in vitro, and then re-inject them back into the patient's body, so as to activate the patient's immune system and take advantage of the immune system to kill tumor cells [16].

4.3.1 Adoptive T cell therapy

Adoptive T cell therapy is to transform the T cells of patients (autologous) or donors (heterologous) in vitro, and then inject them into patients to induce cell proliferation and target antigen-specific tumor cells, so as to improve their immune response to tumors. Chimeric antigen receptor T cell (CAR T) immunotherapy is one of them,which is a novel cell therapy that has been improved and applied to clinic in recent years. CAR T therapies deliver strong and long-lasting lethality to specific tumor cells, whic have shown remarkable efficacy in acute leukemia and non-Hodgkin's lymphoma, and have recently made advances in solid tumors. Many large multinational pharmaceutical companies, such as Novartis, Juno and Kite, have launched CAR-T treatment programs. Although these CAR-T clinical programs are still in phase 1/2, they are generating research and development around the world due to their remarkable therapeutic effects and isolated cases of cure.

4.3.2 Adoptive NK cell immunotherapy

NK cell is an important immune cell, which is directly related to anti-tumor [17]. NK cells can directly secrete perforin and IFN-γ, which have strong inhibitory effect on tumor cells. How to obtain high purity and large number of NK cells is a crucial problem of NK cell immunotherapy. NK cells can act through chimeric antigen receptors, which is similar to T cells, but car-nk therapy has more advantages than car-t cell therapy, which is reflected in the wide source of NK cells and is not limited by autologous cells. In addition, NK cells do not secrete the main cellular factors causing CRS, and have less adverse reactions in the process of tumor treatment [18].

4.3.3 Adoptive DC cell immunotherapy

Dendritic cell (DC) is an important cell with the function of initiating, regulating and maintaining immune response in vivo. It can effectively kill tumor cells. When tumor cells are necrotic, DC cells can release protein B1 to activate dendritic cells, so as to activate the immune function in vivo and promote the immune system to fight tumors [19-20]. Studies have shown that DC vaccine can effectively activate the immune function of the body and promote its anti-tumor effect. The main methods of DC immunotherapy are as follows. First, use T cells to attack tumor cells. IL-12 produced by DC can effectively activate CD4 and CD8 in T cells. In this process, after T cell surface ligands are combined with DC surface molecules, they can produce many cytokines. Under the action of these cytokines, they stimulate a large number of T cells to proliferate and induce specific CTL response, so as to regulate immune response and produce immunity. At the same time, DC can also secrete chemokines to further stimulate T cells, so as to start immune response and induce immune response, so as to kill tumors; Second, use B cells to kill tumor cells. DC also participates in the maturation and differentiation of B cells, so B cells can be used to fight tumor cells. When B cells mature and differentiate, DC can stimulate B cells to secrete a large amount of immunoglobulin, or directly induce initial B cells and memory B cells to differentiate into plasma cells by secreting type I interferon, so it plays a key role in tumor treatment.

5. Conclusions and prospects

Regardless of its academic value or application value, tumor immunotherapy can be called the most noteworthy scientific field today. The progress of science and technology in the field of tumor immunology in recent 30 years has provided knowledge and technical reserves for the development of tumor immune drugs for the treatment of cancer, resulting in the "explosive" growth of tumor immune

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drugs in recent years. As a developing treatment, tumor immunotherapy aims to use the patient's autoimmune system to treat cancer. This method has many advantages, such as low toxicity, long action time and so on. However, there are also some problems in the delivery of immunotherapeutic drugs, such as poor tumor specificity, low tumor deep permeability and low cell uptake rate, which can not produce immune response, or the immune response decreases when tumor cells metastasize, which is difficult to effectively fight recurrent tumor cells. Therefore, further research is needed on tumor immunotherapy. It is believed that with the continuous development of biomolecules and medical technology, tumor immunotherapy will continue to improve, make new breakthroughs, be more standardized and standardized, and make outstanding contributions to human overcoming tumor diseases.

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