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New progress in cancer treatment based on monoclonal antibodies

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Abstract. Monoclonal antibodies (mAbs) have emerged as a promising approach in cancer treatment, offering high specificity, fewer adverse reactions, and improved prognoses compared to traditional chemotherapy and radiotherapy. These drugs utilize monoclonal antibodies to precisely target and bind to cancer-specific markers, enhancing treatment efficacy. Since the approval of the first monoclonal antibody drug in 1986, the field has expanded significantly, with thousands of such drugs now available globally. In China, 53 mAbs have been approved as of 2021. Despite these advances, challenges such as drug resistance and high costs remain. However, continued scientific research and technological innovation are expected to address these issues and further improve treatment outcomes. The integration of individualized treatment plans, tailored to the specific characteristics of patients' tumors, holds the potential to revolutionize cancer care. With ongoing clinical trials and research, mAbs are expected to play an increasingly vital role in cancer therapy, offering new hope to patients and contributing to the global fight against this life-threatening disease.

Keywords: Cancer therapy, monoclonal antibodies, drug resistance.

1. Introduction

Cancer is a major disease that endangers human health worldwide. There are about 4 million new cancer patients in my country every year. The top five cancers with the highest mortality rates among Chinese men and women are: lung cancer, stomach cancer, liver cancer, esophageal cancer, and colorectal cancer. There is a 40% chance that each person will develop cancer in their lifetime. As human life expectancy continues to increase, the probability of people developing cancer will increase further in the future. Cancer is a disease caused by the deterioration of normal cells into cancer cells. Cancer cells have many characteristics, such as:

1) Loss of normal regulation of cell growth and division, which causes cells to proliferate and spread abnormally and crazily;

2) No aging and death. Normal cells spontaneously enter the death program at a certain stage of their life cycle to maintain the stability and health of the tissue structure. However, cancer cells are able to escape death, which allows them to grow and spread indefinitely in the body;

3) Unlimited proliferation potential, angiogenesis, invasion and metastasis, etc.

These characteristics work together to enable cancer cells to form malignant, ever-growing, and immortal tumors in the body, ultimately causing serious harm to the body. Therefore, cancer is one of the diseases that seriously threaten human health and life. In recent years, due to the improvement of

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early screening and cancer treatment methods, especially the progress of immunotherapy such as anti-tumor antibody drugs, the overall cancer mortality rate has gradually decreased. Since the approval of the world's first mAb drug OKT 3 (a mAb drug against human mature T cell common differentiation antigen CD3, mainly used to prevent and treat acute transplant rejection) in 1986, mAbs have become the main direction of development in the field of biopharmaceuticals. In recent years, mAbs have developed rapidly [1]. Currently, there are thousands of mAbs on the market and under development. In 2020, the total sales of mAbs worldwide will be approximately US$170 billion. As of May 2021, a total of 53 mAbs have been approved for marketing in my country, including 31 imported mAbs and 22 domestic mAbs [2].

Compared with traditional chemotherapy and radiotherapy, antibody drugs have the advantages of high specificity, few adverse reactions and good prognosis, and have shown superior anti-tumor effects in the treatment of various tumors. Precision targeted therapy has always been one of the important goals of drug research, and the emergence of mAb technology has provided a good technical means to achieve this goal. Drugs that use the characteristics of mAbs to specifically identify and bind to related targets to achieve the effect of treating diseases are called mAbs. This article will give an overview and summary of the challenges and optimization of mAbs in the treatment of cancer tumors, including a detailed introduction to mAbs and how to use this therapy for special treatment of specific cancers.

2. Basic knowledge of mAbs

2.1. Definition and classification

Antibodies are immunologically active globulins that can specifically bind to corresponding antigens. Conventional antibody preparation is produced by animal immunization and collecting antiserum, so antiserum usually contains antibodies against other unrelated antigens and other protein components in serum. Most general antigen molecules contain multiple different antigenic determinants, so conventional antibodies are also a mixture of antibodies against multiple different antigenic determinants. Even conventional serum antibodies against the same antigenic determinant are still composed of heterogeneous antibodies produced by different B cell clones. Therefore, conventional serum antibodies are also called polyclonal antibodies, or polyclonal antibodies for short [3].

MAbs are highly uniform antibodies produced by a single B cell clone and only target a specific antigen epitope. Hybridoma-hybridoma antibody technology is usually used. On the basis of cell fusion technology, B cells with the ability to secrete specific antibodies and myeloma cells with unlimited growth ability are combined into B cell hybridomas. This hybridoma cell has the characteristics of parental cells. It can proliferate rapidly and immortally in vitro culture like myeloma cells, and it can synthesize and secrete specific antibodies like spleen lymphocytes. Monoclonal lines from single hybridoma cells, i.e. hybridoma cell lines, can be obtained through cloning. The antibodies it produces are highly homogeneous antibodies against the same antigenic determinant, i.e. mAbs. Biologists have conducted a large number of mouse hybrid experiments based on cell fusion, which has enabled people to obtain a large number of stable mouse mAbs, which are divided into: human-mouse chimeric mAbs (first-generation humanized antibodies), complete CDR transplanted antibodies, partial CDR antibodies, surface remodeling antibodies, and fully humanized antibodies.

2.2. The role and mechanism of mAbs

MAbs can specifically recognize and bind to specific antigens (such as specific proteins on the surface of cancer cells). This high specificity enables mAbs to accurately lock cancer cells while having little effect on normal cells. Direct cytotoxicity. Some mAbs can directly cause cell death by binding to cancer cells. This mechanism usually involves antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). After antibodies bind to cancer cells, recruit effector immune cells (such as natural killer cells) to attack and destroy these cells. Antibodies activate the complement system, resulting in the formation of holes in the cancer cell membrane, which ultimately leads to cell lysis. Inhibit signaling pathways. Some mAbs can block growth signaling pathways in

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cancer cells and inhibit tumor growth and spread. For example, mAbs targeting epidermal growth factor receptor (EGFR) can inhibit the proliferation of tumor cells. Promote immune response [4].

MAbs can enhance the body's immune response. For example, some mAbs can activate T cells and enhance their ability to recognize and attack tumors. MAbs can also be used for tumor labeling and imaging. Before treatment, mAbs labeled with radioactive or fluorescent substances can be used for imaging to help doctors better understand the location and size of the tumor. Some mAbs can be combined with drugs to form ADCs. This strategy uses the specificity of antibodies to deliver toxic drugs directly to cancer cells, minimizing damage to normal cells. Anti-tumor antibody drugs that are widely used in clinical practice have a mechanism of action of blocking tumor growth factor signaling pathways or curbing the formation of new blood vessels in the tumor microenvironment by targeting tumor cell surface antigens. At the same time, the effector functions mediated by the antibody constant region, such as ADCC (antibody-dependent cellular cytotoxicity), CDC (complement-dependent cytotoxicity), and ADPC (antibody dependent cellular phagocytosis), can further kill tumor cells. Recent studies have found that for trastuzumab and cetuximab, activation of effector T cells in vivo is also an important mechanism for antibody drugs to kill tumors [5]. It is worth noting that the mechanisms of action of different mAbs targeting the same target are not necessarily exactly the same, and the clinical efficacy and adverse reactions are also different [6]. For example, both trastuzumab and pertuzumab target HER2, but their antigen recognition epitopes are different. The former can inhibit the homodimerization and heterodimerization of HER2 receptors, while the latter only inhibits the heterodimerization of HER2 with EGFR or HER3. Therefore, the combination of the two has a "synergistic effect" in clinical practice; although cetuximab, panitumumab and nimotuzumab targeting EGFR have the same antigen binding epitope, due to differences in affinity and IgG subtype, the skin toxicity caused in clinical practice is also different; ofatumumab and rituximab both target the B cell antigen CD20, but due to the different binding epitopes and slower dissociation rate of ofatumumab, its effector function mediated in vitro is stronger [7].

mAbs can alter T cell responses by targeting immune checkpoint blockade mechanisms, thereby amplifying anti-tumor T cell responses. These mAbs focus on immune checkpoint receptors on the surface of T cells and destroy signals that usually inhibit T cell activation. As a result, they enhance the activation state of T cells and strengthen T cell-driven tumor cell destruction. A prime example is ipilimumab, an FDA-approved mAb designed for melanoma treatment. Ipilimumab specifically inhibits cytotoxic T lymphocyte-associated antigen 4 (CTLA4), a checkpoint receptor found on activated T cells. By blocking CTLA-4, ipilimumab enhances the immune system's response to melanoma cells. MAbs have been widely used in cancer treatment worldwide. Since the first mAb drug was approved in 1986, dozens of mAbs have been approved for clinical use, covering a variety of cancer types. These drugs are often used alone or in combination with other treatments (such as chemotherapy, radiotherapy), significantly improving patient survival and quality of life. Currently, they are mainly used in the treatment of lung cancer, gastric cancer, colorectal cancer, breast cancer and other fields [7].

The application of mAbs in cancer treatment has made significant progress, and the therapeutic effects against different types of cancer have been increasingly recognized. As research deepens and technology develops, more targeted mAbs are expected to be developed in the future to provide more effective treatment options for cancer patients. Certain mAbs can be customized as carriers to specifically deliver cytotoxic substances such as radioactive compounds or potent drugs to cancer cells, thereby protecting healthy cells. For example, Ibrumomab Tiuxetan is an FDA-approved radioimmunotherapy for lymphoma treatment that binds to the CD20 antigen on B cells. This connection helps the yttrium 90 radioisotope bind to the mAB and eliminate cells by emitting beta particles. Similarly, ADCs combine the precision of mAbs with the potency of cytotoxic drugs to target cancer cells. Once these mAbs bind to their targets, the ADC enters the cell. Subsequently, the mAb component breaks down, releasing the cytotoxic drug to eliminate cancer cells while sparing healthy cells. A notable example is brentuximab, which is used to treat relapsed or resistant Hodgkin lymphoma (HL) and systemic anaplastic large cell lymphoma (ALCL). Brentuximab targets the CD30 antigen on cancer cells and releases the anti-mitotic agent monomethyl auristatin E, effectively killing cells [8].

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3. Advantages and disadvantages of mAbs

mAbs offer several advantages in cancer treatment, including high specificity, fewer adverse reactions, multiple mechanisms of action, and potential for personalized treatment. Due to their ability to specifically recognize and target antigens on the surface of cancer cells, mAbs minimize damage to normal cells, making them safer and more effective. Compared with traditional chemotherapy and radiotherapy, mAbs typically result in fewer side effects, improving patient tolerance and quality of life. Additionally, mAbs can directly kill cancer cells, activate the immune system, and inhibit tumor growth signaling pathways, offering multiple therapeutic effects. Moreover, they can be combined with chemotherapy, radiotherapy, and other immunotherapies to enhance overall efficacy. With the discovery of biomarkers, personalized mAb treatments tailored to patients' specific tumor characteristics are now possible, further improving outcomes [9].

Despite these advantages, mAbs have notable drawbacks. High R&D and production costs make these drugs expensive, limiting their accessibility. Drug resistance may also develop over time, reducing treatment efficacy and necessitating alternative therapies. While generally well-tolerated, mAbs can still cause immune-related adverse reactions such as allergies. Additionally, the complex administration methods, often requiring intravenous injections and monitoring in medical institutions, may pose challenges. Furthermore, not all patients benefit equally from mAbs, as efficacy varies depending on tumor type, molecular characteristics, and individual differences [10].

Technological advancements are addressing some of these limitations. For example, combining mAbs with traditional chemotherapy or radiotherapy enhances anti-tumor effects by increasing the sensitivity of chemotherapy drugs. Additionally, combining mAbs with other immunotherapies, such as CAR-T cell therapy, can produce synergistic effects, improving treatment outcomes. Personalized combination therapy, which tailors treatment based on the patient's tumor characteristics, is becoming a research hotspot. The application of biomarkers plays a crucial role in this process by enabling the selection of the most appropriate mAb drug for each patient. Furthermore, advances in genomics provide a basis for precision medicine, where targeted treatments are developed based on tumor genome analysis to maximize efficacy and minimize adverse reactions. Future development in mAb therapies will focus on dynamic monitoring of patient responses, adjusting treatment plans in real-time to achieve more accurate and effective personalized treatments.

4. Conclusion

The application of mAbs in cancer treatment has shown significant progress and potential. Through the in-depth understanding of cancer biology and the continuous innovation of technology, these drugs not only improve the specificity and effectiveness of treatment

In recent years, with the development of new mAbs and the application of combined treatment strategies, cancer treatment will gradually no longer be a major concern for people. The rise of individualized treatment allows us to formulate precise treatment plans based on the specific tumor characteristics of patients, so that patients can overcome the haze of cancer in the near future

Although mAbs have made remarkable achievements in cancer treatment, they still face drawbacks and challenges such as drug resistance and high costs. In the future, with the continuous influx of scientific and technological talents and technological progress, these will promote the further development of mAbs. Through continuous clinical trials and basic research, we have reason to believe that mAbs will play an increasingly important role in the treatment of cancer, bringing hope to more patients, allowing medical professionals in different fields to deal with difficult symptoms and diseases with ease, and relieve the pain of patients' treatment.

In short, the progress of mAbs has not only promoted the transformation of cancer treatment, but also provided us with new ideas to cope with this global health challenge. With the continuous advancement of science and technology, cancer treatment will become more accurate and efficient, helping patients regain hope for life.

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