Problems Facing Monoclonal Antibody Technology

Manlin Zhang *
School of Science and Technology, Hongkong Metropolitan University, Hongkong, China
* Corresponding Author Email: s1337452@live.hkmu.edu.hk

Abstract. Monoclonal antibodies (MABs), which are generated by B cells with precise specificity and strong affinity, have been widely recognized and praised by patients suffering from cancer and immune system disorders, as well as healthcare researchers, since their inception in 1972. These antibodies have been lauded for their exceptional specificity and facile recognition capabilities, which have made them indispensable in the treatment of a wide range of diseases. They are designed to bind to specific antigens, allowing for a more precise treatment, reducing the risk of damage to healthy cells and tissues. Despite their pivotal role in disease treatment, monoclonal antibodies are not without their challenges. One of the most significant issues is their exorbitant cost, which can make these treatments inaccessible for many patients. Additionally, there are potential adverse effects associated with their use, including allergic reactions and immune system complications. Ethical concerns have also been raised, particularly in relation to the use of animals in the production of these antibodies. Another major challenge is the emergence of drug resistance. Over time, some diseases can become resistant to the effects of monoclonal antibodies, reducing their efficacy. This is a significant issue, particularly in the treatment of diseases such as cancer, where the development of resistance can have serious implications for patient outcomes. Despite these challenges, the potential of monoclonal antibodies in disease treatment is undeniable. Ongoing research is focused on addressing these issues, with efforts being made to reduce costs, minimize adverse effects, address ethical concerns, and combat drug resistance.

Keywords: Monoclonal antibody; high specificity; antigen; challenges.

1. Introduction

In recent years, scientists have been conducting more and more in-depth research on immunotherapy for the treatment of many diseases. Immunotherapy mainly utilizes the body's own immune system to fight against many diseases that require the involvement of the immune system, and through the stimulation of the immune system to more effectively fight against pathogens or diseased cells [1], which not only reduces the number of side-effects, but also prevents the recurrence of the disease to a great extent. It has also been used to prevent recurrence of the disease. The most common immunotherapies are usually cellular immunotherapy or antibody immunotherapy. In this article, the authors will focus on MABs as the main research target for antibody immunotherapy. MABs are highly specific and affinity antibodies produced by monoclonal cells. In the 1960's, multiple myeloma was discovered in children, this kind of cancer cells in the body unlimited growth, the cancer cells spread quickly, the mortality rate is high, for people at that time, multiple myeloma is undoubtedly a terminal disease, until the introduction of monoclonal antibodies, the cancer treatment ushered in the dawn. In the 1970s, Argentine biochemist Cesar Milstein and his German postdoctoral researcher, George Kohler, discovered monoclonal antibodies by studying the bone marrow of mice [2]. The process of mouse experiments involves injecting the relevant antigen into the mice, isolating B lymphocytes from the mice before they are stimulated by the antigen, and fusing them with a myeloma cell line, and then continuing to screen the resulting antibody, resulting in a monoclonal antibody [3].These antibodies have the unique ability to bind to a single target and are a valuable medical tool. They can be prepared by in vitro or in vivo methods and are usually isolated from monoclonal cells after immunization in animals or humans. Due to their high specificity and low cross-reactivity, monoclonal antibodies are widely used in medical diagnosis and therapy. Currently, nearly 100 monoclonal antibodies have been approved by regulatory agencies worldwide for the treatment of a variety of diseases, including oncology and autoimmunity [4]. The mechanism of action of monoclonal antibodies is simple and is divided into two main components, antigen binding and immune response modulation, both of which work together. However, this technology faces a number of problems, starting with the high cost of production that makes it difficult for consumers to obtain monoclonal antibodies, and the development of resistance to monoclonal antibodies over time. There is also the issue of perfect storage of MABs, as well as the side effects of monoclonal antibodies and regulatory challenges to consider. Finally, there is also the need to consider the experimental lifeforms that need to be sacrificed in the laboratory (humanitarian vs. experimental process). This review introduces MABs and how it works and the problems it faces.

2. Mechanism of action of monoclonal antibodies

The mechanisms of action of monoclonal antibodies include the following: recognizing and binding to specific antigens, mediating immune effects and MABs coupling.

2.1. Recognize and bind specific antigens

Monoclonal antibody is undoubtedly the best tool for targeted therapy due to its high specificity for target cells. It mainly consists of two fragments, the constant fragment (Fc) and the antigen-binding fragment (Fab). Antigen-binding fragment (Fab) plays a crucial role in the antigen-binding mechanism. Stimulated by the relevant antigen, this antigen searches for a site and binds to the antigen-binding fragment of this monoclonal antibody, forming an antigen-antibody complex [5]. At the same time, due to its high specificity, the monoclonal antibody is able to bind well and accurately to the appropriate target antigen. The high specificity and accuracy of monoclonal antibodies make them ideal for targeted therapy.

2.2. Recognize and bind specific antigens

Monoclonal antibodies regulate the immune response by a variety of mechanisms. Immune cells recognize antigens through specific antibodies on their surface, thus generating a corresponding immune response. Typically, monoclonal antibodies can bind to receptors on the surface of immune cells, thus affecting the corresponding immune response.

Nowadays, monoclonal antibodies have become an important modality in the treatment of cancer, and through its nature and mechanism of action, it can both kill tumor cells and engage with the host's immune system, which is a unique feature that can create a long-lasting antagonism against tumors.

2.3. MABs coupling

Patients proliferate rapidly in vivo, and their main action is usually the coupling of different forms of chemical linkers of ADCs to the heavy or light chain structural domains of the monoclonal antibody, which can deliver the drug specifically to the tumor cells while reducing systemic toxicity [6].

3. The applications of monoclonal antibodies in diseases

Monoclonal antibodies usually have the ability to target specific epitopes [6], so they can target specific antigens on the surface of tumor cells, and at the same time, through the testing of the patient's blood, it is possible to observe the level of monoclonal antibodies directed against specific antigens in the blood, and through the comparison of the levels, it is possible to achieve the diagnosis of the disease.

4. Problems facing the technology of monoclonal antibodies

4.1. Manufacturing cost

The cost of production is the most important consideration. Firstly, the production of monoclonal antibodies requires highly complex technology and equipment, which requires a large amount of capital investment. Secondly, the production of monoclonal antibodies requires long steps such as immunization, fusion, screening, amplification, etc. These numerous steps make the production of monoclonal antibodies time-consuming and costly. In addition, monoclonal antibodies are used in the medical research field, so the quality of monoclonal antibodies is held to a high standard, and a large amount of quality assurance and control work requires a constant flow of funds to ensure. Finally, there is the cost of research and development, as the development of new monoclonal antibodies requires more specialized professionals who need to be rewarded with funds for the brainpower they expend on research.

4.2. Drug resistance

Drug resistance is usually closely related to genes, and mutations or deletions of genes may affect drug resistance [7]. Over time, when there are genetic mutations in genes involved in cancer cell growth or apoptosis, the affinity of the drug to bind to the cancer cells will be decreased, which will result in the inability of the drug to have its full effect. Drug resistance has always been a hot topic and reducing drug resistance in tumor cells is desired. Therefore, before a drug treatment plan is developed, relevant genes should be analyzed to understand, and preemptive consideration should be given to delaying the development of resistance.

4.3. Storage of MABs

The MABs is favored by the public through its good performance, which makes the demand of monoclonal antibody market increase dramatically, so it is also a task to store monoclonal antibodies efficiently. MABs are macromolecular proteins [8], there are two ways to inactivate the protein which are physical degradation and chemical degradation. Physical degradation mainly describes the mechanism that leads to a change in the structure of the protein without having to change or break the covalent peptide bonds. Chemical degradation, on the other hand, describes the change or loss of covalent bonds. A common processing step currently used is freezing the API as a way to enhance the chemical and physical properties of the protein while largely minimizing the potential for other microbial growth [9]. Even so, there is no guarantee that MABS storage will not be compromised at all, and a good way to store MBAs remains to be explored.

4.4. Side effects

Although monoclonal antibodies are well tolerated in humans, there are inevitably side effects. The mechanism of action of monoclonal antibodies consists mainly of antigen binding and immunomodulation, so it is inevitable that there will be adverse reactions when these two mechanisms are used. First of all, most of the well-known cancers, infectious diseases (tuberculosis, progressive multifocal leukoencephalopathy), etc. are related to specific target cells stimulated by monoclonal antibodies. In addition, acute allergic reactions, thyroid disorders, etc. are immune disorders caused by monoclonal antibodies when they are in action [10]. Although monoclonal antibodies can produce side effects, they vary from person to person. Monoclonal antibodies themselves are not toxic, and the side effects they produce are a reaction to some of the body's deficiencies and allow a person to understand his or her own problems.

4.5. Regulatory challenges

Monoclonal antibodies (MABs), as a type of biologic, face many regulatory challenges that make the approval process complex and time-consuming. These challenges stem from the fact that MABs require multiple stages of rigorous testing and evaluation. This includes experimental evaluation of toxicity, carcinogenicity, safety, and efficacy. Each stage is critical to ensure the safety and efficacy of MABs. In addition to these testing requirements, the quality of MABs must meet stringent national and regional regulatory standards. These standards are designed to ensure the consistency and reliability of MABs, and non-compliance may result in product delays or even rejection. The complexity of this approval process can significantly lengthen the time it takes for a new treatment to become available to patients. This is particularly challenging in situations where urgent new treatments are needed, such as in the case of emerging diseases or drug-resistant infections. Despite these challenges, a rigorous regulatory process is essential to ensure the safety and efficacy of MABs, ultimately protecting the health and well-being of patients. Therefore, regulators need to ensure product quality and safety while minimizing approval times to meet patient needs.

4.6. Ethical Issues of Animal Experimentation

The production of monoclonal antibodies (MAB) is a complex process that requires extensive preclinical experiments to ensure the accuracy of the results. These experiments typically involve the use of animals, particularly small mammals such as mice or rabbits. These animals are used to produce antibodies, which are then harvested and purified for research or therapeutic applications. However, these procedures can put the animals under extreme stress and danger. They may be subjected to invasive procedures, kept in unnatural conditions, or exposed to potentially harmful substances. This can cause severe psychological distress to the animals and, in some cases, may even lead to their death. These practices have raised serious concerns about animal welfare among the public and the scientific community. Many believe that causing harm to animals for the purposes of scientific research is unethical, especially when there are alternatives that do not involve. The use of animals. To address these concerns, scientists need to work to develop MABs that do not involve the use of animals.

5. Conclusion

Future research on monoclonal antibody drugs will become more and more intensive. As a novel antibody against tumors and related diseases, monoclonal antibodies play an important therapeutic and research role. It is expected that by 2025, the number of monoclonal antibody drugs marketed worldwide will reach 214 [8, 11]. Although the development of monoclonal antibodies still faces many challenges, the potential of monoclonal antibodies to treat a wide range of diseases makes them a promising area for research and development. With advances in technology and a deeper understanding of disease mechanisms, these challenges can be overcome to develop more effective and safer monoclonal antibody therapies. For example, researchers are investigating how to use gene editing techniques to change the structure of monoclonal antibodies to reduce side effects. In addition, they are also investigating how to use artificial intelligence and machine learning to accelerate the preparation process of monoclonal antibodies and reduce the production cost. In addition to treating diseases, monoclonal antibodies can be used to study the pathogenesis and treatment of diseases. For example, researchers can use monoclonal antibodies to study the growth and spreading mechanisms of tumor cells and how to stop them. In addition, monoclonal antibodies can be used to study treatments for other diseases such as autoimmune and infectious diseases. In conclusion, research on monoclonal antibodies has always been useful. With the continuous development and improvement of technology, monoclonal antibodies will become more comprehensive, and the comprehensive development of monoclonal antibodies can bring the cause of human health to a higher level.

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