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A New Perspective on Alzheimer's Disease Biomarkers in the IVD Field

Ruihai Zhu

Aventura (Beijing) Biological Technology, 102600, Beijing, China

ABSTRACT

As a neurodegenerative disease, early diagnosis of Alzheimer's disease (AD) is essential for delaying the progress of the disease. Due to the limitations of diagnostic methods, new biomarkers and detection technologies are urgently needed. Therefore, this paper mainly discusses the research and development of specific antibodies by lymphocyte hybridoma technology and the application of proximity extension assay (PEA) methodology in the field of in vitro diagnosis (IVD) for early screening detection of AD [1]. By applying Olink proteomic analysis technology with PEA methodology, the potential value of Olink proteomic analysis technology in improving the diagnostic accuracy and early identification of AD is clearly explained, which provided new ideas for future research direction and clinical application.

KEYWORDS

Alzheimer's Disease; Hybridoma technology; Monoclonal antibody; Proximity extension assay; In vitro diagnosis; Olink; Chemiluminescence

1. INTRODUCTION

There are many diagnostic methods for Alzheimer's disease, but effective diagnostic methods need to be broken through. With the deepening of biomarker research, the development of new diagnostic techniques is particularly urgent. This paper focuses on the application of monoclonal antibody technology and proximity extension assay (PEA) in the detection of AD biomarkers and discusses its potential to improve diagnostic accuracy and promote early detection [2].

2. PATHOLOGICAL FEATURES AND DIAGNOSTIC REQUIREMENTS OF ALZHEIMER'S DISEASE

2.1. Pathological basis of Alzheimer's Disease

Alzheimer's disease is a common disease that leads to memory loss and cognitive decline. It affects the function of the brain, making it difficult for patients to remember things and even recognize familiar people. With the development of the disease, the disease will gradually deteriorate, seriously affecting the quality of life of patients. The pathological process of AD also involves many factors, such as neuroinflammation, oxidative stress, and metabolic disorder, which interact with each other and jointly promote the progress of the disease [3]. Understanding the pathological basis of AD is particularly important for developing effective diagnosis and treatment strategies. In addition, they can provide clues for identifying biomarkers in the early stage of the disease. An in-depth study of these pathological features will help scientists better understand the pathogenesis of AD and provide a scientific basis for early diagnosis and treatment.

2.2. Diagnostic Requirements and Limitations of Existing Methods

The diagnosis of Alzheimer's disease needs to be able to identify the disease at an early stage, so as to take timely intervention measures to slow down the development of the disease and to give patients more time to cope with the disease. However, there are many challenges in the existing diagnostic methods. At present, the diagnosis of AD mainly depends on symptom recognition and neuroimaging examination, such as positron emission tomography (PET) and magnetic resonance imaging (MRI). Although these detection methods can help doctors judge the condition, they can only be detected when the condition is serious, which makes it difficult to find in the early stage when the condition is not too serious. Radiotracer is needed for PET scanning, and the high cost of MRI limits its application in large-scale screening [4]. Therefore, it is important to develop a method that can be detected in the early stage of Alzheimer's disease, so that the disease can be found more accurately and the treatment can be started in time.

2.3. The Necessity of New Diagnostic Technology

Because the existing detection methods have their shortcomings, we need to develop some new detection techniques to better find diseases. The ideal diagnostic technique should be able to accurately identify AD in the early stage of the disease, with high sensitivity and specificity, simple operation, and low cost, so as to be widely used in clinics and communities. The new diagnostic technology should also be able to monitor the disease progress and evaluate the treatment effect, and provide support for personalized medical care. With the development of biomarker research, biomarker detection technologies based on blood or cerebrospinal fluid, such as single-molecule array (Simoa) and PEA, have shown great potential and are expected to become important tools for the diagnosis of AD in the future. The development of these technologies will help to realize the early diagnosis of AD and make patients live better [5]. The introduction of new diagnostic techniques will bring revolutionary changes to the diagnosis and treatment of AD and provide more hope for patients.

3. APPLICATION OF HYBRIDOMA TECHNOLOGY IN THE RESEARCH AND DEVELOPMENT OF AD ANTIBODIES

3.1. The basic Principle of Hybridoma Technology

Hybridoma technology, also known as monoclonal antibody technology, is a biotechnology method for producing highly specific antibodies. The core of this technology lies in the use of B cells to generate immune responses to specific antigens and the stable production of monoclonal antibodies through the infinite proliferation characteristics of hybridoma cells. This process first involves immunizing experimental animals to make B lymphocytes in their spleen produce various antibodies. However, B cells cannot survive or proliferate in vitro for a long time, so scientists have developed hybridoma technology, which can stably secrete a single type of antibody by fusing B cells with myeloma cells. In the fusion process, polyethylene glycol or a specific virus is usually used as the fusion agent to promote the fusion of the two cell types. The fused cells were screened in a specific selection medium, and the unmelted cells and self-fused myeloma cells were removed, leaving only hybridoma cells with B cell characteristics [6].

3.2. Screening and Optimization of Antibodies

In the initial screening stage, the specific binding capacity of antibodies in hybridoma cell culture supernatant was evaluated by enzyme-linked immunosorbent assay (ELISA). The specificity and affinity of the antibodies are further verified by more detailed analysis methods, such as Western Blot or IHC. In the optimization stage, it may be necessary to genetically engineer the antibodies to improve their affinity. This can be achieved by site-directed mutation, affinity maturation, and other

technologies. In addition, antibodies with higher affinity can also be screened out by phage display technology.

3.3. Advantages of Traditional Hybridoma Technology and Phage Screening

Traditional hybridoma technology can produce monoclonal antibodies with high specificity and affinity, which are suitable for many applications, including diagnostic reagents, immunodetection, and immunotherapy. However, this process requires the use of experimental animals, and the fusion efficiency and screening workload are large. In contrast, phage screening technology provides a rapid and Qualcomm antibody screening method. Phage display technology can directly screen antibodies by linking antibody genes with the phage surface proteins. This method avoids the use of experimental animals, has high screening efficiency, can quickly obtain a large number of candidate antibodies, and allows multiple rounds of screening to improve the performance of antibodies. The choice of the two technologies depends on the specific application requirements and goals. In some cases, two technologies can be combined to make full use of their respective advantages. For example, phage display technology can be used for preliminary screening, and then monoclonal cell lines can be obtained by hybridoma technology to further optimize and produce monoclonal antibodies [7]. Through this combination, high-quality antibodies with clinical application potential can be developed more effectively.

4. PRINCIPLES AND ADVANTAGES OF PEA

4.1. The Scientific basis of Olink

Olink is an innovative biological detection technology, which is based on the principle of molecular proximity, and achieves high specificity detection by binding specific oligonucleotide probes to two adjacent epitopes on the target molecule. The scientific basis of PEA technology is that only when two probes are bound to the target molecule at the same time and the distance between them is close enough can ligase recognize and connect the two probes into a DNA molecule. This process ensures the high specificity of detection, because only when two specific epitope antibody proteins on the target molecule are recognized at the same time can the signal be triggered. The linked DNA molecules can then be specifically amplified by polymerase chain reaction (PCR). The high sensitivity of PCR enables PEA technology to detect target molecules with extremely low abundance, which can reach the femtogram level. The multiplexing ability of PEA technology is also a major feature. By designing different probe combinations, multiple target molecules can be detected at the same time, which makes it possible to study multiple biomarkers in complex biological samples.

4.2. Advantages (comparison) and Diagnostic Potential of PEA Technology and Traditional Chemiluminescence Detection of AD

Compared with the traditional chemiluminescence immunoassay, PEA technology has shown remarkable advantages in detecting the biomarkers of AD. Chemiluminescence immunoassay usually relies on antigen-antibody reaction and generates signals through labeled luminescent substances, such as acridine ester or luminol, but its sensitivity and specificity are affected by antibody pairs and labeling efficiency. PEA technology is not only through antigen-antibody reaction but also PCR, thus providing higher sensitivity and wider dynamic detection range [8]. This high specificity and sensitivity make PEA technology have great potential in the early diagnosis of AD. The early diagnosis of AD is important for the effective management and treatment of diseases, and PEA technology can detect small changes in the early stage of diseases, which makes it possible for early intervention. The simplicity and cost-effectiveness of PEA technology are also important advantages in the diagnosis of AD. Compared with traditional immunoassay technology, PEA technology does

not need expensive equipment and complicated operations, which helps to reduce medical costs and improve the accessibility of diagnosis.

4.3. Application Prospect in the AD IVD Field

Olink technology has a broad application prospect in the IVD of AD. With the aging of the population, the incidence of AD is increasing year by year, and the demand for early and accurate diagnosis methods is increasing. PEA technology has obvious advantages in the IVD field because of its high sensitivity, high specificity, and multiplexing ability. PEA technology can be developed into a rapid and simple detection kit, which is suitable for clinical use. PEA technology has great value in clinical diagnosis because of its high sensitivity and multiplexing ability. By detecting several biomarkers related to AD, PEA technology helps evaluate the pathological state and progress of the disease more comprehensively [9]. With the progress of technology and the reduction of cost, PEA technology is expected to become an important method in the IVD field. In the future, PEA technology may be combined with artificial intelligence and big data analysis to further optimize the diagnosis process and realize personalized medical care and precise treatment.

5. INNOVATION BREAKTHROUGH AND TECHNICAL CHALLENGE

5.1. Innovative Application of PEA Technology in AD Diagnosis

The innovative application of PEA in the diagnosis of Alzheimer's disease indicates the great progress of biomarker detection technology. PEA technology allows the detection of target biomarkers at the molecular level with high specificity and sensitivity through its unique molecular proximity principle. By designing specific probes for AD-related biomarkers, this technology can identify disease-related molecular changes at an early stage, thus realizing early diagnosis of AD. Compared with traditional ELISA or chemiluminescence immunoassay, PEA technology not only relies on the labeling of antibodies but also generates signals through PCR, which improves the accuracy and sensitivity of detection. The high sensitivity of PEA technology enables it to detect biomarkers in a low sample size, which is especially important for clinical applications that need to minimize invasive operations. These innovative applications of PEA technology provide new tools and methods for early diagnosis, disease monitoring, and treatment effect evaluation of AD.

5.2. Technical Breakthrough and Potential Clinical Value

The breakthrough of PEA technology in AD diagnosis has brought great potential value for clinical diagnosis and disease management. Firstly, the high sensitivity and specificity of PEA technology make it possible to detect disease-related biomarkers in the early stage of AD, even before clinical symptoms appear. This ability of early diagnosis is of great significance for delaying the progress of the disease and improving the prognosis of patients. The multiplexing ability of PEA technology allows multiple biomarkers to be detected at the same time, which helps to evaluate the pathological state of AD more comprehensively and provides the possibility for personalized treatment. By monitoring the changes in multiple biomarkers, doctors can evaluate the treatment effect more accurately and adjust the treatment plan in time. The simplicity and cost-effectiveness of PEA technology make it possible for it to be widely used in clinical environments [10].

5.3. Technical Challenges and Solutions

Although PEA technology shows great potential in AD diagnosis, it still faces some technical challenges in practical application. Firstly, the specificity and affinity of probe design are very important for the accuracy of PEA technology. In addition, non-specific binding of antibodies may also lead to false positive results, while insufficient affinity of antibodies may reduce the sensitivity

of detection. In order to solve this problem, bioinformatics tools and calculation methods to optimize the probe design and carry out strict experimental verification. The signal amplification process of PEA technology needs precise control to avoid excessive background signals. This may require the development of new ligase and PCR optimization methods to improve the specificity and stability of the signal. In addition, multiplexing technology poses new challenges in data analysis, and it is necessary to develop more advanced data processing algorithms and software to accurately analyze complex data sets. The clinical application of PEA technology needs large-scale clinical trials to verify its effectiveness and safety [11]. This requires close cooperation with researchers, clinicians, and regulatory agencies to ensure that the application of technology meets the requirements of medical standards and regulations.

6. CONCLUSION

We deeply discussed the specific antibody produced by monoclonal antibody technology and the application of PEA in the diagnosis of Alzheimer's disease and demonstrated the potential of these innovative methods in improving the accuracy of early identification and diagnosis of diseases [12]. By comparing chemiluminescence with PEA technology, we realized the remarkable advantages of PEA in the IVD field. The technology is expected to be widely used in clinical practice, providing strong support for early diagnosis and personalized treatment of AD, thus improving the quality of life of patients and slowing down the progress of the disease.

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