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Metal-organic Skeleton (MOF) Composite based Using Electrochemical Immunobiosensor to Detect the Important Tumor Marker of Breast Cancer Glycotype Antigen 15-3

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Abstract: Breast cancer is one of the biggest threats to women's life and health in the world, and the mortality rate has reached the second highest in the world. With the development of metal organic skeleton (MOF) and the advantages of the composite in the field of electrochemistry and biosensing, various metal organic skeleton composites have been widely used in electrochemical biosensors. Thus, electrochemical biosensors have received extensive attention and research in the field of rapid breast cancer detection. This article mainly introduces the detection of sugar-type important tumor marker antigen 15-3, and electrochemical immunobiosensor Excellent performance in breast cancer detection and promising prospects for its application.

Keywords: Metal-organic Skeleton (MOF); Biosensors; Breast Cancer; Sugar Antigens 15-3; Electrochemical Immunity.

1. Project Significance and Introduction

Breast cancer has the greatest impact on women's lives and health worldwide One of the serious diseases, there is the famous journal CA (Chemical Abstracts, CA) in 2018 reported that the world throughout the year Breast cancer accounts for about 11.6% of patients with new cancers, and it ranks the second highest mortality rate in the world [1]. It is revealed that breast cancer has become the most common cancer affecting the health of women around the world, and it is also a major problem in women's health care around the world. At present, the most widely used tumor markers in breast cancer patients are carcinoembryonic antigen and glycoprotein 153 (CA153) [2]. First of all, carcinoembryonic antigen is a glycoprotein, mainly found in the pancreas, intestine, and liver of fetuses from 2-6 months of age, so the postnatal tissue content is very low, very low, less than 2.5 nanograms / milliliter. Elevated carcinoembryonic antigen is usually seen in malignant tumors of the digestive tract, such as gastric, colon, rectal, and pancreatic cancer. The second common malignancy is breast cancer. Usually, when the carcinoembryonic antigen is> 20 ng/ml, it is of more therapeutic significance. It means that the possibility of having cancer is higher. The other is CA153, glycoprotein 153, a tumor marker mainly used for the diagnosis and follow-up of breast cancer. If the abnormal increase of CA153 in the early stage of diagnosis, it indicates the possibility of breast cancer, and if the gradual increase of CA125 occurs after surgery or during the follow-up after chemotherapy, it may indicate the possibility of disease recurrence [3]. The breast cancer tumor markers tested in this time are biomolecules that are not normally expressed in the cancer cells of breast cancer cells in different stages of cancer, and play an extremely important role in the early screening and diagnosis of breast cancer. Even through the contemporary conventional breast cancer diagnosis technology including (breast X photography technology, biopsy technology, magnetic resonance imaging, ultrasound scanning, etc.), has reached the effective detection of 80% to 90% of breast cancer. However, these ordinary medical methods have obvious disadvantages in terms of convenience and safety, and limitations in medical cost and professional degree of medical personnel. Therefore, biosensor, which combines sensitive, specific, economical and efficient advantages, has naturally gained extensive attention and exploration [4].

1.1. Research Objectives and Contents

A biosensor is a conversion of biological reaction into objects The signal, and the signal determines the sensing of the target material concentration instrument. Because the biosensors are made rapidly by proceeding directly to the physiological liquid Of non-invasive detection, so biosensors in breast cancer detection There are obvious advantages in testing and diagnosis. The occurrence and progression of cancer are often accompanied by changes in the concentration of tumor markers. However, in the early stage of cancer, the concentration of tumor markers is very low, so the micro (trace) detection of tumor markers is of great significance for the early prevention and treatment of cancer. Biosensors exploit the specific binding of biomolecules to target analytes and transform unvisible biological reactions into readable signals through a transducer. Compared with the traditional detection methods of tumor markers, such as immunohistochemistry and enzyme-linked immunosorbent method, biosensors have the advantages of simple preparation, easy to operate, high sensitivity and low cost. The metal organic skeleton (MOF) has the advantages of diverse structure, adjustable pore structure, large surface area, high porosity, open metal active site, which is widely used in gas selection adsorption and separation, catalysis, fluorescence, sensor and other research directions. However, at the same time, only the mechanical strength of MOF material is not high and the chemical stability is poor, and the use of MOF composite material can effectively make up for the defects of MOF, so the biosensor based on MOF composite material shows great advantages. In the recent studies, the use of

biosensors based on MOF composites to detect tumor markers has attracted wide attention from scholars. Electrochemical immunosensor is an immunoassay method combining immune method and electrochemical detection technology, which can finally microtrace protein tumor markers by measuring the changes of relevant interface current, capacitance, potential and conductance before and after the immune response [5]. To achieve the purpose of increasing detection signal and improving detection specificity and accuracy.

1.2. Key Problems to be Solved

Glycoid antigen 15-3 (CA15-3), is the most important specific marker of breast cancer. Breast cancer often CA15-3 increased, in the early breast cancer sensitivity is not high, about 60%. The positive rate of metastatic breast cancer can be as high as 80%. In Europe, CA15-3 is commonly used as an auxiliary diagnostic index for breast cancer, and it is also an indicator for postoperative follow-up to monitor tumor recurrence and metastasis [6]. CA15-3 is a breast cancer-associated antigen with significant value for the medical diagnosis and postoperative follow-up of breast cancer. But other tumors such as lung cancer, kidney cancer, colon cancer, pancreatic cancer, ovarian cancer, and other tumors may also have varying degrees of elevation. But that CA153 is less significant in these tumors [7]. The serum level of CA15-3 in patients is proportional to the change of breast cancer disease, which can be used as a specific signal for breast cancer recurrence and metastasis, and the expression of this signal is often faster than the onset of clinical symptoms and the detection of similar techniques such as B ultrasound, X-ray or CT. According to relevant data, when the CA15-3 level exceeded 30u / ml, 40u / ml and 50u / ml, the differential breast cancer patients had postoperative local recurrence or distant metastasis, their sensitivity exceeded 90%, specificity was 95%, 99% and 100%, respectively, and the correct judgment rate reached 56%, 83% and 100%, respectively [8]. At the same time, breast cancer patients with increased CA15-3 levels are much more quickly than CA15-3 patients. According to the investigation, breast cancer patients serum CA15-3 levels and its regional lymph nodes and distant metastasis between the identity, especially with distant metastasis, the CA15-3 expression level and positive rate are greatly increase [9], so, CA15-3 has the identification of breast cancer metastasis, when the serum level continues to rise, the need to start or strengthen chemotherapy, radiotherapy or into endocrine therapy, etc [10]. Thus CA15-3 has a strong correlation with breast cancer, because the electrochemical sensor has fast, accuracy and high sensitivity, so the study based on metal organic skeleton (MOF) composite material using electrochemical immune biosensor important tumor markers for breast cancer sugar antigen 15-3 for breast cancer disease detection and postoperative treatment is of great significance. Therefore, in this article, we will propose a based on metal organic skeleton (MOF) composite material using electrochemical immune biosensor important tumor markers for breast cancer sugar antigen 15-3, which to the world of breast cancer detection and postoperative treatment provides a new method, is beneficial to the world of breast cancer early prevention and timely diagnosis and postoperative examination, so as to achieve the goal of saving more breast cancer patients.

2. Proposed Research Method

CA15-3, or carcinoembryonic antigen 15-3, is also a glycoprotein composed of antigen-determining clusters, sugars and polypeptides, and is a type of broad-spectrum tumor markers. So previous research method, UIO-66-NH as the carrier of CA15-3 antibody, build "sandwich" cancer-embryo antigen 15-3, synthesis of Ag-MOF, because it contains a large number of Ag (I), and Ag (I) electrochemical signal is very stable，so Ag-MOF can not only be used as a carrier of fixed antibody, but also can be used as a signal probe, based on this "sandwich" electrochemical immune sensor CA15-3 is established, in potential breast cancer patients or postoperative patients, patients with tumor markers and antibodies fixed on the sensor for specific recognition, finally through the determination of the relevant interface current, capacitor, potential, conductance, etc, the micro trace protein tumor markers sensitive and accurate detection.

In conclusion, the electrochemical immunobiosensor based on MOF composite can effectively replace the traditional breast cancer tumor marker detection method, detect the response of antigen antibody in real time, and realize quantitative measurement, that is, to continuously record the reaction while the antigen antibody response for dynamic analysis. Compared with the conventional breast X photography technology, living tissue examination technology, magnetic resonance imaging, ultrasonic scanning detection methods, have higher convenience and safety, and the use of MOF composite material to build electrochemical immune biosensor, using immobilized bioactive substances as catalyst, makes value expensive reagent can be repeated many times, to a certain extent, overcome the past enzymatic analysis reagent high cost and chemical analysis complex disadvantages. Have (1) Strong specificity, Only only to a specific substrate, And is not affected by the color and turbidity; (2) the fast detection speed, Basically, the results can be obtained in one minute; (3) high accuracy, Generally, the relative error can be as low as 1%; (4) the operation mode is relatively simple, Can easily realize automatic analysis; (5) low cost, At successive tests, The multifaceted significant advantage of using only a small amount of RMB per use, Combined, these advantages can broaden the linear range of detection, reduce the detection limit, The biosensor then combines a variety of functional materials with a simple MOF, Give full play to the unique properties of different materials. Therefore, the experimental scheme is highly feasible.

3. Experimental Pre-results and Discussion

We have developed the metal organic skeleton (MOF) composite electrochemical immune biosensor, in addition to other biological sensors also has high sensitivity, low detection limit of many advantages, strong anti-interference ability is also an important characteristics of immune biological sensor, can be widely used in the bedside detection of tumor markers. Improved sensitivity, lower detection limit; reduce analysis time; simplify analysis process; equipment miniaturization; automated measurement process, can detect immune response and perform fine immunochemical analysis. Therefore, the preliminary results developed by us for the detection of breast cancer specific marker CA15-3 are considerable. In our research plan, the total duration is expected to be: two years; the expected results: in the

treatment of breast cancer diagnosis and postoperative recurrence risk assessment, so that it can be applied to the daily testing in all kinds of hospitals, so as to improve the timely prevention and diagnosis of female breast cancer around the world, to achieve the goal of helping curing breast cancer patients, and make a contribution to the anti-cancer cause around the world.

Although the MOF composites have already been produced The field of object sensors has shown a wide range of application directions, but it is also obvious The disadvantages of weak anti-interference ability and insufficient high-throughput detection ability. So if you want to Continuing to improve the application and performance of such sensors needs to continue to improve the acid resistance of MOF composites Base capacity, designed more reasonable MOF size, and with microarray, microflow Control and other cutting-edge technology combined. More importantly, as scientists continue to dig for new materials And the continuous development of AI, based on the Various biosensors of MOF composites will develop to be more miniaturized and integrated Chenghua, multi-functional, intelligent, ultra-low power consumption, can show better performance in clinical testing, biosafety, food safety, environmental testing and other aspects.

4. Summary and Outlook

At the same time, biosensors have developed rapidly and have been gradually applied in food, industry, environmental testing, clinical medicine and other fields. As an emerging biosensor, immunoelectrochemical sensor is favored by more scholars for its high specificity, sensitivity and stability of identified substances. Its advent has changed the traditional immunoassay. It combines the traditional immunodetection and biologic sensing technology into one, integrating many advantages of both, reduces the analysis time, but also improves the sensitivity and test accuracy, making the measurement process simple, easy to achieve automation, it can be seen that it has a broad application prospect. With the development of bioengineering technology, fusion cells that can secrete monoclonal antibodies to various microorganisms, cell surface antigens or various protein antigens have been developed. The monoclonal antibodies produced by these cells have been widely entered into biology and other fields.

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