Exploratory Research on Constructing a Computational Biological Model Based on Second-generation Sequencing Technology for Monitoring Measurable Residual Disease (MRD) after Breast Cancer Surgery

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Informed Consent Form

Project name: Exploratory Research on Constructing a Computational Biological Model Based on Second-generation Sequencing Technology for Monitoring Measurable Residual Disease (MRD) after Breast Cancer Surgery

Research institution: The Second Affiliated Hospital of Zhejiang University School of Medicine

Dear Sir/Madam

We will invite you to participate in this clinical scientific research, which has been reviewed by the Medical Ethics Committee of our research institution. This informed consent form provides you with detailed information to help you decide whether to participate in this project. Please read carefully and ensure that you fully understand the content of the document or that your questions have been satisfactorily answered before making a decision. If you have any questions, please feel free to consult with the researchers (research doctors, research nurses, etc.), and we will provide you with comprehensive explanations.

1、 Research background, purpose, and content introduction:

Since 2020, breast cancer has become the largest cancer in the world, accounting for about 11.7% of all malignant tumors and 24.5% of the total number of new female cancer cases. The incidence and death rate of female cancer rank first, seriously threatening women's life and health. With the

continuous development of liquid biopsy technology, liquid biopsy technology based on cfDNA multi omics has shown great potential in postoperative cancer detection. Meanwhile, deep learning techniques can more accurately analyze and predict cfDNA multi omics data, providing a more reliable and accurate method for monitoring tumor recurrence after liquid biopsy technology. Clinical oncologists using this method can detect the presence of cancer 2-3 years in advance, with simple sampling, fast detection speed, and high accuracy, making it very suitable for monitoring postoperative recurrence of single cancer.

At present, scientific research in breast cancer MRD monitoring related fields has not been carried out on a large scale in China. Therefore, through the research of this project, we expect to establish a computational biological model based on second-generation sequencing technology to monitor breast cancer MRD, and verify the accuracy of this model in clinical application.

2、 Research process, methods, and timeline

After screening and evaluating your condition, the research doctor confirmed that you are eligible for inclusion in this study and signed an informed consent form. Then take 5ml of peripheral venous blood from you. A total of 11 follow-up visits were conducted in this study, with 5ml of peripheral venous blood collected from you each time, lasting for 3 years.

This study was conducted at our research institution and recruited a total of 80 participants to participate in this clinical research. The expected duration is from June 2023 to June 2026.

The criteria that meet the selection criteria include:

1) Age ≥ 18 years old, gender not limited;

2) Obtain plasma samples from the subjects during a 3-year follow-up period;

3) The subjects fully understand the study and voluntarily sign the informed consent form;

4) Can cooperate with a 3-year follow-up visit to the hospital;

5) . The physical fitness status score (ZPS) of the ECOG scoring criteria for the subjects must be ≤ 1;

6) Expected lifespan ≥ 5 years;

7) Subjects who meet the following criteria: a Histopathology confirmed primary breast cancer (unlimited molecular type); b. Radical breast cancer resection is expected; c. Adopting postoperative adjuvant therapy or preoperative neoadjuvant therapy;

The research participants who cannot be selected for this study include:

1) The subject is pregnant or breastfeeding;

2) Severe mental illness or drug abuse.

3) Unable to obtain plasma from the subject during that period;

4) The subject had a non primary malignant tumor of the breast with a clear pathological diagnosis within the 5 years prior to enrollment;

5) The subject has suspected non breast malignant tumors (such as B-ultrasound, CT, etc.) on imaging within the past year of enrollment, but without pathological confirmation;

6) Clinical suspicion of distant metastatic lesions;

7) The subject has received any blood product infusion therapy within the past 30 days;

8) Known carriers of pathogenic genetic mutations;

9) Participate in other interventional clinical studies within 3 months;

10) Subjects with poor compliance or deemed unsuitable by researchers to participate in undergraduate clinical trials;;

If you voluntarily participate in this study and sign this informed consent form, the study doctor will screen you before enrollment. If you meet the enrollment criteria but do not meet all exclusion criteria, you will be included in this study, and we will collect your information ☑ Blood, oral tissue samples, □ urine, feces □ pleural and peritoneal fluid, □ cells, □ clinical history data □ other: specimens (hereinafter referred to as specimens). The collection of specimens for this study is conducted simultaneously with your routine medical examination. In addition to meeting the requirements of routine examination and pathological diagnosis, we will keep some of your specimens for this clinical study. After testing, the test samples will be destroyed according to the regulations of the research center.

3、 Risk and discomfort:

（1）This study requires blood collection during the research phase, and the risks of blood collection may include fainting, pain, redness, swelling, and/or bruising at the acupuncture site. In rare cases, small blood clots or infections may occur at the acupuncture site.

（2）The above-mentioned organizational, blood sample collection, testing, or related examination procedures involved in the study are diagnostic examination items for research purposes (i.e., if you do not participate in this study, you do not need to undergo these examinations).

The above-mentioned sample collection, testing, or related examination procedures involved in the study are for routine diagnostic purposes. Even if you do not participate in this clinical study, as long as you accept this

examination item, these side effects/adverse reactions may occur. The research will not add any extra risk to you.

However, due to the limitations of current medical development, many research results may temporarily be unable to explain, which may bring you some anxiety and psychological pressure.

4、 Possible benefits:

Participating in this study may not have direct guiding significance for your current treatment. The results of medical research may have certain guiding significance for your future treatment plan selection, efficacy evaluation, prognosis prediction, etc. If the test results indicate the need to adjust your medical plan, we will promptly provide feedback to you and have your attending physician guide your personalized treatment (if there is no impact, we will not inform you separately).

Scientific research work mainly promotes the progress of science and technology, without generating direct economic benefits or welfare. If any patent rights or commercial interests are derived from the research results, all rights and interests will not be related to you.

5、 Costs and compensation for damages:

The specimen testing fee for this project will be borne by the researcher.

If any research related damages occur due to participating in this clinical study and following the instructions of the research doctor, the initiator of the

study will bear the relevant treatment costs and provide compensation in accordance with laws, regulations, and mutual agreement.

To compensate for the loss of blood collection, you will receive a nutritional compensation fee of 50 yuan per time. Please contact the researcher to obtain this compensation.

6、 Privacy issues:

If you decide to participate in this study, your participation in the experiment and personal information during the experiment will be kept confidential. Your identity information will not be disclosed to members outside of the research team unless authorized by you. All research members and sponsors are required to keep your identity confidential. Your file will be stored in a locked filing cabinet for researchers to access only.

To ensure that the research is conducted in accordance with regulations, if necessary, members of the ethics committee, management departments of research institutions, national regulatory agencies, and sponsors may access the original medical records containing your personal information and your signed informed consent form for research or regulatory purposes. These inspectors have all assumed the responsibility of confidentiality of subject information.

If this study is published in a research journal, your name and other identifiable information will be removed and replaced with subject numbers. The subject number is linked to your identification information, but only the personnel mentioned above can directly access your original medical records. Your identity will not be disclosed, and unauthorized individuals theoretically cannot identify your identity. We will make every effort to protect the privacy of your personal medical information within the scope permitted by law.

7、 Voluntary choice to participate in research and withdrawal from research midway

Whether to participate in the research is entirely up to your voluntary decision, and you can discuss it with your family or friends before making a decision. Before making the decision to participate in the study, please try to ask your doctor as many questions as possible until you fully understand the contents of this informed consent form.

You can withdraw from the study at any time without providing any reason. This will not affect the relationship between you and the doctor, nor will it cause any loss of your medical or other interests. We will retain and use the research data collected up to the time of your exit.

If the study is no longer in your best interest or due to other scientific or safety reasons, the study doctor or study sponsor also has the right to decide to withdraw you from the study. If your research doctor terminates your participation in this study, he/she will discuss the main reasons with you.

8、 How to obtain more information?

You can raise any questions about this research at any time. Your research doctor will leave you his/her phone number so that you can contact him/her.

If there is any important new information during the research process, including but not limited to adverse events and significant findings, that may affect your willingness to continue participating in the study, your doctor will notify you promptly. You will be required to sign a new informed consent form

to record any updates you have received and your willingness to continue participating in this study.

9、 If you have any questions, who should you contact?

If you have any questions about the research process, rights during the research, or if you believe you have suffered any harm related to the research, please contact your research doctor. You may be required to undergo relevant examinations, which is beneficial for protecting your health.

Research Doctor：

Contact Number：

For any questions regarding the rights and interests of participants in this study, please contact the Medical Ethics Committee at 0571-87783914, Research Department, 8th Floor, Caitong Building, 111 Jiefang Road, Hangzhou, China. Email address: keyanlunli_zheer@163.com ）.

As a research participant, you are required to provide truthful information about your medical history and current physical condition, and inform the researcher of any discomfort you may have experienced during the study period; Tell the researcher whether they have recently participated in other studies or are currently involved in other studies.

Thank you for reading the above materials. If you decide to participate in this study, please inform your doctor and he/she will arrange all the relevant affairs for you to participate in this study.

Signature page

I have read this informed consent form.

I have the opportunity to ask questions and all of them have been answered. I understand that participating in this study is voluntary.

I can choose not to participate in this study, or withdraw at any time after notifying the researcher without discrimination or retaliation, and my medical treatment and rights will not be affected as a result.

If I need other treatments, or if I do not follow the research plan, or if there are any research related injuries or other reasons, the research physician may terminate my participation in this study.

I will receive a signed copy of the 'informed consent form'.

Subject Name (in regular script):

Subject Signature:

Contact Information:

Date:

If the subject is unable to read and sign the informed consent due to reasons such as lack of legal capacity, or if the subject is a minor, their guardian shall act as a proxy for the informed process and sign.

Guardian Name (in regular script):

Guardian Signature:

Relationship with Subject:

Contact information:

Date:

If the subject lacks the ability to read the informed consent form (such as illiterate subjects), a witness shall witness the informed process and sign it.

Witness Name (in regular script):

Witness Signature:

Contact information:

Date:

ID card number of witness (or provide a copy of ID card):

I have accurately informed the subject of this document, and he/she has read this informed consent form accurately, demonstrating that the subject had the opportunity to ask questions. I prove that he/she voluntarily agreed.

Researcher Name (in regular script):

Researcher Signature:

Contact Information:

Date:

Informed Consent Form

Signature page

I have read this informed consent form.

I have the opportunity to ask questions and all of them have been answered. I understand that participating in this study is voluntary.

I can choose not to participate in this study, or withdraw at any time after notifying the researcher without discrimination or retaliation, and my medical treatment and rights will not be affected as a result.

Subject Name:

Subject contact phone number:

You can choose to fill in the above name and contact phone number on your own.

If you are willing to participate in this study, please check the following option to continue filling out:

□ Agree to participate in this study

If you are unwilling to participate in this study, please check the following option and choose to exit:

□ Disagree to participate in this study

The subjects have accurately read this informed consent form, had the opportunity to ask questions, and had sufficient time to consider whether to participate in this study. The researchers ensure that the subjects voluntarily agree to participate in this study.

Researcher Name:

Researcher's contact phone number：