Informed Consent Form for Subjects

Topic	Mapping of Genomic Structural Variations in Major Birth Defects
Research center	Peking Union Medical College Hospital
Principal Investigator	Qingwei Qi
Informed Consent Form Version	V1.0
Subject Name	
Subject ID	

Dear subject:

We would like to invite you to participate in a clinical study titled "Mapping of Genomic Structural Variations in Major Birth Defects". Before deciding whether to consent to participate, please carefully read this informed consent form. You may ask the investigator about any concerns you have, or consult your family members, friends, or other individuals. Once you decide to participate in the study, you are required to sign this informed consent form.

Research background

Conducting etiological research on birth defects is crucial for their prevention and control. Apart from environmental factors, genetic variations are a significant cause of defective offspring in healthy parents. The WES technology based on second - generation short - read sequencing lacks comprehensive coverage of genetic variation types, leading to limitations in genetic diagnosis.

Structural Variations (SVs), characterized by high mutation rates, large variation degrees, and strong pathogenicity, have become a research hotspot in life sciences in recent years. Currently, commonly used genetic testing methods in clinical practice have insufficient resolution for long repeat sequence regions and SVs, which may result in missed diagnoses, necessitating the introduction of new technical approaches.

Long - read sequencing is the development direction for genomic variation (especially SV) analysis. In addition to technological innovation, genetic etiological research on major birth defects in the Chinese population still requires overcoming two technical challenges. One of them is the need to construct a genomic reference map. There are significant differences in genomic structure and sequence among different populations, yet the current human genomic reference map is based on Caucasian samples. Applying it to identify genomic SVs in the Chinese population may lead to serious misinterpretations.

Therefore, it is urgently necessary to establish a pan - genomic reference map for the Chinese population. This study will focus on difficult cases with unclear genetic diagnoses, conducting long - read DNA sequencing data analysis of birth defect cases and family samples. It will prioritize the extraction and identification of individual - specific genomic features, develop detection algorithms for all types of structural variations (SVs) including complex SVs, and establish a pan - genomic reference map exclusive to the Chinese population. This will support the identification of pathogenic SVs in birth defect cases and family samples of the Chinese population, and map the fine structure of SVs associated with major birth defects in the Chinese population.

What is the purpose of this clinical study?

For complex cases with unclear prenatal genetic diagnosis, this project aims to conduct long - read DNA sequencing data analysis of birth defect cases and family samples. It focuses on the extraction and identification of individual - specific genomic features and develops detection algorithms for all types of structural variations (SV), including complex SV. It will establish a pan - genomic reference map exclusive to the Chinese population to support the identification of pathogenic SV in birth defect cases and family samples of the Chinese population, and map the fine SV spectrum of major birth defects in the Chinese population. The project will also deeply analyze the genetic and pathogenic roles of different types of SV in birth defects, providing a theoretical basis for promoting early warning, intervention, and prevention of major birth defects in China.

Method

(1) This study will not interfere with the current clinical diagnosis and treatment of the subjects.

(2) Inclusion criteria for this study:

① Single pregnancy with fetal structural abnormalities confirmed by ultrasound.

② Negative results from all routine prenatal genetic tests.

③ Alternatively, only one heterozygous pathogenic variant is detected in a suspected recessive genetic disorder, and no second suspected pathogenic variant is identified.

(3) Exclusion criteria:

① Twin/multiple pregnancies;

② Absence of interventional prenatal diagnosis;

③ Refusal of further testing by both parents.

(4) Adverse effects: The study used only the remaining available samples, posing no adverse effects to the patients.

(5) This project plans to enroll approximately 50 subjects for the study.

(6) Third - generation long - read sequencing was employed to analyze the family samples.

Research process

(1) This study will commence only after clinicians have obtained your prenatal diagnostic test results and confirmed that the results meet the study's inclusion criteria.

(2) Prior to initiating any study-related activities, you must first receive an introduction to the study project from the investigators, have your questions addressed, and sign the informed consent form.

(3) During the process of signing the informed consent form, you will have the right to choose whether to receive the results related to third - generation sequencing testing and make a declaration.

(4) During the screening phase, the investigator will inquire about and collect your personal information, medical history, genetic testing results.

(5) Retrieve any remaining samples from your previous prenatal diagnosis and perform third - generation sequencing testing.

(6) With your consent, this study will provide genetic counseling in the form of outpatient consultation based on the results of third - generation sequencing testing.

How to end the study

(1) If you complete the full follow - up of this study, you will be informed of your third - generation sequencing results and provided with adequate genetic counseling. After that, you will undergo subsequent clinical management in line with standard clinical practice.

(2) This study will conclude upon the completion of all treatments for the last participant. Your estimated duration of participation in the study is 3 years.

(3) You may choose to withdraw from the study at any time during the study period. The study physician may also request your withdrawal for your health and well - being.

(4) During the study, the research physician, the sponsor, the regulatory authority, and the ethics committee may terminate the study.

Benefits

(1) Participating in this study may allow you to obtain a more accurate fetal genetic diagnosis, which can serve as a reference for subsequent prenatal diagnosis and the selection of interventions.

(2) Participating in this study may offer guidance for your next pregnancy.

(3) Your participation in this study may help physicians gain further insights into the clinical efficacy of third - generation sequencing technology. Patients with the same or similar conditions may potentially benefit from this information in the future.

Risks and inconveniences

All research involves known or unknown risks. Some may be mild and transient, while others could be severe and permanent. The likelihood of risk occurrence, the specific risks involved, and their severity vary from individual to individual. Your research physician will implement all necessary preventive measures and closely monitor your condition. If you experience any discomfort, please inform your research physician immediately so that timely and appropriate treatment can be administered.

1. The samples used in this study were residual samples from prenatal diagnoses of pregnant women, and no specific physiological discomfort was reported by the subjects.
2. Failure to obtain results on time or test failure

   (1) Even when strictly adhering to technical specifications, testing may fail in rare cases due to sample quality issues or other unpredictable factors.

   (2) Due to uncontrollable factors such as pandemic control measures, sample testing may not be conducted, resulting in delayed research outcomes.
3. Test Results

   (1) The results of third - generation sequencing may include genetic diagnostic findings beyond the intended purpose or results with unclear clinical significance. This could potentially introduce uncertainty in subsequent clinical diagnosis, treatment, and counseling, thereby exerting psychological pressure or anxiety on the subjects and their families. During the informed consent process in the study enrollment phase, subjects have the right to choose and declare whether to accept test results with unclear clinical significance, or even whether to receive any information about test results.

   (2) The subject was not assured of 100% accuracy of the test results.

   (3) The subject was informed that the test results are only valid for the current sample and cannot serve as the basis for final clinical diagnosis.

New information in the research process

During the study, if researchers obtain the latest and most relevant information related to the study, we will promptly inform you, and it is up to you to decide whether to continue participating in this study.

Related costs

The testing and monitoring expenses during the study process are free of charge, and you will not be required to bear any additional costs. We will cover the costs of third - generation sequencing tests required for your participation in this study. If the test results indicate the need for further examinations, you will be notified accordingly. The costs associated with further examinations will be your responsibility.

What benefits will you receive for participating in this program?

Since participating in this study poses no health risks to you or your fetus, you will not receive any financial compensation upon enrollment.

How to handle my sample

(1) This study will utilize the remaining samples from your previous prenatal diagnosis for

testing.

(2) The sample usage in this study is as shown in the table below:

Sample type	Sample volume	Test method
Remaining amniotic fluid	8ml	Long - read DNA sequencing

(3) Samples collected during the study will undergo testing and analysis at our institution. The remaining samples after use will be stored in a sample bank for long - term preservation and may be utilized for future medical research upon obtaining ethical approval.

Confidentiality system

(1) In this study, your personal information and medical information may be collected or processed, including but not limited to: your name, gender, date of birth, address, telephone number, diagnosis, treatment, etc.

(2) Your personal information will be used solely for the purposes described in this study protocol and this informed consent form.

(3) The medical information obtained from your participation in this study will be kept confidential. No personally identifiable information will be disclosed when the research findings are published in academic journals.

(4) The investigators will be responsible for the storage and use of all your personal data in this study. The research supervisors, ethics committee, or clinical research regulatory department of Peking Union Medical College Hospital may access your personal data.

Principle of voluntariness

Your participation is entirely voluntary. You may opt out of or withdraw from the study at any time during the research process, and this will not affect your relationship with the healthcare providers or your regular medical care.

Matters needing attention

(1) Please truthfully disclose your pregnancy and childbirth history, family history of genetic diseases, and other relevant information to the research physician.

(2) If the laboratory receives samples that do not meet the requirements, you must actively cooperate with re-collection and re-testing.

Contact information

If you experience any discomfort or have any questions regarding the study, you may contact the investigator:

Research Assistant	Jiazhen Chang	Tel:+86-010-69156230

If you have any questions regarding the rights of participants, you may contact the ethics committee：

Ethical Secretary	Jiayue Li	Tel:+86-010-69156874

Thank you for reading and for considering participating in the study.

Signature page

Participant

I confirm the following:

I have read and understood the above informed consent information, and I have had sufficient time to consider whether to participate in the study.

All my questions have been answered to my satisfaction.

I voluntarily participate in this study and will comply with the research procedures.

I understand that I may withdraw from this study at any time without providing a reason, and my treatment or benefits will not be affected.

I have received an informed consent form and signed it for my own records.

I agree to the collection and use of my sample as described in this informed consent.

I consent to the collection and use of my personal information in this study.

I acknowledge that I may be contacted in the future to obtain my consent for this study or any related sub - studies.

I have been fully informed and have considered the matter, and hereby make the following declaration regarding the disclosure of the study test results.

☐ Please inform me of all genetic diagnostic results that meet the requirements of the third - generation sequencing test report in this study.

☐ Please inform me of all results that meet the requirements of the third - generation sequencing test report in this study and have been clinically determined to have clear clinical significance.

☐ I do not wish to receive any results from the third - generation sequencing test.

By signing this document, I agree to participate in this study in accordance with the informed consent information and the statements in the consent form.

Subject signature:_____ Date:_____

This section is only applicable to subjects without legal capacity, requiring the signature of a guardian.

Subject name_____The relationship between the guardian and the subject is_____]

Guardian's name_____ Tel：_____

Guardian's signature_____ Date:_____

This is only applicable to subjects without reading or writing ability, requiring a signed witness.

Witness name_____ Tel：_____

Witness signature_____ Date:_____

Researcher/Authorized Person Signature：_____ Date:_____