Study Consent Form
Clinical Utility of Prenatal Whole Exome Sequencing NCT03482141
Document Date: 5/27/2021

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: ***Clinical Utility of Prenatal Whole Exome Sequencing***

Maternal consent form

Research Project Director:	Mary Norton, MD, Professor of Obstetrics, Gynecology and Reproductive Sciences, UCSF 350 Parnassus Avenue, Room 810, CA. 94143-0132 Phone: (415) 353 7865; e-mail: nortonm@obgyn.ucsf.edu
Study Coordinator:	Billie Lianoglou, LCGC Phone: (415) 476 2461 Billie.lianoglou@ucsf.edu

Dr. Mary Norton and her team are conducting a clinical research study. Research studies include only people who choose to take part. You can take your time deciding if you want to participate. If you have any questions, please ask a member of the study team.

You are being asked to take part in this study because an ultrasound during your pregnancy has found a birth defect in your fetus, and you have completed routine genetic testing that has not uncovered the cause.

What is the purpose of the study?

If you decide to participate, we will study the genes in your fetus' DNA using a new test called exome sequencing. Genes are the instructions passed from a parent to child that determine how our bodies are built and grow. Some medical conditions are caused by differences in genes. The exome sequencing test tries to find those differences.

This test will be done on a sample that has already been obtained for prenatal diagnosis (CVS, amniocentesis or testing performed after pregnancy interruption or loss). We are offering this test because other tests so far were not able to find a cause of the birth defect in your fetus. To understand the importance of variations found in your fetus' genes, we will also study the genes in your DNA and DNA from the fetus' biologic father.

Exome sequencing is different from most genetic tests. It studies <u>many</u> genes in your body all at once instead of one gene at a time. The goal of this research study is to see if finding the genetic cause of birth defects before delivery will help health care providers to 1) counsel women about the long-term outcomes for their children, 2) improve care during pregnancy and at delivery, and 3) plan for the medical needs of the baby. We want to see if having a better understanding of the genetic causes of birth defects can help pregnant women and their families make pregnancy-related decisions. We also want to see if a diagnosis made before birth can lead to better treatment of the mother and fetus during the pregnancy or immediately after delivery.

We also want to understand the effect genetic information has on families. The study may help other pregnant women whose fetuses have birth defects or genetic conditions in the future. We are particularly interested in learning how to provide services to families from different backgrounds.

This study is being paid for by the National Institutes of Health, the federal agency that pays for health research in the U.S.

How many people will take part in this study?

The study will include about 300 pregnant women and their partners, 600 to be consented in total. Women receiving care at a clinic affiliated with the University of California, San Francisco will be invited. This includes the UCSF Betty Irene Moore Women's Hospital (BIMWH), UCSF Benioff Children's Hospital at Mission Bay, UCSF Benioff Children's Hospital Oakland, Zuckerberg San Francisco General Hospital or UCSF Fresno Community Medical Center.

What will happen if we take part in this research study?

1) The purpose of this form is to explain the study. We will review this consent form with you in person, by video consultation, or over the phone. You will have the chance to ask questions about the study and to decide whether you would like to join the study.

2) If you decide to take part in the study, the team will collect health information about you, your pregnancy, your prenatal care, and your family. Medical records from your pregnancy will be requested. This information will be used by the study team and the laboratory to interpret findings from the genetic test.

3) Study staff will ask for a sample of blood, saliva or a cheek swab from you, and the fetus' biologic father. A blood sample will be drawn by inserting a needle into a vein. The blood sample will be about 1 teaspoon. We collect saliva by asking you to spit into a tube. Cheek swabs are collected by brushing the inside of your cheek with a small brush. Genetic material will be extracted from these samples. Samples from both parents are used to help understand genetic differences found in your fetus. It is most helpful to have a sample from both parents but testing can be done with sample from just one parent. Your health care provider or Dr. Norton, the study director, may also ask for DNA samples from other family members (including siblings) to help complete the testing process.

4) Each parent providing a sample will be asked to sign a consent form.

5) When the results from the test are available (about 3-5 weeks after we receive the samples), we will contact you to arrange discussion of your results. Results may or may not explain the cause of the birth defect found in your fetus. These results will be explained by the study team, including a genetic counselor, during an in person meeting or through a telehealth consultation. If we provide preliminary results by telephone, we will arrange to meet with you again when you are next at UCSF for a clinic visit. The physician and/or genetic counselor will explain the test results and what they mean for your fetus, your pregnancy, and your family. They will discuss

with you any important genetic change found in you or another family member who had testing. They may also make recommendations for follow-up with our team or another specialist. These results will become a part of your medical record and a copy of the results will be made available to you.

6) When we review the test results with you, we may ask you if someone from our study team may also observe. We may also ask if we can audio record the visit. We may show you the results displayed with a special computer program, or App, on an iPad. The purpose is to learn how to improve how we give results to families.

7) We will ask you to complete a couple of short surveys after you receive the results. Surveys may be done in person, by phone, and may be emailed, or mailed to you after the clinic visit. We want to learn about your experience with genetic testing and whether your test results affected your decision making during the pregnancy, improved your prenatal care, improved the ability of the medical team to plan for specific care needs for the baby, led to any different treatments, tests, or studies during your pregnancy, and whether the results have helped you or your family.

8) You will receive $50 total in gift cards if you complete the surveys. You will get $20 for the first survey after receiving the results and $30 for the second survey at 6-12 month follow-up.

9) You may also be asked to participate in one or two interviews. Only a small number of families will be invited. We want to learn how the results have affected your family. If you are invited, you will receive $35 in gift cards for each interview, or $70 if you agree to be interviewed twice.

10) Total personal involvement with study activities should take approximately 2-3 hours including the consent, return of results and follow up surveys.

11) It is possible that additional studies may be done by the study researchers on leftover samples or using results from your exome sequencing test. You have the choice to agree or decline to have your samples used for this kind of future research. If future studies are done by researchers using your data, those results will not be given back to you.

How long will my child be in the study?

Your participation in this study will take place over 9-12 months.

What kind of results will we get from exome sequencing?

Results related to your fetus' medical condition
The goal of this test is to find out if there are genetic differences that explain your fetus' medical condition. Knowing the cause of the condition may lead to changes in your prenatal care. You may also learn the chance that other family members have the same medical condition and the chance that you could have another child with the same condition.

Every person's DNA has many genetic differences. These differences may be unique to an individual, found only in one family, or present in many healthy people. Most of these variants do not cause disease.

The exome test can provide different kinds of results. We might find:

1. Genetic differences known to cause or contribute to the birth defect found in your fetus
2. Genetic differences that do not cause or contribute to any medical condition—in other words, they are normal variations of the gene.
3. Genetic differences that are new or rare, so that we do not know whether they cause or contribute to the birth defect(s) found in your fetus.
4. In many cases, no genetic differences will be found in your fetus

Genetic differences that are not related to the birth defects in your fetus

There is a chance that we could find a genetic difference that causes medical problems but that is not related to the reason you were offered the exome sequencing test. These differences might be important for your fetus now or in the future. They may also be important for your health or for the health of other family members. Some of these genetics differences mean there is a chance your fetus may develop cancer or heart problems later in life. If these differences are found, doctors may recommend tests to find cancer or heart disease early or suggest ways to prevent it. Only a small number of people have these differences found, and it is your choice whether you want to learn about whether these are present in your fetus.

Results from biological parents

Sometimes exome sequencing finds an important genetic difference that the fetus inherited from a parent. If that happens, we can tell you which parent it came from. If the lab finds a genetic difference in a parent that is important for your health, we will help refer you to a doctor who can provide care for that condition.

What are the limits of the exome sequencing test?

Most often this test does not find a clear genetic cause of the fetus' condition. This is sometimes because the test cannot find all genetic differences that are important for health. We may not find the cause of the condition in your fetus because of limits to our knowledge about human genes and disease. It is also possible that we will find a genetic difference and not be sure what it means or if it is the cause. Even when we find a genetic difference that we think is medically important, we may not be able to predict how severe it will be.

Can we change our mind about being in the study?

Yes. You can decide to stop being in the study at any time. Tell the study team if you decide to stop participating in any part of the study.

The study doctor may suggest that you stop being in this study if she believes it is in your best interest, or if you are not able to continue to complete the study visits.

What side effects or risks are there?

- Drawing blood for the exome sequencing may be uncomfortable or cause bruising, infection, or fainting. The risk is not different from the risk of a routine blood test.
- Information about family relationships can be learned during testing. Testing may reveal unexpected information about blood-relatedness. It may reveal situations where a father or another relative has no biological relationship with the fetus, meaning that the father is someone unexpected. UCSF researchers may discover additional information about your family's health.
- Genetic testing or other unexpected events may involve a risk to privacy. UCSF takes many steps to keep personal health information confidential.
- Some people worry that genetic information might be used against them. A federal law called the Genetic Information Nondiscrimination Act (GINA) gives some protection. The law says that employers and health insurance companies cannot use genetic information when making decisions. Life insurance, long-term care insurance, and disability insurance are not included in this law's protections. GINA does not cover those serving in the military. California law also includes protection against genetic discrimination, but legal protections are not complete.
- There may be unknown risks to participating in the study and having exome sequencing.

Are there benefits to taking part in the study?

You may benefit if we find a genetic difference that is important to your health, the health of your fetus and/or the health of your family. In this case, you, your fetus and your family may benefit from having that information.

Even if you receive no direct benefit, your participation may help doctors and scientists improve genetic testing. We hope that this will help future patients.

What other choices do I have if I do not take part in this study?

- Your choices include: Not having exome sequencing, and continuing your pregnancy with routine care.
- Getting exome sequencing paid for by your insurance or by paying out of pocket.
- Entering a different research study if one is available.

Will information obtained from the study be shared with others?

Yes, your results will be shared with your doctors to help with your clinical care. We may also share information about your pregnancy and the test results to help with future medical research.

Clinical: The exome sequencing test is a clinical test. This means that the results will be placed in your medical record and, if the testing is not completed until after you deliver, in your child's medical record. Doctors, nurses, and others carrying for you and your baby will have access to results.

Also, limited information about your test results may be placed in a genetic laboratory resource run by the National Institutes of Health, a U.S. government health agency. Sharing genetic information in this way helps doctors to look at many people's test results. This allows them to understand genetic differences more fully and may help them develop new treatments or forms of prevention. If you decide to participate in the study, this sharing is required.

Research: Sharing genetic information is important for advancing medical research. Therefore, we will share your family's health and genetic information in the following ways:

1) We will share your and your family's health and genetic information with other clinicians and scientists inside UCSF. If you decide to participate in the study, this sharing is required. Every effort is made to keep your identity private as much as possible.

2) We will share your and your family's health and genetic information with trusted research partners from other institutions that work with UCSF. If you decide to participate in the study, this sharing is required. Every effort is made to keep your identity private as much as possible.

3) We will share your and your family's health and genetic information in a research database run by the National Institutes of Health, a U.S. government health agency. Sharing this information will enable researchers to better understand genetic differences between people. Every effort is made to keep your identity private as much as possible. This sharing is optional, and you will be asked to check a box at the end of this form if you prefer not to share this information.

We never include your name or other personal information when sharing data. However, genetic information is unlike other information. Your detailed genetic information is unique to you and could possibly be re-identified. We believe the risk of someone figuring out who you are is low. The purpose of sharing data is to allow doctors to learn more about genetic differences that cause medical conditions.

If you would like to withdraw from the study and no longer want your information shared as part of the study please notify the study team in writing. We will not be able to retrieve information that has already been shared and we will not be able to remove results tha have already been placed in the electronic medical record.

How will my family's health and genetic information be protected?

Whenever we share information with other researchers we will not include your name or date of birth or other personal identifiers. When we publish or discuss the results of this research study, we may show a family tree and who is affected with a genetic condition, but we will not include any information that could identify you or your family members. At all times, we will do all we can to make your family less recognizable.

Is sharing my information risky?

Sharing your private medical information involves some risks. People involved with your and your family's care, including insurance companies, may learn that your family participated in this study and may learn the test results. Information about you and your family will be handled as confidentially as possible. Information that could be used to identify you or your family will be physically secured. Electronic data will be password protected and secured behind a firewall. As with any electronic data storage, there is a chance of a security breach. This might result in a loss of privacy. There is also a risk of discrimination if someone learns you or someone in your family has a health problem.

Can researchers be forced to disclose my information?

According to National Institutes of Health policy, researchers cannot be forced to disclose information that may identify you or your family members, even if that information is requested with a court subpoena. This applies to federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

When may researchers disclose information about me and my pregnancy without my permission?

Researchers may not withhold information from the federal government needed for auditing or evaluating federally funded projects or information needed by agencies that assure the safety of medical care.

May I or a family member voluntarily release information?

You or a member of your family may voluntarily release information about your and your family's involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not withhold that information.

Are there any costs to participating in this study?

Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care and clinic visits, including any follow up clinic visits and genetic counseling services. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out of network. Any procedures done only for research, including exome sequencing, will not be charged to you or your insurer. Exome sequencing done as part of this study is paid for by the National Institutes of Health.

Will I benefit financially from taking part in this study?

It is possible that the research done on your sample may help doctors to develop medical tests or treatments that have commercial value. You will not receive any money that might result from such research.

What happens if I am injured as a part of this study?
It is important that you tell the study doctor if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call her at 415-476-0445. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415-476-1814.

What are my rights if I take part in this study?

Whether or not to take part in this study is your choice. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your or your family's medical care from our institution. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

You can call the study team about any questions, concerns or complaints you have. If you want to ask questions about the study or your rights as a research participant with someone outside the research team, or if you want to discuss any problems or concerns you may have about the study, please call the UCSF Institutional Review Board at 415-476-1814. You will be given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

A description of this clinical trial is available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. The website will include a summary of the results. You can search this website at any time using the clinical trial number assigned to this research study, NCT03482141

Special federal laws protect the privacy of your family's personal health information. You will be asked to sign a separate form allowing the University of California, San Francisco to access, use, or share health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right not to participate or to leave the study without penalty or loss of benefits to which you are otherwise entitled. If you wish to participate in this study, please sign below.

_____
Date Participant's Signature for Consent

_____
Date Legally Authorized Representative

Date Person Obtaining Consent

Date Witness – Only required if the participant is a non-English speaker

We want to make certain we understand your choices. Please answer the following questions:

Exome sequencing tests sometimes show additional findings. Some of these findings may be medically significant. Would you like to learn about medically significant additional findings discovered in you and/or your fetus? You might learn that you or your fetus are at risk for a condition like cancer or heart disease. See page 4 for more details. Please initial yes or no.

YES, I want additional findings	*NO, I do not want additional findings*
Initial:_____	Initial:_____

As part of this research study we will share your health and genetic information with a research database run by the National Institutes of Health, a U.S. government health agency. Sharing this information will enable researchers to better understand genetic differences between people. See page 5-6 for more details. Initial the box below if you'd prefer not to share this information.

NO, I do not want my information to be shared with a research database to aid future research.
Initial:_____

My samples and health information may be used in future research to learn about, prevent, or treat birth defects and genetic conditions.

YES	*NO*
Initial:_____	Initial:_____

I am willing to donate an extra tube of blood for the additional research described above.

YES	*NO*
Initial:_____	Initial:_____

I give my permission to be contacted about participation in future research by UCSF or UCSF research collaborators.

YES	*NO*
Initial:_____	Initial:_____