

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals**Primary consent form for blood or saliva/buccal swab collection for whole-genome/exome sequencing to identify the genetic cause of Mendelian diseases**

H-29697- GENOME SEQUENCING TO ELUDICATE THE CAUSES AND MECHANISMS OF MENDELIAN GENETIC DISORDERS

Background

The person being asked to take part in this research study may not be able to give consent to be in the study. You are therefore being asked to give permission for this person to be in the study as his/her decision maker. In the following paragraphs, "you" may refer to you or your child/dependent.

You are invited to take part in a research study. Please read this information and feel free to ask any questions before you agree to take part in the study.

We are asking you to take part in a study that involves genetic analysis. Genes are pieces of DNA that provide the instructions for building the proteins that make our bodies work. These instructions are stored in the form of a code, the genetic code. This is the code that you inherit from your parents and that you may pass on to your children. Mutations are errors in these instructions that could cause a protein to not be produced or to not work properly. In these ways, mutations may cause a disease, or make someone more likely to develop a disease.

Your doctor has decided that it is very likely that you have a mutation in your genetic code and that this has led to a genetic disease. Your family members may also have the same mutation. However, the mutation or affected gene has not yet been identified. We will try to find the mutation or affected gene using new methods called exome sequencing and whole-genome sequencing. These new methods will allow us to look at all or the most important pieces of your genetic code. In this way, we will try to find the exact genetic change that causes the genetic disease in your family.

Purpose

The purpose of this study is to find the genetic changes that have occurred in your genetic code and the genetic code of some members of your family that have led to a genetic disease. Because we may find many possible changes in your genetic code, it is very helpful to look at the genetic codes of your family members, both those with the disease and those without. This will give us more information about which one of the mutations is the main cause of the genetic disease.

The research done in this study will also help us to understand more about your disease and genetic diseases in general and how new technologies can be used to provide better medical diagnosis and appropriate patient care.

Procedures

The research will be conducted at the following location(s): Baylor College of Medicine, TCH: Texas Children's Hospital.

What samples will be collected?

You will be asked to provide a small amount of blood, a cheek swab, or a saliva sample. If possible, you will be asked to provide about 20 ml of blood (about 4 teaspoons). We may ask for additional samples if they are needed for further studies, but this would be no more than every 3 months. If we can't collect blood, or if the blood we collect isn't enough, it is possible that we can get DNA from a swab of your cheek using a brush or a saliva DNA collection kit. We may use your sample to create

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a cell line. This means that we would treat the cells from your sample in a way that allows us to grow them in the laboratory. These cells would also be stored and used for research.

What information will be collected?

Basic Information: We will ask you for some basic information, such as name, age, sex, etc. We will also ask about your family's health history.

Clinical Information: We will collect information from your medical records that is related to your health and/or disease history. Some examples include results of tests, medical procedures, images (such as X-rays), and medicines you take. We may request to look at your medical record from time to time to update this information.

Who will have access to my samples and information?

We will remove your name and any other information that could directly identify you from your samples. We will replace this information with barcodes or numbers. We will keep the samples in freezers in locked buildings at Baylor College of Medicine. We will keep health information and research data on secure computers that have many levels of protection. Your samples will be kept indefinitely unless you request that they be destroyed.

Over time your sample may run out or we may find something in your genome that we would like to study further. To do this, we may need to collect another sample from you and/or we may want to collect more clinical information. In some cases, we may also ask for your help to enroll your family members into this or other future studies. We would ask you to discuss your research experience with your family and provide them with our contact information. If any family member is interested, they may contact us for more information. If you agree, we may re-contact you and/or ask you to help enroll other family members for future research opportunities.

Yes ____/No ____ You consent to be contacted in the future.

In the future, other researchers may wish to study the samples you provided for other future studies. You may choose to participate in these studies or not. If you agree, your samples may also be put in a tissue bank at Baylor College of Medicine. A tissue bank is a place where samples from many people are stored for research. Researchers can apply to the tissue bank to get samples for their studies. If a researcher's study is approved, the tissue bank will give him or her samples and some information. These materials will always be labeled only with codes or numbers; the tissue bank will not give out any information that directly identifies you, like your name or address, without your permission. Please indicate below whether you agree to the use of your samples in future research.

Yes ____/No ____ You consent to have your specimens used for future research studies.

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Will I get the results of my DNA analysis?

Analysis of your DNA can reveal many things about you, including the mutations that have caused the disease that you or members of your family have. Some of the information may be important to your present or future health, some of it may have nothing to do with your health, and for much of it we will not know how it might or might not affect your or your family's health.

There is a potential risk in this genetic analysis for unwanted information to be discovered about parentage (the identity of someone's parents) or specific risk of disease. Some people who are healthy may find out that they have a mutation or DNA change that they did not know that could cause a risk of disease. People have different opinions about whether or not they want to know if they have these genetic changes. Therefore, this information will only be given to you if you let us know that you want to know the information. Please initial one or more of the spaces below:

_____ I do NOT wish to be informed of any DNA changes I have.

_____ I wish to be informed of ANY DNA changes I have that are found during the study that may explain my current medical condition. Contact me at the phone number / e-mail below.

Phone number / E-mail : _____

_____ I wish to be informed of DNA changes I have that are very likely to cause or put me at substantial risk of developing disease in the future and for which there is a cure or treatment.

Contact me at the phone number / e-mail below.

Phone number / E-mail : _____

_____ I wish to be informed of DNA changes I have that are very likely to cause or put me at substantial risk of developing disease in the future and for which there is a NO cure or treatment, including carrier status for diseases. Contact me at the phone number / e-mail below.

Phone number / E-mail : _____

_____ I wish to think further and decide later during the study whether I want to receive the information about any DNA changes I have that are found during this study.

Who will have access to my genetic information?

Researchers can do more powerful studies when they share with each other the information they get from studying human samples. They share this information with each other by putting it into scientific databases. These databases store information from many studies conducted in many different places. Researchers can then study the combined information to learn even more about health and many different diseases. This information is most valuable when it is linked to information about your medical history (clinical information).

There are many scientific databases where your genetic and clinical information may be released; some of these databases are publicly accessible and others are restricted to approved researchers

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only. If you agree, de-identified parts of your genetic information and, in some instances, some clinical information, will be released into one or more scientific databases, such as the database of Genes and Phenotypes (dbGaP). Your name and other information that could directly identify you (such as address or social security number) will not be placed into any scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Researchers will always have a duty to protect your privacy and to keep your information confidential.

As part of this research study, your data will be released into public and/or restricted scientific databases in a de-identified form for the benefit of medical research, unless you explicitly indicate the opposite. Please indicate whether you agree to the de-identified release of genetic and/or clinical information into scientific databases.

Yes You agree to the de-identified release of genetic and/or clinical information into publicly accessible scientific databases.

Yes You agree to the de-identified release of genetic and/or clinical information into restricted-access only scientific databases.

If we learn more information about your disorder through this research study, we may publish and/or present this information to other medical professionals through public scientific presentations and/or medical and scientific journals. You will never be identified by name.

I give consent to have my clinical information, genetic information, and family tree published in a medical or scientific journal

I give consent to have my photograph published in a medical or scientific journal if I am not identifiable in it.

I give consent to have my photograph published in a medical or scientific journal even if I am identifiable in it.

If you decide to leave this study early, Baylor College of Medicine reserves the right to use the health information that it had acquired prior to your decision to leave, if this information is needed for this study or any follow-up activities.

Baylor College of Medicine and the federal government do not have programs to pay you if you are hurt or have other bad results from being in this study.

If you have health insurance: The costs of any treatment or hospital care you receive as the result of a study-related injury will be billed to your health insurance company. Any costs that are not paid for by your health insurance company will be billed to you.

If you do not have health insurance: You will be billed for the costs of any treatment or hospital care you receive as the result of a study-related injury.

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The National Human Genome Research Institute (NHGRI) of the National Institutes of Health (NIH) has given us a Certificate of Confidentiality for this study. This certificate of confidentiality adds special protection for research information that allows us, in certain circumstances, to refuse to give out information that could identify you as a research subject without your consent, when such information is sought in a federal, state, or local court or public agency action. Still, we may disclose identifying information about you if, for example, you need medical help.

Potential Risks and Discomforts**Physical risks:**

The only physical risk in this study is related to the collection of blood samples. No potential major risks are associated with blood drawing; however mild bruising or bleeding can rarely occur; in very rare cases, it may result in fainting. You may have some small discomfort from the needle used to draw blood. A small blood clot may form where the needle enters or there may be swelling in the area. There is a very small chance that you may develop an infection where the needle went in. Medicine will be prescribed if infection occurs. There are no known risks associated with cheek swabs or saliva collection.

Risks related to pregnancy:

There are no direct risks to an embryo or fetus by taking part in this study. However, if you are a pregnant woman, no information from this genome sequencing study will be available to you or your healthcare provider over the course of your pregnancy. This research does not replace any routine medical or genetic testing you may have during your pregnancy.

Other risks and discomforts:

There is the potential that DNA analysis will reveal unwanted information, for example about ancestry, parentage, other non-medical physical or personality traits, etc. The data may also reveal that you may be at risk for certain genetic diseases or if you are a carrier of disease associated mutations. Also, predictions about health and disease made from DNA sequencing are not 100% accurate.

The DNA sequencing and analysis performed by Baylor College of Medicine in no way guarantees your health or the health of your living or unborn children. You should not rely only on the results of this study to make decisions about your health or the health of your family, or medical care for yourself or your family.

This genome-wide sequencing study will be done for research purposes only. Because this is research and we do not understand the meaning of all mutations or changes that we find in genes, we may not give all the results of your research tests to you. In addition, any results that we may find in your tests would need to be confirmed in a clinical certified laboratory. Study team members would help you find clinical testing if you want, however your insurance would need to pay for this testing.

If you have given us permission to contact you about your genetic information related to your family's genetic disease or other mutation likely to cause a serious medical condition other than the condition that led you to take part in this study, the information you learn may upset you. This

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information may also upset members of your family who may have the same genetic changes or mutations. There will be board certified genetic counselors and board certified geneticists available to answer any questions you may have about these results. You will not be responsible for the cost of this genetic counseling.

There is a potential risk that knowing your risk of disease could affect your insurance. The Genetic Information Nondiscrimination Act (GINA) generally protects you against discrimination based on your genetic information when it comes to health insurance and employment. We have a strict policy not to disclose any information to insurance companies. Your sample and related information will be assigned a barcode or number to protect your identity. All your personal and clinical information will be stored in password protected computers and a locked filing cabinet in a locked office; only some research staff will have access to this information. Also, there is a potential risk of being identified and information traced back to you or your family from the genetic and/or clinical information released into scientific databases. The current risk is small and we will take all precautions to prevent this from happening. However, even with the protections provided by GINA and the best efforts of the research team, there may still be a risk of insurance coverage denial or other kind of discrimination.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study.

Potential Benefits

You will receive no direct benefit from your participation in this study. However, your participation may help the investigators better understand the genetic cause of your disease. If you choose to receive your genetic results, they may be helpful in learning more about you and your family's health risk. If we find that you are a carrier for disease associated DNA changes, this may help your doctor guide your treatment in the future. However, you may receive no benefit from participating..

Alternatives

You may choose to not participate in this study.

Subject Costs and Payments

You will not be asked to pay any costs related to this research.

You will not be paid for taking part in this study.

This institution does not plan to pay royalties to you if a commercial product is developed from blood or tissue obtained from you during this study.

Subject's Rights

Your signature on this consent form means that you have received the information about this study

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and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

Your Health Information

We may be collecting health information that could be linked to you (protected health information). This protected health information might have your name, address, social security number or something else that identifies you attached to it. Federal law wants us to get your permission to use your protected health information for this study. Your signature on this form means that you give us permission to use your protected health information for this research study.

If you decide to take part in the study, your protected health information will not be given out except as allowed by law or as described in this form. Everyone working with your protected health information will work to keep this information private. The results of the data from the study may be published. However, you will not be identified by name.

People who give medical care and ensure quality from the institutions where the research is being done, the sponsor(s) listed in the sections above, representatives of the sponsor, and regulatory agencies such as the U.S. Department of Health and Human Services will be allowed to look at sections of your medical and research records related to this study. Because of the need for the investigator and study staff to release information to these parties, complete privacy cannot be guaranteed.

The people listed above will be able to access your information for as long as they need to, even after the study is completed.

If you decide to stop taking part in the study or if you are removed from the study, you may decide that you no longer allow protected health information that identifies you to be used in this research study. Contact the study staff to tell them of this decision, and they will give you an address so that you can inform the investigator in writing. The investigator will honor your decision unless not being able to use your identifiable health information would affect the safety or quality of the research study.

The investigator, JAMES R LUPSKI, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: JAMES R. LUPSKI at 713-798-6530 during the day and Wojciech Wiszniewski at 832-824-1000 (#6397) after

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hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

If your child is the one invited to take part in this study you are signing to give your permission. Each child may agree to take part in a study at his or her own level of understanding. When you sign this you also note that your child understands and agrees to take part in this study according to his or her understanding.

Please print your child's name here _____

CONSENT FORM

HIPAA Compliant

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Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject Date

Legally Authorized Representative
Parent or Guardian Date

Legally Authorized Representative - Adult Date

Investigator or Designee Obtaining Consent Date

Witness (if applicable) Date

Translator (if applicable) Date