

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

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

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### **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 various methods to look for changes in DNA, RNA and proteins. 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 and 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

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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 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.

You may be asked to provide a skin sample. For a skin biopsy: Your skin will be numbed with a local anesthetic medicine, such as Lidocaine, and a small sample of skin will be removed using a punch biopsy instrument. This instrument cuts the top layers of the skin to remove a sample of skin about the size of a pencil eraser. We will use this sample to create 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. We will then use these cells in our research.

\_\_\_\_\_ I agree to have a skin biopsy (please initial)

For collection of a surgical specimen: If any tissue will be removed during a surgical procedure you have agreed to undergo as part of your routine clinical care, you allow us to use it to extract DNA or RNA for the purposes of this research. No extra tissue will be taken from you during your surgery for use in this study.

For collection of a surgical specimen: If any tissue will be removed during a surgical procedure you have agreed to undergo as part of your routine medical care, you allow us to use it to extract DNA or RNA for the purposes of this research. No extra tissue will be taken from you during your surgery for use in this study.

\_\_\_\_\_ I agree to release residual surgical tissue for research (please initial)

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?

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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 which may or may not be directly related to the reason you are being enrolled in this study. 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. Investigators may also wish to study chemicals from your blood/tissue in order to better understand the cause and/or effect of your disease. 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.

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 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 an unexpected (incidental) 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

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know if they have these genetic changes. This research is aimed to identify the genetic cause of disease in your family. This means that we are not specifically looking at your other genes which might be unrelated to the suspected disease in your family. However, since we will have information on part or all of your DNA sequence, there is the potential for us to discover changes or mutations that put you at risk for some genetic disease unrelated to the reason for your inclusion in the study. Therefore, this information will only be given to you if 1) the incidental genetic change(s) has/have a clear and known association with serious or life-shortening disease for which cure or medical treatment is available AND 2) you let us know that you want to know the information. We will not give you information related to genetic disease for which there is no known cure or treatment at the time this study is completed.

Any incidental results would need to be confirmed in a clinical laboratory. The study team members can help you coordinate clinical testing on a fresh blood sample, if you so desire, however you or your insurance would need to pay for this testing.

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 the medical condition that led me to take part in this study. 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 other than the medical condition that led me to take part in this study and for which there is a known cure or treatment at the time the study is completed. 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.

Please note that even though we will have most of your genetic information, we will not be checking every gene exhaustively. So, we cannot guarantee that even if you are at risk for a genetic condition that we will be able to detect it. Study staff will be able to give you more information about this fact, if desired.

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.

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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).

As part of this project, we will release deidentified genetic and clinical information into restricted scientific databases, such as the database of Genes and Phenotypes (dbGaP). However, there are many other scientific databases where release of your deidentified genetic and clinical information would benefit medical research. With your permission, we may also release your deidentified data into other databases in addition to restricted access only databases. Some of these databases are controlled but publicly accessible. 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.

Please indicate whether you agree to the de-identified release of genetic and/or clinical information into controlled, public scientific databases.

Yes\_\_\_\_\_ You agree to the de-identified release of genetic and/or clinical information into controlled public 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.

In the event of injury resulting from this research, Baylor College of Medicine and/or the Harris

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Health System are not able to offer financial compensation nor to absorb the costs of medical treatment. However, necessary facilities, emergency treatment and professional services will be available to you, just as they are to the general community.

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.

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.

**Research related health information**

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine and TCH: Texas Children's Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Photographs, videotapes, and/or audiotapes of you

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, TCH: Texas Children's Hospital, and NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) and their representatives.

**Use or Disclosure Required by Law**

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other

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proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure of N/A to state or local authorities.

Baylor College of Medicine and TCH: Texas Children's Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and TCH: Texas Children's Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research does not involve treatment. Baylor College of Medicine and TCH: Texas Children's Hospital may not condition (withhold or refuse) treating you on whether you sign this Authorization.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) and their representatives, regulatory agencies such as the U.S. Department of Health and Human Services, Baylor College of Medicine, and TCH: Texas Children's Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: James R Lupski MD PhD; Baylor College of Medicine; One Baylor Plaza room 604B; Houston, TX 77030

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

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No publication or public presentation about the research described above will reveal your identity without another authorization from you.

**Potential Risks and Discomforts**

Physical risks:

The physical risks in this study related to the collection of samples are:

**Blood Draw:** 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.

**Skin biopsy:** The physical risks related to the collection of the skin biopsy are mild bruising or bleeding; in very rare cases, it may result in fainting. You may have some discomfort from the punch biopsy instrument used to take the skin biopsy. There may be swelling in the area. There is a chance that you may develop an infection where the biopsy was taken from; medicine will be prescribed if infection occurs.

**Surgical specimen:** There are no risks to you for allowing us to use residual surgical specimens in our research since they will be taken as part of a routine surgical procedure to which you have already agreed.

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



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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 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. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

**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.

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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 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.

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 or Betty Fernandini at 713-798-3723.

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 \_\_\_\_\_

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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 Date  
Parent or Guardian

\_\_\_\_\_  
Legally Authorized Representative - Adult Date

\_\_\_\_\_  
Investigator or Designee Obtaining Consent Date

\_\_\_\_\_  
Witness (if applicable) Date

\_\_\_\_\_  
Translator (if applicable) Date

**Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals****Secondary consent form for collection of skin biopsy and/or surgical specimen.**

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**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 or changes that cause the genetic disease in your family. In order to find out the effect of a mutation and the reason it is causing disease we will need to test the function of the gene.

**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. Experiments that test the function of the genetic changes found are necessary.

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 and TCH: Texas Children's Hospital.

You will be asked to provide a skin sample. For a skin biopsy: Your skin will be numbed with a local anesthetic medicine, such as Lidocaine, and a small sample of skin will be removed using a punch biopsy instrument. This instrument cuts the top layers of the skin to remove a sample of skin about the size of a pencil eraser. We will use this sample to create a cell line. This means that we would treat the

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cells from your sample in a way that allows us to grow them in the laboratory. We will then use these cells in our research.

For collection of a surgical specimen: If any tissue will be removed during a surgical procedure you have agreed to undergo as part of your routine clinical care, you allow us to use it to extract DNA or RNA for the purposes of this research. No extra tissue will be taken from you during your surgery for use in this study.

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The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Photographs, videotapes, and/or audiotapes of you

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, TCH: Texas Children's Hospital, and NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) and their representatives.

**Use or Disclosure Required by Law**

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the

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researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure of N/A to state or local authorities.

Baylor College of Medicine and TCH: Texas Children's Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and TCH: Texas Children's Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research does not involve treatment. Baylor College of Medicine and TCH: Texas Children's Hospital may not condition (withhold or refuse) treating you on whether you sign this Authorization.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) and their representatives, regulatory agencies such as the U.S. Department of Health and Human Services, Baylor College of Medicine, and TCH: Texas Children's Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: James R Lupski MD PhD; Baylor College of Medicine; One Baylor Plaza room 604B; Houston, TX 77030

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

**Potential Risks and Discomforts**

Physical risks:

The physical risks related to the collection of the skin biopsy are mild bruising or bleeding; in very rare cases, it may result in fainting. You may have some discomfort from the punch biopsy instrument used to take the skin biopsy. There may be swelling in the area. There is a chance that you may develop an infection where the biopsy was taken from; medicine will be prescribed if infection occurs.

There are no risks to you for allowing us to use surgical specimens in our research since they will be taken as part of a routine surgical procedure to which you have already agreed.

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Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

**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 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.

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.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB)

**CONSENT FORM**

HIPAA Compliant

**Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals**

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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 \_\_\_\_\_



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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 Date  
Parent or Guardian

\_\_\_\_\_  
Legally Authorized Representative - Adult Date

\_\_\_\_\_  
Investigator or Designee Obtaining Consent Date

\_\_\_\_\_  
Witness (if applicable) Date

\_\_\_\_\_  
Translator (if applicable) Date

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### **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 various methods to look for changes in DNA, RNA and proteins. 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 and 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

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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 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.

You may be asked to provide a skin sample. For a skin biopsy: Your skin will be numbed with a local anesthetic medicine, such as Lidocaine, and a small sample of skin will be removed using a punch biopsy instrument. This instrument cuts the top layers of the skin to remove a sample of skin about the size of a pencil eraser. We will use this sample to create 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. We will then use these cells in our research.

\_\_\_\_\_ I agree to have a skin biopsy (please initial)

For collection of a surgical specimen: If any tissue will be removed during a surgical procedure you have agreed to undergo as part of your routine clinical care, you allow us to use it to extract DNA or RNA for the purposes of this research. No extra tissue will be taken from you during your surgery for use in this study.

For collection of a surgical specimen: If any tissue will be removed during a surgical procedure you have agreed to undergo as part of your routine medical care, you allow us to use it to extract DNA or RNA for the purposes of this research. No extra tissue will be taken from you during your surgery for use in this study.

\_\_\_\_\_ I agree to release residual surgical tissue for research (please initial)

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?

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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 which may or may not be directly related to the reason you are being enrolled in this study. 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. Investigators may also wish to study chemicals from your blood/tissue in order to better understand the cause and/or effect of your disease. 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.

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 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 an unexpected (incidental) mutation or DNA change that they did not know

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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. This research is aimed to identify the genetic cause of disease in your family. This means that we are not specifically looking at your other genes which might be unrelated to the suspected disease in your family. However, since we will have information on part or all of your DNA sequence, there is the potential for us to discover changes or mutations that put you at risk for some genetic disease unrelated to the reason for your inclusion in the study. Therefore, this information will only be given to you if 1) the incidental genetic change(s) has/have a clear and known association with serious or life-shortening disease for which cure or medical treatment is available AND 2) you let us know that you want to know the information. We will not give you information related to genetic disease for which there is no known cure or treatment at the time this study is completed.

Any incidental results would need to be confirmed in a clinical laboratory. The study team members can help you coordinate clinical testing on a fresh blood sample, if you so desire, however you or your insurance would need to pay for this testing.

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 the medical condition that led me to take part in this study. 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 other than the medical condition that led me to take part in this study and for which there is a known cure or treatment at the time the study is completed. 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.

Please note that even though we will have most of your genetic information, we will not be checking every gene exhaustively. So, we cannot guarantee that even if you are at risk for a genetic condition that we will be able to detect it. Study staff will be able to give you more information about this fact, if desired.

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

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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).

As part of this project, we will release deidentified genetic and clinical information into restricted scientific databases, such as the database of Genes and Phenotypes (dbGaP). However, there are many other scientific databases where release of your deidentified genetic and clinical information would benefit medical research. With your permission, we may also release your deidentified data into other databases in addition to restricted access only databases. Some of these databases are controlled but publicly accessible. 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.

Please indicate whether you agree to the de-identified release of genetic and/or clinical information into controlled, public scientific databases.

Yes \_\_\_\_\_ You agree to the de-identified release of genetic and/or clinical information into controlled public 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.

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In the event of injury resulting from this research, Baylor College of Medicine and/or the Harris Health System are not able to offer financial compensation nor to absorb the costs of medical treatment. However, necessary facilities, emergency treatment and professional services will be available to you, just as they are to the general community.

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.

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.

**Research related health information**

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine and TCH: Texas Children's Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Photographs, videotapes, and/or audiotapes of you

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, TCH: Texas Children's Hospital, and NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) and their representatives.

**Use or Disclosure Required by Law**

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that

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may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure of N/A to state or local authorities.

Baylor College of Medicine and TCH: Texas Children's Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and TCH: Texas Children's Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research does not involve treatment. Baylor College of Medicine and TCH: Texas Children's Hospital may not condition (withhold or refuse) treating you on whether you sign this Authorization.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) and their representatives, regulatory agencies such as the U.S. Department of Health and Human Services, Baylor College of Medicine, and TCH: Texas Children's Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: James R Lupski MD PhD; Baylor College of Medicine; One Baylor Plaza room 604B; Houston, TX 77030

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this



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authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

**Potential Risks and Discomforts**

The physical risks in this study related to the collection of samples are:

**Blood Draw:** 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.

**Skin biopsy:** The physical risks related to the collection of the skin biopsy are mild bruising or bleeding; in very rare cases, it may result in fainting. You may have some discomfort from the punch biopsy instrument used to take the skin biopsy. There may be swelling in the area. There is a chance that you may develop an infection where the biopsy was taken from; medicine will be prescribed if infection occurs.

**Surgical specimen:** There are no risks to you for allowing us to use residual surgical specimens in our research since they will be taken as part of a routine surgical procedure to which you have already agreed.

**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

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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 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. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

**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 your 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.

**Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals  
 Primary consent form for blood, saliva/buccal swab or pathological specimen collection  
 for whole-genome/exome/transcriptome sequencing to identify the genetic cause of  
 Mendelian diseases (Children and non-viable neonates)**

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

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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 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.

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.

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 \_\_\_\_\_

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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.

\_\_\_\_\_  
Parent Date

\_\_\_\_\_  
Parent Date

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Legally Authorized Representative  
Parent or Guardian Date

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Legally Authorized Representative - Adult Date

\_\_\_\_\_  
Investigator or Designee Obtaining Consent Date

\_\_\_\_\_  
Witness (if applicable) Date

\_\_\_\_\_  
Translator (if applicable) Date

**Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals****Secondary consent form for collection of skin biopsy (Children and non-viable neonates).**

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**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 or changes that cause the genetic disease in your family. In order to find out the effect of a mutation and the reason it is causing disease we will need to test the function of the gene.

**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. Experiments that test the function of the genetic changes found are necessary.

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 and TCH: Texas Children's Hospital.

You will be asked to provide a skin sample or allow us to use a surgical specimen. For a skin biopsy: Your skin will be numbed with a local anesthetic medicine, such as Lidocaine, and a small sample of skin will be removed using a punch biopsy instrument. This instrument cuts the top layers of the skin to

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remove a sample of skin about the size of a pencil eraser. We will use this sample to create 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. We will then use these cells in our research.

For collection of a surgical specimen: If any tissue will be removed during a surgical procedure you have agreed to undergo as part of your routine clinical care, you allow us to use it to extract DNA or RNA for the purposes of this research. No extra tissue will be taken from you during your surgery for use in this study.

**Research related health information**

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine and TCH: Texas Children's Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Photographs, videotapes, and/or audiotapes of you

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, TCH: Texas Children's Hospital, and NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) and their representatives.

**Use or Disclosure Required by Law**

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your

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family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure of N/A to state or local authorities.

Baylor College of Medicine and TCH: Texas Children's Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and TCH: Texas Children's Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research does not involve treatment. Baylor College of Medicine and TCH: Texas Children's Hospital may not condition (withhold or refuse) treating you on whether you sign this Authorization.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) and their representatives, regulatory agencies such as the U.S. Department of Health and Human Services, Baylor College of Medicine, and TCH: Texas Children's Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: James R Lupski MD PhD; Baylor College of Medicine; One Baylor Plaza room 604B; Houston, TX 77030

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

**Potential Risks and Discomforts**

**Physical risks:**

The physical risks related to the collection of the skin biopsy are mild bruising or bleeding; in very rare cases, it may result in fainting. You may have some discomfort from the punch biopsy instrument used to take the skin biopsy. There may be swelling in the area. There is a chance that you may develop an infection where the biopsy was taken from; medicine will be prescribed if infection occurs.

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There are no risks to you for allowing us to use surgical specimens in our research since they will be taken as part of a routine surgical procedure to which you have already agreed.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

**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 your 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..

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