

Clinical Utility of Pediatric Whole Exome Sequencing
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**UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
 CONSENT TO PARTICIPATE IN A RESEARCH STUDY**

Study Title: *Program in Prenatal and Pediatric Genome Sequencing (P³EGS)*

Guardian consent form

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

You are being asked to take part in this study because you are the parent of a child with a condition that may have a genetic cause.

What is the purpose of the study?

The purpose of the study is to understand the effects genetic information has on families. The study may also help other children with genetic conditions in the future. We are particularly interested in learning how to provide services to families from diverse backgrounds.

Genes are the instructions passed from a parent to child that determine how our bodies are built and grow. Some medical conditions are caused by differences in genes. Exome sequencing is a method of looking for those differences to try to find a genetic cause for your child’s condition. Exome sequencing can be called a genetic test. Exome sequencing is often used as a test for children with medical conditions thought to have a genetic cause.

Exome sequencing is different from many genetic tests. It studies most of the genes in your body all at once instead of one gene at a time. Learning if your child has a genetic cause for their health problems with exome sequencing could help doctors to care for your child.

If you decide to join the study, we will study your child’s genes using exome sequencing. We may also study your genetic information. We are studying your genes to help understand the importance of differences found in your child’s genes. We will also ask you questions to learn more about how the genetic test results affect your family.

Who is paying for the study?

This study and the exome sequencing test is being paid for by the National Institutes of Health (NIH), the federal agency that pays for health research in the U.S.

How many people will take part in this study?

The study will include about 700 children and their biological parents. Sometimes other family members will be included. Families will be enrolled through clinics at UCSF Benioff Children's Hospital Mission Bay, UCSF Benioff Children's Hospital Oakland, UCSF Fresno, or Zuckerberg San Francisco General Hospital.

What will happen if my child takes part in this research study?

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

If you choose to participate in this study:

- 1) The team will collect health information about you and your family. This information will be used by the study team and the laboratory to interpret the results from the exome sequencing. The team may ask permission to take a photo of you or your child.
- 2) You will be asked to sign this consent form.
- 3) Study staff will ask for a sample of blood, saliva or a cheek swab from you, your child, and your child's other biological parent if available. Genetic information, called DNA, will be extracted from these samples. The amount of blood taken from your child will depend on body weight, but the most that is taken is a small amount, about 1 teaspoon. The blood sample will be drawn by inserting a needle into a vein. If you do not wish your child to have a blood sample drawn, your child can give a cheek (buccal) swab sample or a saliva sample. Cheek swabs are collected by brushing the inside of the cheek with a small brush. Saliva is collected by spitting into a tube.

Exome sequencing will be done for your child. The lab may also do genetic testing on your sample to help us to better understand genetic differences found in your child. Exome sequencing may be done on your sample, or more limited testing might be done to determine if you also have a genetic difference that was identified in your child. It is most helpful to have a sample from both parents, but testing can be done with just one parent's sample. Your health care provider may also ask for DNA samples from other family members (including brothers and sisters) to help complete the testing process.

- 4) The exome sequencing results will come back in 3-5 months. Sometimes it may be sooner. We will schedule an appointment to go over the results with you. You will be given a copy of your child's results.

- 5) We would like to see you and your child for a follow-up appointment 5-7 months after we give you your child's test results. The follow-up appointment is for the study team to get an update on your child and to find out if the testing was useful for your family.
- 6) At the appointment where we review the test results with you, we may ask if someone from our study team can observe the appointment. We may also ask if we can audio record the visit. It is your choice whether or not to allow a study team member to observe or record the appointment. We may show you the testing results displayed with a special computer program, or App, on an iPad. The purpose is to learn how to improve how we give results to families. The surveys and recordings are for research and are not part of clinical care.
- 7) We will ask you to complete surveys as part of each of your clinic visits. These may be done in person, by phone, or emailed or mailed to you after the clinic visit. The surveys ask demographic questions and also ask about your family's experience with genetic testing. You can skip questions that you do not want to answer or stop the survey at any time. We will keep your answers confidential and will not share your personal information with anyone outside the research team. You will receive \$50 total in gift cards if you complete the surveys. You will get \$20 for the first survey and \$30 for the second. The surveys are for research and are not part of clinical care.
- 8) You may also be asked to participate in interviews. Only a small number of families will be asked. We want to learn how the results have affected your family. If you are asked, you will receive \$70 in gift cards if you agree to be interviewed twice. That is \$35 for each interview. Participating in the interviews is optional. You do not have to agree to participate in the interview to continue participating in the study. The interviews are for research and are not part of clinical care.
- 9) We will share your child's data from these surveys with the NIH and other researchers. We will share the health information and exome sequencing results that we have collected with the NIH and other researchers, as part of this study is to work out if exome sequencing is useful for clinical care. We will also share data from other family members who take part in this study. We will discuss how we plan to protect your health information in detail later in this form.

What kind of results will my child get from exome sequencing?

Results related to your child's medical condition

The goal of exome sequencing is to find a genetic difference that explains your child's medical condition. Knowing the cause of the condition may lead to changes in his or her medical care. Examples of changes to medical care include seeing a new specialist, starting a new medication, or stopping a medication your child is already taking. You may also learn the chance that other family members have the same medical condition. You may learn the chances of having another child with the same condition.

Results that are not related to your child's medical condition (additional results)

There is a small chance that we could find a genetic difference that causes medical problems that are not related to your child's current medical condition. We call these additional results. They might be important for your child's health now or in the future. They may also be important for your health or for the health of other family members. Examples of additional results you could learn about include genetic differences that cause a high chance for developing cancer or heart problems. These are all conditions where doctors can take preventive measures if they know about the genetic difference. For example, they may offer regular testing to try to catch cancer early or suggest options to prevent it. We expect that only a handful of people will get results like this. You can decide if you want to learn about these conditions or not. You can make your choice on the last page of this form.

Results from biological parents

Sometimes exome sequencing finds an important genetic difference that the child inherited from a parent. If that happens, the report will indicate which parent it came from. Sometimes we learn that a parent has the same diagnosis as their child. If the lab finds a genetic difference in a parent that is important to health, we will help make a referral to a doctor.

What are the limits of the exome sequencing test?

Most often patients do not receive a clear genetic diagnosis from this test. This test could still miss genetic differences that are important for your child's health. The test cannot find all types of genetic differences. We may not find a genetic difference that is causing your child's condition because of limits to our knowledge about human genes and disease. It is possible we will find a genetic difference and not know if it is the cause of your child's condition or not. It will be many years before we understand the importance of all differences found in genes. Even when we find a genetic difference we think is medically important, it may not predict how severe a condition will be or when a person will become ill.

How long will my child be in the study?

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

Can my child stop being in the study?

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

What side effects or risks are there?

- Drawing blood may be uncomfortable or cause bruising, infection, or fainting. The risk will not be any different from the risk of a routine blood test.
- You may learn that family relationships are not what you thought. For example, sometimes we discover that someone's biological father is not who they thought.
- You may feel upset or disappointed at the results of the test. However, the study providers will do their best to explain the meaning of any results to you in language you can understand and will offer support.
- We may discover additional unexpected information about your family's health. For example, we could learn that you have a medical condition you did not expect.
- Genetic testing and information sharing may involve a risk to privacy. UCSF takes many steps to keep personal health information confidential. Unexpected events could lead to a loss of privacy.
- Some people are concerned that genetic information might be used against them. A federal law called the Genetic Information Nondiscrimination Act (GINA) gives some protection. The law says that employers and health insurance companies cannot use genetic information when making decisions. GINA has limits. Life insurance, long-term care insurance, and disability insurance are not included in the law's protections. GINA does not cover those serving in the military. California law also includes protection against genetic discrimination, but legal protections are not complete.
- There may be unknown risks both to being in the research study and to genetic testing.

Are there benefits to taking part in the study?

We may find a genetic difference that explains your child's condition. This may help your child's doctors to provide better care, or it may not change your child's care. However, we may not find a genetic difference that explains your child's condition.

Even if you or your child receive no direct benefit, your participation may help doctors and scientists improve genetic testing and understand if exome sequencing is useful. We hope that this will help future patients.

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

Your choices include:

- Getting another genetic test.
- Getting exome sequencing paid for by your insurance or by paying out of pocket.
- Entering a different research study if one is available.

Will information obtained from the study be shared with others?

Yes, it will be shared for clinical care. We will also share information about your and your child's test results as part of this study and to help with future medical research.

The exome sequencing results will be used for clinical care. This means that the results will be placed in your child's medical record. Doctors, nurses, and others caring for your child will have access to results.

Also, limited information about your child's test results may be placed in a genetic laboratory resource run by the NIH. Sharing genetic information in this way helps doctors to look at many people's test results all together. This allows them to understand genetic test results more fully and may help them develop new treatments or forms of prevention. Most labs require this type of sharing if you decide to have exome sequencing.

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

- 1) We will share your family's health and genetic information with other clinicians and scientists, including the lab that does the exome sequencing, inside UCSF. If you decide to be in the study, this sharing is required.
- 2) We will share your family's health and genetic information with research partners from other institutions that are part of the Clinical Sequencing Evidence Generating (CSER2) research consortium that this study is a part of. If you decide to be in the study, this sharing is required.
- 3) We will share your child's health and genetic information in a research database run by the NIH. We will also share your genetic and health information in the database if genetic testing is done on your sample. Sharing this information will enable researchers to better understand genetic differences between people. If you do not want your family's information to be shared in this way, just let us know. You will be asked to check a box at the end of this form if you'd prefer not to share this information.

Apart from sharing with the exome sequencing lab, in which your child's name and date of birth will be used to identify their sample for testing, we will not include your child's or your name or other personal information when sharing data. However, genetic information is unlike other information. Your child's detailed genetic information is unique to your child and could possibly be re-identified. We believe the risk of someone figuring out the identity of your child is low. The purpose of sharing data is to allow doctors to learn more about genetic differences that cause medical conditions.

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

What will happen to my child's samples?

Your child's sample will be sent to the Genomic Medicine Laboratory at UCSF, where exome sequencing will be done. Your child's sample will be sent with personal identifiers such as your child's name, date of birth, and medical record number so that the laboratory can verify that the

sample belongs to your child. Once they have verified that the sample is your child's, they will remove the identifiers and code the sample with a number.

The laboratory saves leftover samples after completing the test. These samples are used for improving the test and for educational purposes. To protect your privacy, these samples are "de-identified," meaning they are not stored with your child's name or other personal information.

The leftover de-identified samples may also be used for future research studies. You have a choice about whether to allow your child's sample to be used for future research studies. You can make your choice at the end of this form. Results from future studies done by researchers using your data will not be offered to you.

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

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

Is sharing my child's information risky?

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

Can researchers be forced to disclose my child's information?

This research is covered by a Certificate of Confidentiality from the National Institutes of Health, which means that researchers cannot be forced to disclose information that may identify you or your child, even if that information is requested with a court subpoena. This applies to federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

There are some important things that you need to know. The Certificate does not stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate cannot be used to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate does not stop disclosures required

by the federal Food and Drug Administration (FDA). The Certificate also does not prevent your information from being used for other research if allowed by federal regulations.

When may researchers disclose information about my child without my permission?

There are times when researchers may disclose information about you and your child without your consent, if required by law. For example, we will report child abuse. We will also report if we learn that someone intends to hurt your child or others. Also, researchers may not withhold information from the federal government needed for auditing or evaluating federally funded projects or information needed by agencies that assure the safety of medical care.

May I or a family member voluntarily release information?

You or a member of your family may voluntarily release information about your child 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 withhold that information.

Are there any costs to being in this study?

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

Will my child benefit financially from taking part in this study?

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

What happens if my child is injured as a part of this study?

It is important that you tell the study doctor if you feel that your child has been injured because of taking part in this study. You can tell the doctor in person or call the study team at 415-476-2201. If your child is injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415-476-1814.

What are my child’s rights if he/she takes part in this study?

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

You can call the study team about any questions, concerns or complaints you have. If you want to ask questions about the study or your rights as a research participant with someone outside the research team, or if you want to discuss any problems or concerns you may have about the study, please call the UCSF Institutional Review Board.

A description of this clinical trial is available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This website will not include information that can identify you. The website will include a summary of the results. You can search this website at any time using the clinical trial number assigned to this research study, NCT03525431.

Special federal laws protect the privacy of your family’s personal health information. You will be asked to sign a separate form allowing the University of California, San Francisco to access, use, or share health information about you or your child. You have been given copies of this consent form and the Experimental Subject’s Bill of Rights to keep.

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

Date Parent or Guardian’s Signature for Consent

Date Legally Authorized Representative

Date Person Obtaining Consent

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

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

Exome sequencing tests sometimes show additional findings. Some of these findings may be medically significant. Would you like to learn about medically significant additional findings discovered in you and your child? You might learn that you or your child are at risk for a condition like cancer or heart disease. Offering these additional findings is a part of clinical care, however, a goal of this research study is to learn more about the impact of these kinds of results. See page 4 for more details. Please initial yes or no.

<p><i>YES, I want additional findings for my child.</i></p> <p>Initial: _____</p>	<p><i>NO, I do not want additional findings for my child.</i></p> <p>Initial: _____</p>
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With your permission we would like to use leftover samples from this test for future research, for example, for studies to better understand how genetic differences cause health conditions. See page 7 for more details. Please make your choice below.

<p><i>YES, my child's samples can be used for future research.</i></p> <p>Initial: _____</p>	<p><i>NO, I do not want my child's samples used for future research.</i></p> <p>Initial: _____</p>
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Are you willing to be contacted about being in future research studies at UCSF or UCSF research collaborators? Please make your choice below.

<p><i>YES, it is okay to contact me about future research.</i></p> <p>Initial: _____</p>	<p><i>NO, I do not want to be contacted about future research.</i></p> <p>Initial: _____</p>
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We may share your child's health and genetic information with a research database run by the National Institutes of Health, a U.S. government health agency. Sharing this information will enable researchers to better understand genetic differences between people. See page 6 for more details. Initial the box below if you'd prefer not to share this information.

NO, I do not want my child's information to be shared with a research database to aid future research.

Initial: _____