If you are using Epic for this study, fax a copy of the signed consent form to 410-367-7382.

Patient I.D. Plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **Genome-wide Sequencing to Identify the Genes Responsible for Mendelian Disorders**

Application No.: **NA_00045758**

Sponsor: **National Institutes of Health (NIH)**

Principal Investigator: David Valle, MD
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1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.

- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.
- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.
- If children and adults can join this study, the word "you" in this consent form will refer to both you and your child.
- The person being asked to be in this research study may not be able to give consent to be in this study. You are therefore being asked to give permission for this person to be in the study as his/her decision maker.

2. Why is this research being done?

This research is being done to identify the genetic cause for inherited syndromes and health conditions (called "Mendelian disorders"). We look for the genetic cause of these Mendelian disorders by studying the DNA of an affected individual and/or members of their family. We will obtain the DNA from a sample of the cells of participants' bodies (such as blood cells, skin cells, cells in the saliva, or other body cells). DNA is an abbreviation for deoxyribonucleic acid; DNA carries information that directs the growth, development or function of our body in the form of a code. We inherit this code from our parents and pass the code on to our children. The DNA is divided into genes.

Genes contain the information to produce the proteins in our body that allow us to grow, develop and function. A person's complete set of genes is called their genome. An abnormality in a gene, known as a mutation or variant, may produce defective proteins that do not work properly in the body. In this case, mutations can result in problems in growth, development and function that may be recognized as a syndrome or health condition.

- As part of this study, we will collect health information and biologic samples that will be stored in a Biologic Repository at Johns Hopkins or Baylor College of Medicine and used for research now and in the future.
- During this study, you will not have access to certain medical information and test results collected for study purposes. Researchers will study biologic samples and information from many people; it will take many years before we know if the results have any meaning. However, in the future it may be possible for us to give you your personal genetic research results and relate them to medical problems in you or your family. There is also a small chance that researchers will find something that could possibly change your medical management based on current knowledge. If this happens, we will contact you with this information if you indicate later in this consent form that you want us to do so.
- As part this study, genetic information from your biologic samples and health information may be sent to a controlled public database, such as the Database of Genes and Phenotypes (dbGaP). This type of controlled database is accessible only to legitimate investigators who meet criteria established by the National Institutes of Health (NIH). Furthermore, information that identifies you directly, such as your name, address, birthdate or social security number, will not be sent to any database. Please see the last page of this consent form for information about genome-wide sequencing and your data.

You may take part in this study because you have a rare syndrome or disorder that appears to be inherited, but for which we do not know the responsible gene. We will try to find the genetic cause for the rare syndrome or disorder by studying all or nearly all your genes through a new method called genome-wide sequencing. In genome-wide sequencing, we will look for disease causing mutations in your entire genome.

People of any age with any rare syndrome or health condition in themselves or their family members may join this research.

How many people will be in this study?
Up to 100,000 people will be in this study, with 50,000 people from Johns Hopkins.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

Donate either an existing or new cell sample (blood, skin, saliva, or other body tissue) for DNA extraction and/or to establish a cell line (cells that can be grown forever in the laboratory) for genome-wide sequencing to identify the gene or genes responsible for a genetic condition in you or your family. DNA can be used immediately or stored indefinitely for sequencing. A cell line provides a limitless supply of DNA that can be extracted from the stored cells at any time in the future. Establishing a cell line means that we do not need to collect more blood from you for future genetic studies that we may not be able to foresee today. It is possible that this cell line may be made by manufactured by Hopkins or its research partners for further study to design treatments for a given disorder or medical condition. If this should happen, we will not publicly identify you as the source of the cell line.

Blood Sample: Blood may be collected during a clinical visit or a research study visit. Blood or other tissue may also be collected during a surgical procedure that is being done for other purposes. The total blood collected from you for this study will be 3 cc/kg of your body weight, up to 2 tablespoons (30 cc).
Skin Biopsy for fibroblast cell lines: Your skin will be numbed with a numbing medicine (Lidocaine) and a small sample of skin will be removed using a punch biopsy instrument. The punch biopsy instrument is like a circular cookie cutter that cuts the top layers of skin to remove a piece of skin about the size of a pencil eraser. You will be asked to sign a separate clinical consent describing the risks of this procedure.

Your cell sample, DNA and/or cell line may be stored indefinitely in a Biologic Repository at Johns Hopkins or Baylor College of Medicine, our collaborating site for this project.

To help identify the gene responsible for the disorder in you or a family member, we will also collect medical information from you and your family members.

We may also perform a physical examination of you.

We may ask for permission to obtain photographs of you.

If we learn more information about your disorder through this research, we may publish and/or present this information to other medical providers through public presentations and medical journals. The information we may present could include photographs, X-rays, or other test results. Your name will never be written on any of these pieces of information in a public presentation or a medical journal. Please initial ALL lines indicating what type of photographs you agree we can show in a public presentation or medical journal.

_____ Yes, you can show a photo of my whole body, including my face, with my clothes on.

_____ Yes, you can show a photo of my whole body with my clothes on, but covering or cutting out certain parts.

_____ Yes, you can show a photo of my whole body, including my face, with my clothes off.

_____ Yes, you can show a photo of my whole body with my clothes off, but covering or cutting out my face.

_____ Do not show any photographs of any part of my body.

We retain the right to analyze and publish all results following the above restrictions.

This genome-wide sequencing will be done for research only. Because this is research and we do not understand the meaning of all mutations or variants that we find in genes, we may not release the results of your research tests to you. We will however return your results from this research if we discover one of the two following types of results and you respond here that you want to be contacted. If shown on this consent, we will try to contact you within one year of the end of this study (December 31, 2020) if we find:

1) the genetic cause for the rare disorder or medical condition that lead you or your family to take part in this research, or;

2) a previously validated genetic cause for other serious medical conditions which you will likely develop as a result of a mutation we discover.

Either of these results would need to be confirmed in a clinical laboratory, and study team members would help you with clinical testing, if you want, though your insurance would need to pay for this testing.

Please initial next to the statement(s) that meets your wishes for our study of the rare disorder or medical condition in you or a member of your family:

_____ Please contact me if you discover the genetic cause for my disorder or medical condition

_____ Please contact me if you discover that I have a genetic mutation likely to cause in me a serious medical condition other than the condition that lead me to take part in this study.

If you are a **family member who does not have the rare syndrome we are studying in your family,** please initial here next to this statement if you would like for us to contact you:

_____ Please contact me if you find a genetic mutation likely to cause in me a serious medical condition other than the condition in my family that lead me to take part in this study. We would assist you as needed with this clinical testing for which you or your insurance will pay.

All study members are board certified clinical geneticists or genetic counselors and qualified to discuss these results with you.

As part of this research, we plan to send out an electronic newsletter every 3-6 months to inform study participants about our overall research progress (and not including any information about your specific research results). Please initial here and write your email address if you would like to receive these electronic updates.

_____ Initial _____ Email address

- You will have the option of allowing future contact with our research team based on the results of your evaluation.

Will you allow us to contact you about future research?

YES ☐ _____
Signature of Participant

NO ☐ _____
Signature of Participant

It is important to understand that it may take many months, or even years, before we complete our research. So, it may be several months or years before we may contact you about any important results. This study will continue through December 31, 2020 and we may contact you for up to one year after that date. It is possible that we may never contact you.

Your samples and medical information may be stored forever for current and future research or they may be destroyed if no longer needed for future study.

How long will you be in the study?
Taking part in this study will require one visit with the study staff to complete informed consent, collect medical information, and obtain a blood, saliva, or skin sample. Once enrolled, you will be in this study forever unless you request otherwise. If you withdraw from this study, your request will not affect the use of your information or samples that have already been shared with the NIH or other researchers.

The Genetic Information Nondiscrimination Act (GINA) may help protect you from health insurance or employment discrimination based on genetic information.

The law provides that health insurance companies and group health plans
- may not ask for genetic information from this research and
- may not use genetic information when making decision about eligibility or premiums

The law will not stop health insurance companies from using genetic information to decide whether to pay claims. The law also will not help you get other types of insurance (such as: life, disability or long-term care).

4. What are the risks or discomforts of the study?

Blood collection: Taking blood may cause discomfort, bleeding, infection or bruising where the needle enters the body; in rare cases, it may result in fainting.

Skin Biopsy for fibroblast cell lines: You will be asked to sign a separate clinical consent describing the risks of this procedure.

Saliva collection: There are no known side effects or risks of providing a saliva sample.

There may be side effects and discomforts that are not yet known.

Return of Individual Results: If you have initialed above giving us permission to contact you if we learn information about the cause of your/your family member's disorder, or if we learn that you have a genetic mutation likely to cause in you a serious medical condition other than the condition that led you to take part in this study, the information you learn may be distressing to you. This information may also cause distress for members of your family who may carry the same genetic mutations. There will be board certified genetic counselors and board certified physicians with specific expertise in genetic medicine available to answer any questions you may have about these results.

Despite the GINA protections and the best efforts of the research team, there may still be a risk if information about you were to become known to people outside of this study.

5. Are there risks related to pregnancy?

There are no direct risks to an embryo or fetus by taking part in this study. However, you should know that if you are a woman able to become pregnant, no information from this genome-wide sequencing 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.

6. Are there benefits to being in the study?

While we hope to identify the genetic cause of the disorder present in you or your family, there may be no direct benefit to you from being in this study. If you take part in this study, you may help others in the future.

7. What are your options if you do not want to be in the study?

You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

No.

9. Will you be paid if you join this study?

No.

10. Can you leave the study early?

Yes, you can withdraw from the study at any time. To withdraw, you must contact the PI of this study (contact information listed on the last page of this consent) and request that your information and biologic sample(s) be destroyed. You will no longer receive electronic updates about the overall research results, if you indicated earlier that you wanted to receive these electronic updates.

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.
- If you leave the study early, Johns Hopkins may use or give out your health information that it already has if the information is needed for this study or any follow-up activities**.**

11. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records ([which may include information about HIV, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study. If you are in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

12. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers. You will be asked to give us a list of other health care providers that you use.

13. What if there is a Certificate of Confidentiality for this study?

NHGRI at the NIH has given us a Certificate of Confidentiality for this study. This Certificate adds special protection for research information that identifies you and allows us, in some 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.

We may also disclose identifiable information about you as described in Section 12 of this form or in other cases. For example, the government may see your information if it audits us, and the research team will voluntarily comply with Maryland disclosure laws and will tell the local or state authorities:

- if they suspect abuse or neglect of a child or dependent adult;
- if certain diseases are present; and
- if the team learns that you plan to harm someone. In this case, the team also may warn the person who is at risk.

This Certificate does not mean the government approves or disapproves of this research project.

14. What treatment costs will be paid if you are injured in this study?

Johns Hopkins and the federal government do not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

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

By signing this form you will not give up any rights you have to seek compensation for injury.

15. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?
Call the principal investigator, Dr. David Valle at *410-955-4260.* If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?
If you think you are injured or ill because of this study, call Dr. David Valle at phone (410-955-4260) or pager (410-283-5897).

If you have an urgent medical problem related to your taking part in this study, call Dr. David Valle at phone (410-955-4260) or pager (410-283-5897)

To use a pager number, dial the number listed, then after the tone, enter the phone number where you can be called, press the # key, and hang up.

d. What happens to Data and Biospecimens that are collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

16. Assent Statement

This research study has been explained to my child in my presence in language my child can understand. He/she has been encouraged to ask questions about the study now and at any time in the future.

17. What is a Genome-Wide Sequencing Study?

This research is being done to identify the genetic cause for rare disorders and health conditions that appear to be inherited. We look for the genetic cause of disorders and health conditions by studying the DNA in our body cells. DNA is divided into thousands of genes. Genes contain the information to produce the proteins in our body that allow us to grow, develop and function. The entire collection or set of a person's genes is referred to as the genome. If there is an unusual form of a gene, known as a mutation or variant, then the gene may not work properly. Mutations in genes can cause problems in growth, development or function that may be responsible for a genetic disorder or medical condition. Each of us has many genetic variants or mutations that do not appear to cause a problem. But certain variants or combinations of variants can cause medically significant disorders. We will try to find the genetic cause for the disorder in you or your family by studying all your genes through a new method caused genome-wide sequencing. In genome-wide sequencing, we will look for mutations in your entire genome or key parts of your genome in a single study.

As part this study, genetic information from your biologic samples and health information will be sent to a public, controlled database, such as the Database of Genes and Phenotypes (dbGaP) maintained by the National Institutes of Health (NIH). It is possible that parts or all of your sequenced genome may be submitted to dbGaP. Standard identifying information (such as your name, address, birthdate, social security number) will not be sent to any database. The submitted data will be coded and will not contain information that identifies you directly. Genome-wide sequencing data will be shared with other qualified researchers at other institutions through this controlled database. The Principal Investigator of this study (Dr. Valle) will keep the key to the code that links your name to the data. However, dbGaP will never receive this code or any other information that could identify you directly. Johns Hopkins will not be informed of what types of research will be done with the data that is sent to dbGaP.

18. What are the risks of data being stored for Genome-wide Sequencing?

The storage of your data in the Genome-wide Sequencing repository has some possible risks to your privacy and to the privacy of your relatives.

Although it would be unlikely, the following could occur with your coded data:

- Your identity could become known to people outside of this study either through a lapse in security or by virtue of the collection of genetic variants in your genome that are specific to you.
- Information could be revealed that could lead to denial of employment or insurance for you or a relative.
- Information about you could be released to law enforcement agencies.

Any researcher who uses the data will be required to abide by confidentiality restrictions.

The possible loss of privacy could also cause stress, anxiety or embarrassment.

The data will be deposited to dbGaP, a limited access database controlled by the NIH and accessible only to scientists who have been granted access through a rigorous application process, or other similarly controlled databases.

19. Are there benefits to being in this Genome-wide Sequencing study?

The storing of your data in the Genome-wide Sequencing registry may not be a direct benefit to you. However, the information that may be learned from the data could lead to a greater understanding of health and disease and this may benefit you or others in the future.

20. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form; you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time
Signature of Person Obtaining Consent	(Print Name)	Date/Time
Signature of Legally Authorized Representative (LAR) **For ADULTS NOT CAPABLE of GIVING CONSENT** (*Persons from the following categories in order of priority may be a Legally Authorized Representative: Health Care Agent; Legal Guardian; Spouse; Adult child; Parent; Adult sibling; Friend or other relative)*	(Print Name)	Date/Time
Relationship of LAR to Participant (indicate why the LAR is authorized to act as a surrogate health care decision-maker under state or applicable local law)		Date/Time
Signature of Parent	(Print Name)	Date/Time
Signature of Legally Authorized Representative (LAR) **For CHILD PARTICIPANT**	(Print Name)	Date/Time
Description of LAR's authority under state or applicable local law to act as surrogate health care decision-maker for child research participant (for example, Legal Guardian, court-ordered representative)		Date/Time
Signature of Parent #2 (required if DHHS 45 CFR 46.406 or 46.407/FDA 21 CFR 50.53 or 50.54 study)	(Print Name)	Date/Time
Signature of Child Participant (optional unless IRB required)	(Print Name)	Date/Time
Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

Signature of Participant, LAR or Parent/Guardian	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider (Print Name) Date/Time

Signature of Participant (Print Name) Date/Time

Signature of Legally Authorized Representative (LAR) (Print Name) Date/Time
For ADULTS NOT CAPABLE of GIVING CONSENT (*Persons from the following categories in order of priority may be a Legally Authorized Representative: Health Care Agent; Legal Guardian; Spouse; Adult child; Parent; Adult sibling; Friend or other relative)*

Relationship of LAR to Participant (indicate why the LAR is authorized to act as a surrogate health care decision-maker under state or applicable local law) Date/Time

Signature of Parent (Print Name) Date/Time

Signature of Legally Authorized Representative (LAR) (Print Name) Date/Time
For CHILD PARTICIPANT

Description of LAR's authority under state or applicable local law to act as surrogate health care decision-maker for child research participant (for example, Legal Guardian, court-ordered representative) Date/Time

Signature of Parent #2 (Print Name) Date/Time
(required if DHHS 45 CFR 46.406 or 46.407/FDA 21 CFR 50.53 or 50.54 study)

Signature of Child Participant (optional unless IRB required) (Print Name) Date/Time

Signature of Witness to Consent Procedures (Print Name) Date/Time
(optional unless IRB or Sponsor required)

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.