Investigation into the Natural History and Metabolic and Molecular Basis of RASopathies

NCT04395495

Principal Investigator:
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CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER
INFORMED CONSENT/PARENTAL PERMISSION/ASSENT
FOR PARTICIPATION IN A RESEARCH STUDY

STUDY TITLE: INVESTIGATION INTO THE NATURAL HISTORY AND METABOLIC AND MOLECULAR BASIS OF RASOPATHIES

SPONSOR NAME:
Cincinnati Children's Hospital Medical Center
Department of Pediatrics
Division of Human Genetics

INVESTIGATOR INFORMATION:

K. Nicole Weaver, MD	513-636-4760 ask for "geneticist on call"
Name of Principal Investigator	Telephone Number

PARTICIPANT NAME: _____

RESEARCH ID: _____ DATE OF BIRTH: _____

Throughout this document, "you" refers to the research participant. The signature(s) at the end will clarify whether the participant is signing this consent form on their own behalf or via a parent, legal guardian, or legal personal representative.

INTRODUCTION:
We are asking you to be in a research study so that we can learn new information that may help others. If you decide not to be in this study, we will still take good care of you. If you decide to be in this study, you may change your mind at any time during the study and you can stop being in the study. Take all the time you need to make your choice. Ask us any questions you have. It is also okay to ask more questions after you decide to be in the study. You can ask questions at any time.

WHY ARE WE DOING THIS RESEARCH?
In this research study we want to learn more about a group of genetic disorders called the Rasopathies. The Rasopathies are a group of genetic conditions that are caused by genetic typos, called mutations, in a person's DNA. Sections of our DNA make up our genes. There are many genes that are related to the Rasopathies. Mutations in these genes cause cells to have problems talking to each other within a pathway called the RAS/MAPK pathway. The Rasopathies include Noonan syndrome, Noonan syndrome with multiple lentigines (LEOPARD syndrome), cardiofaciocutaneous (CFC) syndrome, Costello syndrome, Legius syndrome, neurofibromatosis type 1, and other related

disorders.

The goal of this research study is create a repository to store tissues, blood, urine, saliva, and medical information. Researchers can request samples and information from the repository to do research about the Rasopathies. We are asking you to participate because we hope that researchers using this repository may be able to develop better ways to detect and treat patients who have a Rasopathy diagnosis.

WHO IS IN CHARGE OF THE RESEARCH?

K. Nicole Weaver, MD is the researcher at Cincinnati Children's Hospital Medical Center (CCHMC) who is in charge of this study.

Funds to conduct this study are being provided by the Rasopathy program at Cincinnati Children's Hospital Medical Center (CCHMC).

WHO SHOULD NOT BE IN THE STUDY?

You cannot be in this study if:

1) You do not have a suspected or confirmed Rasopathy diagnosis OR
2) You do not have a relative with a suspected or confirmed Rasopathy.

WHAT WILL HAPPEN IN THE STUDY?

If you qualify and decide you want to be in the study, you will come to CCHMC as you normally would for your clinical care and procedures. Rarely, we may ask you to come in for a research visit.

These are the things that will happen to you while you are in the study:

You will be asked to donate a saliva sample and/or a blood sample. We may also request a urine sample. You cannot eat, drink, smoke or chew gum for 30 minutes before your saliva sample. If you decide to provide a blood sample, up to 15 mL (about three teaspoons) of blood will be collected for genetic analysis. We will take special care not to draw more blood than is safe for you. In the rare case that there is a technical problem with the blood sample in the laboratory, the blood sample you provide is all used, or we're not able to collect enough blood during your first procedure, we may collect more blood at a future visit/procedure. Blood, skin, buccal cells (cheek swab), sputum, and urine may be collected during a regular clinic visit or just for this research. If you agree to be a participant you will not be asked to donate blood, buccal cells, sputum, and/or urine more than three times per year for research purposes only.

If you require a procedure (e.g. surgery or catheterization), a blood or saliva sample may be obtained during the pre-operative visit, during the procedure, or at a follow-up appointment. In addition to collecting blood, we may collect any discarded tissue, various body fluids (e.g. urine), or prosthetic/graft material from the procedure in order to store it for future research. There is no additional risk for tissue or material collection during the procedure, researchers will only be collecting some of the samples are collected for clinical reasons. No additional tissues or materials will be removed for the purposes of this

research study. In the event that you have procedure at a later date, this consent allows us to collect discarded tissue, blood and urine at that time.

The discarded specimens that you provide may be collected a little different than usual so that the cells remain healthy for our research studies. However, this will not affect the medical care you receive or change the amount or number of samples collected.

Samples for this study will be stored once testing for your medical care is finished. If your clinical care requires the use of any entire sample, the sample will not be stored for research purposes.

Saliva, blood, urine and tissue specimens will be stored for future use in the Cincinnati BioBank at Cincinnati Children's Hospital Medical Center. Your samples will be de-identified, which means your personal information will be removed. Samples that are not used for initial laboratory analysis will be stored in the BioBank indefinitely. If you withdraw (or are withdrawn) from the study, the sample will be kept unless you request that the sample be discarded. The sample will not be available to you for other testing.

Study coordinators will also review your medical record for medical and surgical history and any imaging, laboratory or genetic testing. Study coordinators may ask you for your email address and contact number. This will be used in the future as a way to contact you/your child for re-consenting if your child turns 18 while the study is still being conducted. Newsletters may also be mailed out via email.

Information from your medical record that is related to your Rasopathy diagnosis will be entered into a secure database. You may be asked to complete questionnaires about your or your child's health, skills, or well-being. The study doctor or a designee will choose which questionnaires are appropriate for you/your child. These questionnaires can be sent via paper documents or electronically via text or email. Electronic questionnaires may take place during study or clinic visits using CCHMC resources (tablet, computer). Your responses and scores from these assessments will be entered into the secure database.

Genetic Studies: If you agree to allow your specimens to be used for future research, there is a chance that your specimens may be used to study changes in genetic material that are passed on in families or that are not passed on in families but are influenced by environment and lifestyle. The results can then be studied to identify changes in genetic material that influence the development of diseases, including Rasopathies, or the effectiveness of specific treatments.

Results from genetic studies and other testing done as part of a research study will not be returned to you.

CCHMC may use/disclose (release) images/video/audio recordings for the purposes described below:

- CCHMC communications, such as marketing, advertising, public relations, fundraising, or other related purposes. This may include publications (print or

electronic), presentations (at public or private events, on television), or internet sites (e.g., CCHMC websites, partner websites, or social media sites).
- These records may be used for purposes of study, research, and teaching and may be published in scientific publications or on the Intranet or Internet. The patient's or family's name may not be used. This release is effective until revoked in writing by the undersigned. Such revocation shall only be effective to prevent any expanded future use of the records.
- Professional audiences, such as publications (print or electronic), presentations or related internet sites.

Collection of specific samples and images (photo/audio/video) is optional. You can give your permission or refuse the collection/use of specific samples/images in the *Consent for Sample/Image Collection and Future Use* section below. You can change your mind at any time by notifying the study team of your updated choice in writing.

Using Stored Samples and Medical Information for Research

In addition to the research being carried out by Dr. Weaver and her co-investigators, these samples may also be provided to other investigators either at Cincinnati Children's Hospital Medical Center or at other hospitals or research laboratories who have a study approved by their Institutional Review Board. These investigators may be studying other cell functions or diseases.

Researchers who want to use your samples for research must request the samples from a committee who will review the request before allowing them to be used. To use your samples in research, researchers may need to know some things about you like your age, sex, race, past medical treatments and tests. Your samples and medical information may be given to researchers at other institutions (outside CCHMC). None of your identifying information will be given to them.

Future Studies: With your permission:
- Your samples may be used for future research studies to learn more about what causes Rasopathies and about how to make treatment better.
- Your samples may be used to help researchers learn more about other diseases.
- Researchers may want to contact you in the future to ask if you would like to take part in more research.
- Your samples may be used for genetic studies.

WHAT ARE THE GOOD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

Being in this study may not help you right now. When we finish the study, we hope that we will know more about Rasopathies. This may help other people with Rasopathies later on.

WHAT ARE THE BAD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

For participants in this study, the tissue or material (if applicable) analyzed for this study will be obtained during a procedure that is clinically scheduled. The tissue or material that is collected will be tissue or material that would ordinarily be discarded. As such, there will

be no additional risk in obtaining a portion of the tissue or material for research use.

For all participants, the only physical risks present in this study involve drawing blood from a vein, usually from the arm. Rarely bleeding (usually a very small amount) or infection, just like any other small scratch, may occur. There also may be mild discomfort from the needle stick and a minor risk of bruising from the stick.

There is a small risk for the loss of confidentiality. However, study personnel will make every effort to minimize this risk. Please see the section "How Will My Information Be Kept Private And Confidential" for a detailed explanation on how we will minimize this risk.

You may be asked questions that make you uncomfortable or cause you to remember situations that were upsetting to you. You do not need to answer any questions that you do not wish to answer and you can stop the testing at any time. If you become very upset during the testing at any time, we will end the testing. We will also offer to have you speak to someone about what you are feeling. If the study team notes concern for suicide or that you could harm yourself or others, the study staff will contact your doctor and/or Psychiatric Intake Response Center (PIRC) at Cincinnati Children's Hospital for further review and advice. Your health and well-being is very important to us.

There may be other risks that we do not know about yet. Study staff will update you in a timely way on any new information that may affect your health, welfare, or decision to stay in this study.

WHAT OTHER CHOICES ARE THERE?

Instead of being in this study, you can choose not to be in it. If you choose not to participate, your care will not be affected in any way.

HOW WILL INFORMATION ABOUT YOU BE KEPT PRIVATE?

Making sure that information about you remains private is important to us. To protect your privacy in this research study:

All patient identifiers will be removed to the greatest extent possible from medical records, questionnaires, and samples and replaced with a study identification number; only the study team will have access to the study files and database; all documents, files, and computer devices will be kept in a secured location at CCHMC.

Information from this research study may be published; however, you will not be identified in such publications. The publication will not contain information about you that would enable someone to determine your identity as a research participant without your permission.

A copy of this consent form will be included in your medical record. You will be registered in the Cincinnati Children's Hospital Medical Center's computer system as a research subject.

By signing this consent form you are giving permission for representatives of the Cincinnati Children's Hospital Medical Center ("CCHMC"), the Investigator and CCHMC employees involved with the research study including the Institutional Review Board and the Office for Research Compliance and Regulatory Affairs, and any sponsoring company or their appointed agent to be allowed to inspect sections of your medical and research records related to this study.

WHAT IF WE LEARN NEW INFORMATION DURING THE RESEARCH?

The results of research studies using your blood and/or tissue will not be made available.

The study doctor will tell you if they find out about new information from this or other studies that may affect your health, safety or willingness to stay in this study.

WILL IT COST YOU ANYTHING EXTRA TO BE IN THE RESEARCH STUDY?

There is no cost to participate in this study. You will not be charged for the tests that are done for research purposes; however, you will still be responsible for the usual costs of medical care including any follow-up care that is indicated as a result of learning about your diagnosis.

WILL YOU BE PAID TO BE IN THIS RESEARCH STUDY?

You will not be compensated for participation in this study.

Tissues or body fluids collected for this research may result in the development of a product that could be patented/licensed and sold. You will not be paid if this happens.

WHAT HAPPENS IF YOU ARE INJURED FROM BEING IN THIS STUDY?

If you believe that you have been injured as a result of this research you should contact Dr. K. Nicole Weaver as soon as possible to discuss the concerns. Treatment for injuries is available at CCHMC. If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in a research study. If possible, you should give them a copy of this consent form.

CCHMC follows a policy of making all decisions about compensation for the medical treatment of physical injuries that happened during or were caused by research on an individual basis.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

For questions, concerns, or complaints about this research study you can contact the study person listed on page 1 of this document.

If you would like to talk to someone that is not part of the research staff or if you have general questions about your research study rights or questions, concerns, or complaints about the research, you can call the CCHMC Institutional Review Board at 513-636-8039.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this research study you must also give your permission (or authorization) to use and disclose (or share) your "protected health information" (called PHI for short).

What protected health information will be used and shared during this study?
CCHMC will need to use and share your PHI as part of this study. This PHI will come from:

- Your CCHMC medical records
- Your research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnosis, and medications
- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- If applicable, information concerning HIV testing or the treatment of AIDS or AIDS-related conditions, drug or alcohol abuse, drug-related conditions, alcoholism, and/or psychiatric/psychological conditions (but not psychotherapy notes).

Who will share, receive and/or use your protected health information in this study?

- Staff at all the research study sites (including CCHMC)
- Personnel who provide services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor and organizations that the sponsor may use to oversee or conduct the study.
- The members of the CCHMC Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.

How will you know that your PHI is not misused?
People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can you change your mind?
You may choose to withdraw your permission at any time. A withdrawal of your permission to use and share your PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share PHI you need to notify the study doctor, listed on the first page of this document, in writing. Your request will be effective immediately and no new PHI about you will be used or shared. The only exceptions are (1) any use or sharing of PHI that has already occurred or was in process prior to you withdrawing your permission and (2) any use or sharing that is needed to maintain the integrity of the research.

Will this permission expire?
Your permission will expire at the end of the study. If the study involves the creation or maintenance of a research database repository, this authorization will not expire.

Will your other medical care be impacted?
By signing this document you are agree to participate in this research study and give permission to CCHMC to use and share your PHI for the purpose of this research study. If you refuse to sign this document you will not be able to participate in the study. However, your rights concerning treatment not related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

Consent for Sample/Image Collection and Future Use:

Yes ☐ No ☐ I consent to a collection of extra **bone marrow** from myself/my child. This extra sample will only be taken if it is indicated as part of your/your child's standard of care or treatment.

Yes ☐ No ☐ I consent to a collection of **skin tissue** from myself/my child. This sample may be obtained as part of your/your child's standard of care or treatment or may be obtained directly for research purposes.

Yes ☐ No ☐ I consent to a collection of **buccal cells** from myself/my child. This sample may be obtained for research purposes only or as leftover cells.

Yes ☐ No ☐ I consent to a collection of **blood** from myself/my child. Whenever possible, blood will be collected from you/your child at the same time as blood is being collected as part standard of care or treatment or may be obtained directly for research purposes.

Yes ☐ No ☐ I consent to a collection of **urine** from myself/my child. This sample may be obtained for research purposes only or as a leftover sample.

Yes ☐ No ☐ I consent to a collection of **sputum** from myself/my child. This sample may be obtained for research purposes only or as a leftover sample.

Yes ☐ No ☐ I consent to the **research use of leftover specimens** collected from your/your child's clinical care.

Yes ☐ No ☐ I consent to the use and/or disclosure (release) of **photographs/images/video/audio recording** of me/my child.

Yes ☐ No ☐ I consent to allow the use of my/my child's samples or components of samples to be used for **research to learn about, prevent, or treat Rasopathies or related conditions**.

Yes ☐ No ☐ I would be willing to have a researcher associated with Cincinnati Children's Hospital Medical Center specimen repository **contact me/my child in the future** to ask me/my child to take part in more research.

Yes ☐ No ☐ I am willing to allow my/my child's specimens to be used for **future genetic research studies**.

SIGNATURES:

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you should participate in this research, you will document your consent by signature below.

You will receive a copy of this signed document for your records.

_____

Printed Name of Research Participant

_____ _____

Signature of Research Participant Indicating Consent or Assent (if applicable) Date

_____ _____

Signature of Parent/Legally Authorized Representative* Date

_____

* If signed by a legally authorized representative, a description of such representative's authority must be provided

_____ _____

Signature of Individual Obtaining Consent Date