The Children's Hospital *of* Philadelphia®

Informed Consent Form and HIPAA Authorization

Study Title: LeukoSEQ: Whole Genome Sequencing as a First-Line Diagnostic Tool for Leukodystrophies

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You and your child may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time.

In the sections that follow, the word "we" means the study doctor and other research staff. In general, "you" refers to all members of the family, except when specifically noted as "your child".

Why are you being asked to take part in this study?

You are being asked to take part in this research study because your neurologist thinks your child may have a leukodystrophy or other heritable disorders affecting the white matter of the brain. These disorders can have many causes - some known and some unknown. Recent studies have shown that advanced genetic testing, such as whole genome sequencing, is able to identify these causes more often than standard diagnostic tests. However, it remains unclear what impact these more advanced tests will ultimately have on changes in a patient's future care.

You have already agreed to participate in the Myelin Disorders Biorepository Project (MDBP), and you expect to have whole genome sequencing done as part of your clinical care. Your decision to participate should be based on an interest in helping further the research on leukodystrophies. There may be no information gained specifically about your present or future health risks.

What is the purpose of this research study?

The purpose of this study is to establish whether whole genome sequencing leads to an improvement in the quality of care patients receive following their diagnosis, as well as how rapidly that care is delivered compared to patients who received standard diagnostic testing.

How many people will take part?

Enrollment is limited to 150 individuals with suspected leukodystrophies or genetic disorders affecting the white matter of the brain. The study team will also enroll each individual's biological parents as "healthy controls".

What is involved in the study?

How long will you be in this study?

If you agree to take part, your participation will involve collection of information from your medical records and regular contact with study staff via emails, phone calls and/or online surveys for approximately 14 months. You can participate without having to come to CHOP. Your data may be kept indefinitely.

What are the study procedures?

Tests that are part of your regular, routine medical care will continue to be performed. The study involves the following procedures.

Review of Medical Records: We will review your medical records to get information about your diagnosis, treatment, follow-up, clinic visits and results from tests and procedures. This will include the findings from your family's genetic testing, and any MRI studies you have had. We may also ask your physician about your clinical care. You may be asked to sign additional release of information forms to allow us to request this information on your behalf.

Financial information, including charges for diagnostic testing, medical visits, and additional radiologic, neurophysiologic and functional testing ordered both prior to and as a result of a diagnosis, will be collected for cost analysis. No personal financial information will be collected.

Questionnaires: We will ask you to complete weekly surveys for approximately 14 months following study enrollment. These questions will focus on changes in clinical management, both before and after the results of your diagnostic testing have been returned to you.

Surveys may be completed online, using the REDCap database system. You will receive an email at the end of each week, containing a unique link to the survey. Each survey will generally take 5-10 minutes to complete. You may also complete the survey by phone if you do not have access to a computer or smartphone.

What are the risks of this study?

Taking part in a research study involves inconveniences and risks. If you have any questions about any of the possible risks listed below, you should talk to your study doctor or your regular doctor.

While enrolled in this study, you may encounter the following risks:

Risks of Completing Surveys: Some of the survey questions may cause you to experience momentary embarrassment or discomfort. You do not have to answer any questions that make you too uncomfortable.

Risk of Breach of Confidentiality: As with any study involving collection of medical data, there is the possibility that protected health information (PHI) may be disclosed unintentionally. The study investigators take this very seriously, and have taken various precautions to ensure that your PHI remains protected during and after your enrollment in the study.

You have been assigned a unique alphanumerical study identification number that will be used on data collection forms and in the database instead of your name and other protected health information. Only the study team has access to the list that links each participant's name to the study identification number.

Are there any benefits to taking part in this study?

There will be no direct benefit to you from taking part in this study. The knowledge gained from this study may help doctors determine whether whole genome sequencing leads to an improvement in the quality of care patients receive following their diagnosis, as well as how rapidly that care is delivered compared to patients who received standard diagnostic testing.

Do you need to give your consent in order to participate?

You must sign this form if you wish to participate in this study. A copy will be given to you to keep for your records.

What are your responsibilities?

Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study.

What happens if you decide not to take part in this study?

Participation in this study is completely voluntary. You do not need to participate in order to receive clinical care at CHOP.

If you decide not to participate, or if you change your mind about participating later on, there will be no penalties or loss of benefits to which your family would otherwise be entitled.

Can you stop your participation in the study early?

You can withdraw from the study at any time by submitting a written request to the investigator. You do not have to give a reason.

What choices do you have other than this study?

There are options for you other than this study including:

- You may receive clinical diagnostic testing without releasing that information for research.
- You may participate in another study (if available) about your specific leukodystrophy.

Please speak with your local physician and/or a member of the study team if you are interested in pursuing other options.

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about your family members will be collected. This will include information from your medical records and interviews. We will do our best to keep your personal information private and confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research, to assure the quality of the data, or to analyze the data. These groups include:

- Members of the research team and other authorized staff at CHOP;
- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services, Office for Human Research Protections;
- The National Institutes of Health who is funding this research;
- If you agree, your data will be shared through databases that may be publicly available to anyone. The data will not include identifiers like your name, medical record number or date of birth. To use your data, researchers must promise not to try to re-identify you. You can tell us at the end of this form whether you will allow is to share your data in this way;
- We may wish to share your data with other investigators or national databases for future research. The shared information will not include identifiers like your name, medical record number or date of birth. The other investigators will not know who you are. This information shared with them will include information about your diagnosis and genes.

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

There is no set time for destroying the information that will be collected for this study.

Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

A Certificate of Confidentiality (CoC) issued by the NIH covers this research. A CoC helps protect your identifiable information and biological samples.

A CoC protects your private information from all legal proceedings. Unless you consent, information from this research study that identifies you will not be shared outside this research.

- No one can be forced to share your identifiable information or biological samples for a lawsuit.
- Your information can't be used as evidence even if there is a court subpoena.

If you consent, your information or biological samples could be shared for further research, analysis, or quality assurance with the people or organizations listed above.

The CoC does not prevent some disclosures.

- The researchers can't refuse requests for information from those funding this research. The National Institutes of Health may need information to assess this project.
- You can still share information about yourself. You can also freely discuss your involvement in this research.

  The researchers must disclose things required by law. This includes suspected child abuse and neglect, harm to self or others, or communicable diseases.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you tell the investigator in writing.

Dr. Adeline Vanderver, MD
The Children's Hospital of Philadelphia
Abramson Pediatric Research Center 516H
3615 Civic Center Blvd.
Philadelphia, PA 19104-4318

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. You may also elect to withdraw from the study completely, which will result in all previously collected data and samples being destroyed. Please note that we may not be able to destroy data and/or samples that have already been shared anonymously with other researchers.

Financial Information

While you are in this study, the cost of your usual medical care – clinical procedures, medications, and appointments – will continue to be billed to you or your insurance.

Will there be any additional costs?

The costs of the genetic testing will be paid for by the study and will not be billed to you or your insurance.

Will you be paid for taking part in this study?

Your family will not receive any compensation for taking part in this study.

We may share your data with third parties, either other academic institutions or for-profit companies). If there are patents or products that result from the research, the third parties may make money from the research. You will not receive any financial benefit from research performed using your data.

Who is funding this research study?

The Children's Hospital of Philadelphia (Division of Neurology) and The National Institutes of Health are funding this research.

What if you have questions about the study?

If you have questions about the study, call the study doctor, Dr. Adeline Vanderver, MD at 215-590-1719. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

Sharing Data with the National Institutes of Health (NIH)

Why will my data be shared with the National Institutes of Health (NIH)?

For people with certain types of leukodystrophies, the NIH may fund parts of this study. The study team will discuss this with you in more details if it applies to you. The NIH's goal is to maximize the benefits that come from the research.

The NIH repository stores genetic information and phenotypic data from many studies. The NIH then shares that information with researchers. We will send the information about you and the other participants to a repository at the NIH. The information will be de-identified (no names or other direct information about you will be included). The NIH will not be able to re-identify you or any other individual.

The NIH intends to share the collected information with other researchers. The researchers who receive data must promise to keep the data confidential and to use it only for the purpose approved by NIH. They must also promise to not try to re-identify anyone.

The goal of genetic studies is to look for genetic connections that may explain how to identify, prevent, and treat health problems. For example, genetic data may be used to find out:

- who is more likely to develop a certain illness, such as asthma, cancer, or diabetes, or a condition like high blood pressure or obesity;
- what genes affect the progress of a certain disease or condition; and
- what genes may affect treatments which now may or may not work in certain people.

Risks Associated with Sharing Data with the NIH

There are risks associated with sharing your data with the NIH but they are very unlikely to occur. There is only a very small chance that someone could find out that the data came from you. If that happened, it's possible that someone could deny you a job or health insurance. Or you could experience stress, anxiety or embarrassment.

Benefits Associated with Sharing Data with the NIH

Sharing your information for future research will not directly benefit you. It is hoped that it will lead to a greater understanding of the interaction between genes and health. This knowledge could help others in the future.

Controlled or Unrestricted Access

The data about you can either be made available by the NIH through controlled access or unrestricted. Controlled access means the data are made available for other research only after investigators have obtained approval from NIH to use the requested data for a particular project. Data for unrestricted access are publicly available to anyone (e.g., The 1000 Genomes Project).

Consent to Share Data with the NIH (<u>each party initial separately</u>)

Please indicate whether you will allow us to share your information with the NIH by putting your initials next to one of the following choices:

_____ (initials) No, I do not consent to sharing my de-identified information with the NIH

_____ (initials) Yes, I do consent to sharing my de-identified information with the NIH for controlled access

_____ (initials) Yes, I do consent to sharing my de-identified information with the NIH for unrestricted access

CONSENT TO TAKE PART IN THIS RESEARCH STUDY AND AUTHORIZATION TO USE AND DISCLOSE HEALTH INFORMATION FOR THE RESEARCH

The research study and consent form have been explained to you by**:**

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to take part in this research study and if you are giving permission for a child or consent for an adult to participate in this research study, you are legally authorized to consent to the child's or adult's participation. You are also agreeing to let CHOP use and share the health information that will be collected for this study, as explained above. If you don't agree to the collection, use and sharing of health information, you cannot participate in this study.

NOTE: *A foster parent is not legally authorized to consent for a foster child's participation.*

Consent for Child's Participation

Name of Subject	
Name of Authorized Representative	Relation to subject: ☐ Parent ☐ Legal Guardian ☐ Legally Authorized Representative
Signature of Authorized Representative	Date

Consent for Parents' Participation

Name of Mother	
Signature of Mother	Date
Name of Father	
Signature of Father	Date

Assent to Take Part in this Research Study

For children (or adults with diminished capacity) capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Conducting Assent

_____ _____
Signature of Person Conducting Assent Date

This study has been explained to me and I agree to take part.

_____ _____
Signature of Subject (optional) Date

For children (or adults with diminished capacity) unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

_____
Person Responsible for Conducting Assent

_____ _____
Signature of Person Responsible Date

Consent to Take Part in this Research Study and Authorization to Disclose Health Information for Research (non-English Speakers)

_____
Name of Child Subject

_____ _____
Name of Authorized Representative (if different than subject)

Relation to subject:
☐ Parent ☐ Legal Guardian
☐ Legally Authorized Representative

_____
Name of Mother Subject

_____
Name of Father Subject

The research study and consent form have been explained to the subject or parent/legal guardian/legally authorized representative.

By signing this form, you are indicating that you have answered the subject's or parent's/legal guardian's/legally authorized representative's questions, they have agreed to take part in this research study and they are legally authorized to consent to their, their child's, or the adult's participation. They have also agreed to let CHOP use and share the health information as explained above. If they don't agree to the collection, use and sharing of the health information, they cannot participate in this study.

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date:

Interpreter

By signing this form, you are indicating that

- The information in the Summary Document as well as any additional information conveyed by the person obtaining consent was presented to the subject in a language preferred by and understandable to the subject; and
- The subject's questions were interpreted and the responses of the person obtaining consent were presented in a language preferred by and understandable to the subject.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as any additional information conveyed by the person obtaining consent (including responses to the subject's questions) and responded affirmatively.

Name of Interpreter	Signature of Interpreter
	Date:

Assent to Take Part in this Research Study

For children (or adults with diminished capacity) capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

Person Obtaining Assent	
Signature of Person Obtaining Assent	Date

For children (or adults with diminished capacity) unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

_____
Person Responsible for Obtaining Assent

_____ _____
Signature of Person Responsible Date

Witness/Interpreter

By signing this form, you are indicating that

- The information in the Summary Document as well as any additional information conveyed by the person obtaining assent was presented to the subject in a language preferred by and understandable to the subject; and
- The subject's questions were interpreted and the responses of the person obtaining assent were presented in a language preferred by and understandable to the subject.

At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as any additional information conveyed by the person obtaining assent (including responses to the subject's questions) and responded affirmatively.

_____ _____
Name of Witness/Interpreter Signature of Witness/Interpreter

_____
Date