

 **The Children's Hospital of Philadelphia[®]**
Informed Consent Form and HIPAA Authorization

Study Title: **PediSeq:** The Pediatric Genetic Sequencing Project (IRB 12-009169)

Version Date: April 10, 2013

Principal Investigator: Nancy Spinner, PhD Telephone: 215-590-4177

Co-Investigator: Ian Krantz, MD Telephone: 215-590-2931

You, or 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. If you are a parent or legal guardian who is giving permission for a child, please note that the word “you” refers to 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 you are

A patient at the Children's Hospital of Philadelphia (CHOP) and you may have a genetic condition caused by a change or alteration in one or more of your genes.

A family member of a patient cared for at CHOP.

What is the purpose of this research study?

The purpose of this research study is to learn more about newer types of genetic testing called *Exome Sequencing* and *Genome Sequencing*. Current genetic testing usually examines one gene or a few genes at a time. Exome and genome sequencing allow us to test most of a person's genes at one time with a single test.

This testing might identify the reason for a person's unexplained condition or primary diagnosis. The testing might also identify genetic changes related to other current or future health conditions in the person tested or his or her relatives.

The purpose of this study is to identify the best methods for:

- Educating patients and families about exome and genome sequencing
- Analyzing exome and genome sequencing data to identify results relevant to patients
- Giving results to families in a clear, appropriate, and informative manner

How many people will take part?

Up to 1,000 children seen at the Children's Hospital of Philadelphia and their family



members and clinicians will take part in this study.

What is involved in the study?

If you decide to participate in this study, you will be asked to provide a blood, saliva, or tissue sample for genetic testing, to answer questions about your medical history and to give permission for us to review your medical records. You and your parents may be asked to complete several surveys and interviews regarding your experiences with genetic testing and learning your results. You, your parents, your other family members, and your clinicians may also be audiotaped during your study visits, and we may interview your primary care physician or other physician.

How long will you be in this study?

If you agree to take part, your direct participation will last for about 3 to 6 hours over a period of approximately 2 years and will involve at least 2 study visits. Genetic testing and data analysis will continue until the completion of the study, which could be several months or years after you receive the results of your genetic testing.

What are the study procedures?

The study involves the following tests and procedures.

Medical History Interview: A member of our study team or one of your CHOP healthcare providers will take your medical history to better understand how the disease affects you (as a patient or a family member). In some cases, this information may be obtained from your medical record or during your clinic visit.

Review of Medical Records: We will review your paper and electronic medical records on an ongoing basis until the completion of the study. As part of our analysis, we may link to and extract information directly from your electronic medical record. This will allow us to compare results from your genetic analysis with your clinical information.

Photographs: If you are willing, we would like to obtain photographs of you to document your physical features. Even if you choose not to do this, you can still participate in the study.

Blood Sample: You will have approximately 2-4 teaspoons (18mL) of blood drawn for this study. If possible, we will try to coordinate this with a clinical blood draw or use left overs of clinical draws.

Additional Samples: In rare cases, we may be able to obtain a saliva or cheek swab sample or a pre-existing tissue sample, such as tissue from a previous skin or muscle biopsy, instead of a blood sample.

We will isolate genetic or biochemical material (such as DNA, RNA, or proteins) from your samples. This material will be used for genetic analysis, including exome or genome sequencing.

A portion of your sample may be used to create a cell line and/or a cell pellet. This is done by growing blood cells in the laboratory and then freezing and storing them. The cell lines and cell pellets allow us to do



additional genetic or biochemical analysis for this or for future studies (if you agree below).

Additional genetic or biochemical testing might be performed on your samples in order to help us confirm or better understand the results of exome or genome sequencing. We cannot guarantee what specific testing will be performed or when testing will be completed.

Surveys and interviews: For patients, we will ask you and your parents to complete and sign a questionnaire indicating which of your genetic testing results you want us to return to you. You will receive a copy of the completed questionnaire.

Parents of patients under the age of 18 will also be asked to complete several surveys about your family's experiences with genetic testing and learning your test results. Surveys can be completed via email or mail.

Some adolescent or adult patients and participating parents of patients under the age of 18 will be asked to complete a phone (or rarely in person) interview to discuss their impressions of the test results and the results discussion. Interviews will be audiotaped. These surveys and interviews will be conducted by study team members at the University of Pennsylvania (UPenn).

Some participants will also be asked for permission for us to interview their healthcare provider about his/her understanding and impressions of exome/genome sequencing and its impact on caring for you.

Audiotaping of study visits: We may audiotape the enrollment visit during which the study is explained to you or the visit when the results are given to you. These audiotapes will be analyzed by the study team to understand what is discussed during these visits and what kinds of questions are raised by families.

What results can you expect to receive from this study?

Your sample will be studied in our research laboratory to look for alterations or changes in your genes that may be associated with your or your family member's primary diagnosis. *Our main focus will be to identify the genetic basis of this primary diagnosis.* However, as a result of studying many different genes, we may also identify incidental findings that are unrelated to the primary diagnosis. Incidental findings could tell us about other diseases that a person may have or might develop, as well as the potential risks of having a child with a specific genetic disease. Identifying incidental findings is not the main purpose of this study.

By participating in this study, you will automatically receive results related to your primary diagnosis and incidental findings with an immediate and major impact on your health ("immediate medical actionability"). Receiving results of incidental findings without immediate medical impact is completely voluntary; you may choose the types of information you wish to receive.

It is important to remember that we cannot guarantee what specific results this testing will be able to identify. *Exome and genome sequencing do not identify all genetic*



alterations or disease risk. Therefore, there may be genetic alterations that will not be identified or reported. It is possible that this study will be unable to identify the cause of your or your family member's condition or other health problems. We estimate that we will only identify the cause of a person's primary diagnosis in about 10 to 30 percent of participating families (1 out of every 3 to 10 families who participate). Failure to identify a result cannot exclude the possibility that you have an unidentified alteration in a gene/s or a risk of developing disease in the future.

We may not release certain types of results, including:

- Inconclusive or uncertain incidental findings,
- Results that cause a difference in response to medication or a minor increased risk for common adult onset diseases, such as heart disease or Alzheimer's disease,
- Results that do not have associated health problems, such as baldness,
- Results related to certain untreatable adult onset disorders, such as dementia or other neurodegenerative disease,
- Results related to incidental findings in family members, or
- Other results that the study team determines are inappropriate to release, such as those restricted by patents or regulations.

How and when will study results be verified and returned to you?

Throughout this study, a group of experts in genetics, patient care, sequence data analysis, ethics, and bioinformatics will review and verify all findings before they are released to you or your clinicians. This group will carefully review and consider all results before making a final decision about which results will and will not be released.

We will return the results to you based on what you indicated in the results questionnaire.

We expect your initial genetic testing to take 6- 12 months to complete. When the analysis is nearing completion, one of your CHOP healthcare providers or a member of the study team will contact you to set up a time to discuss the results.

Your results will be made available to you as part of a genetic counseling session at CHOP. If you choose to receive genetic counseling due to questions or concerns about results of this study, it will be provided by a clinician who is associated with this study at no cost to you. If you seek genetic counseling at an outside institution, you will be responsible for payment for these services.

After you receive your results, data analysis may continue until the completion of the study. Although unlikely, it is possible that we could identify additional results after your results visit. If this occurs and you indicated that you wanted these types of results and consented to future contact, then we will contact you to see if you would like additional information at that time.

Who else will take part in this study?

For patients, with your permission, your family members, including your parents, siblings and others, may be asked to provide a blood sample or other source of genetic material. Analysis of samples from family members can significantly improve our understanding



of results from your testing. The uses of the samples from family members will be the same as those described above. In addition, your CHOP clinicians who explained this study to you may be asked to complete a survey about their experiences with the consent and return of results process. With your permission, we may also release your test results to your pediatrician and/or another health care provider and interview them about their impressions of the testing and results.

Visit Schedule

The table below provides a brief description of the purpose and duration of each part of the study.

Visit	Purpose	Main Procedures	Duration
Enrollment Visit	Screening and Consent	Review of medical records (Ongoing) Consent Sample Collection (Blood or Saliva)	45 minutes to 2 hours
2 – 3 days later	Parent Survey	Complete survey about consent visit	20 minutes
Visit 2 6-12 months later	Return of Results	Review results with CHOP clinician Parent Survey	~ 2 hours
4 months after return of results	Telephone Interview	Parent Interview Adolescent/Adult Patient Interview (if applicable) Pediatrician Interview (if applicable)	30 to 45 minutes each
12 months after return of results	Parent Survey	Survey about genome sequencing and test results	20 minutes

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.

Risks associated with Sample Collection:

Blood draws: Taking blood may cause some pain, bleeding or bruising at the spot where the needle enters your body. Rarely, taking blood may cause fainting or infection. If possible, the research blood sample(s) will be taken at the same time you have blood drawn for clinical care or through an existing catheter already inserted into a vein.

Saliva and Cheek Swab Samples: The physical risks of these are all minimal. A cheek swab could include irritation in the cheek where the swab was taken.

Tissue Samples: Only tissue that is leftover from a previous clinical or research test will be used. There are no additional risks from the collection of these samples.

Risks associated with genetic testing: For some individuals, undergoing genetic testing or receiving genetic test results might cause frustration, anxiety, depression, anger or fear. We would be happy to arrange for you to speak with a genetic counselor or another mental health specialist if you would like to discuss any



concerns related to this study. You may speak with a genetic counselor who is a member of the study team free of charge. If you speak with a counselor who is not a member of the study team, a counseling fee may be billed to you or your insurance.

- Undergoing genetic testing could confirm that your condition is hereditary, raising questions about risks to family members and family planning. It could impact your relationships with family members or upset relatives who learn that they may be at risk for a disorder. It could also identify unexpected results that are unrelated to your or your family member's reason for participating in this study.
- New information about parentage may be discovered by this research. This could include unknown adoption and paternity (fatherhood). These types of findings will not be shared with you unless there are medical concerns or if required by law. We will not reveal this information to any third party, including other family members.

Risks to Personal Privacy and Confidentiality: Research that uses information from medical records and that involves genetic testing can affect your privacy. Your participation in this research will be held strictly confidential and only a code number will be used to identify your stored samples and data. However, because there will be a link between the code and your identity, confidentiality cannot be guaranteed.

Since future research studies will involve genetic analyses, potential risks include stigmatization of individuals or groups of individuals. It could also affect your insurability. The protections in place minimize those risks. Only coded samples will be stored and used for future research.

There is also a Federal law, called the Genetic Information Nondiscrimination Act (GINA), which generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law may protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Some genetic information may be unique to you and your family. Therefore, although we will not share your identity with anyone outside of this study, there is a chance that sharing coded genetic information could allow someone to identify you or your biological relatives, particularly if you have a rare condition or a rare genetic alteration (change).

We cannot predict how genetic information will be used in the future. It is possible that



this risk could increase over time, as technology improves. Before sharing data, we will verify that measures are in place to protect your privacy and confidentiality to the greatest degree possible. Once data is placed in a public location, such as a database or publication, there is no way to remove it or to completely control its use.

There may be other risks that are not known at this time. Tell the study investigator or study staff right away if you have any problems.

Risks associated with review of medical records/history, obtaining photographs, participating in surveys/interviews and audiotaping study visit sessions:

There is a possibility that participation in this study may make you feel uncomfortable. You do not have to answer any survey or interview questions that you do not wish to answer. You are not required to consent to obtaining photographs.

Are there any benefits to taking part in this study?

You will not receive any direct benefit by participating in this study. There is a possibility that you will learn about the genetic cause for your primary diagnosis or other health problems. However, we may not identify the genetic cause for your diagnosis. Even if we do identify a result related to your diagnosis or health, these results may not lead to improved prognosis or treatment.

The knowledge gained from this research may help doctors improve the way exome and genome sequencing are provided to patients in the future. This study may also increase our understanding of the genes responsible for genetic diseases and contribute to medical care, treatment, and prevention of problems in children with similar genetic disorders or symptoms.

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

If you decide to participate in this study, you must consent to participate by reviewing and signing this form. A copy will be given to you to keep as a record. Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study. Minors who turn 18 during the study will be given the opportunity to re-consent to participation.

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

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP.

If you decide not take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason.

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

As part of this research, health information about you will be collected. This will include information from your paper and electronic medical records, tests performed on your



biological specimens, and surveys and interviews administered as part of this research. 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. Your data and information may also be shared with other researchers or internal and external scientific databases or repositories, including AudGenDB (a genetic database for hearing loss) and the NIH database of Genotypes and Phenotypes (dbGap). Sharing these materials will allow for further research and a better understanding of genetic disease. We will keep your identity private if we share the data in any publication or presentation, as well as with outside researchers and databases.

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 or samples. These groups include:

- Members of the research team and other authorized staff at CHOP and UPenn;
- 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 sponsoring this research.

To help us protect your privacy, we have applied for a *Certificate of Confidentiality* from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

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

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

By law, CHOP and UPenn are 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 and UPenn 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 finished.

Will genetic test results be placed in your medical record?

Only validated results that are directly relevant to your care at CHOP will be placed in the medical record. These will include results related to your primary diagnosis and incidental findings that require an immediate medical action (IMA). These are findings with an immediate impact on your health or healthcare in childhood.

Because these results could significantly impact your health and your care at CHOP, we are obligated to inform you and your clinicians and to place these results in your medical record in order to make sure that you are provided with appropriate medical care. We may release these results whether or not you indicate in the questionnaire that you would like to receive these types of results. Other incidental findings identified solely for the purpose of this research study, including results for adult onset disease and carrier status, will NOT be placed in your medical record as a part of this study.

The certificate of confidentiality described above will not protect the results placed in your medical charts.

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, you must tell the investigator in writing.

Dr. Nancy Spinner
The Children's Hospital of Philadelphia
Department of Pathology and Laboratory Medicine
34th Street and Civic Center Blvd., Abramson Research Bldg. 1007
Philadelphia, PA 19104

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. If you withdraw your permission to use your personal health information, you may be withdrawn from the study.

Financial Information

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

Will there be any additional costs?

There will be no additional costs due to taking part in this study.

Will you be paid for taking part in this study?

Each participant (patients, healthcare providers, and parents of children under the age of 18) will be given a \$25 Amazon gift card for completing each telephone interview, and parents of children under the age of 18 will be given a single \$25 Amazon gift card for completing all three parent surveys.



Who is funding this research study?

The National Institutes of Health (NIH) is providing financial support for this study and the procedures described above.

Financial Information - Two investigators involved in part of this study have invented software applications that may be used to collect data relevant to the research. If CHOP decides to license or sell the software, the inventors will be entitled to a share of royalties earned by CHOP.

What if you have questions about the study?

If you have questions about the study, you can call the Project Coordinator at 267-426-8379 or one of the study investigators: Dr. Nancy B. Spinner at 215-590-4177 or Dr. Ian Krantz at 215-590-2931. You may also talk to your own doctors or genetic counselor about your 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.

Future Analysis

Researchers' understanding of exome and genome sequencing is improving with time. Therefore, it is possible that future testing or re-analysis of prior test results may find results that are not identified or understood on current testing. If your symptoms or diagnosis change significantly in the future, please feel free to contact us so that we can consider the possibility of pursuing additional analysis on your samples. In addition, you and your doctor can also discuss the possibility of additional clinical testing that may be relevant in the future. Due to financial and time constraints, we cannot guarantee when or if additional analysis will be performed on your samples for the purposes of this study.

Consent for Use of Data or Specimens for Future Research

As part of the study, we will collect information and biological samples, such as blood, saliva, or tissue. We may wish to use your information and samples in future studies. The information and samples will be given a unique code and will not include any personal identifiers.

We will maintain a master list of study participants and the numbers assigned to their records and samples in a secure location in the laboratories of Nancy Spinner or Ian Krantz. Information that can identify you or your samples may be kept permanently in a lab or computer database at CHOP.

Only the study doctors and those working with them on this study will be able to see information that can identify you.

If you leave the study, you can ask to have your samples destroyed. You can also ask us to remove information that identifies you from the data or samples. Data collected prior to your removal will continue to be included in the study. At the completion of the study, all samples not approved for additional use will be destroyed. Personal identifiers and



links to personal identifiers will be permanently removed from data not approved for additional use. The data may be maintained indefinitely. Please indicate whether you will allow your data or samples to be used for future research by putting your initials next to one of the following choices:

_____ (initials) My data and specimens may be used for this study only.

_____ (initials) My data and specimens may be used for other future research studies related to genetic research. I understand that if the data or specimens are shared outside of CHOP, my personal identifiers will not be shared.

Consent to Future Contact

As we learn more about genetic testing and genetic disease, we might like to contact you about additional information related to this study, because we need additional information or samples, or about participating in another study. We will only contact you if you are willing. You can decline further participation at that time.

_____ (initials) I give permission to be contacted again.

_____ (initials) I do not give permission to be contacted again.

Consent for Photographs

Many children have physical features that reflect their underlying diagnosis, making photographs useful for research and teaching purposes. If you are willing, we would like to take photographs of your physical features, which may include your face, your body, or specific regions of your body.

If a photograph has been taken as part of your evaluation and diagnosis, we are requesting your permission to use the photographs as part of this study.

A number of different groups of people could see the photographs including members of the general public, scientists and medical researchers. Although these photographs will be used without identifying information such as names, it is possible that someone might recognize you.

Please let us know if you will allow us to take your photograph or use photographs of you that were taken for clinical purposes by putting your initials next to one of the following choices:

_____ (initials) Yes, I give permission to have photographs taken or existing ones used.

_____ (initials) No, I do not want to have photographs taken or used.

If you will allow us to use your photographs, please read and choose an option below.

I allow the photographs (“images”) to be used and released by representatives of The Children’s Hospital of Philadelphia and/or its affiliates (“CHOP”) for the purpose(s) I have initialed below. CHOP may use and release the Images (and other information I give permission for in this form) for the purposes I authorize below until CHOP no longer has the images.

Yes, I agree to the use of my photographs/images (initial all that apply):



1. _____ (initials) as part of this research.
2. _____ (initials) for teaching purposes.
3. _____ (initials) in publications.

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 you are legally authorized to consent to your child's participation. You are also agreeing to let CHOP use and share your child's health information as explained above. If you do not agree to the collection, use and sharing of your child's health information, your child cannot participate in this study. **NOTE: A foster parent is not legally authorized to consent for a foster child's participation.**

 Name of Subject

 Signature of Subject (18 years or older)

 Date

 Name of Authorized Representative
 (if different than subject)

Relation to subject:

Parent Legal Guardian

 Signature of Authorized Representative

 Date



Child Assent to Take Part in this Research Study

For children 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

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

Signature of Subject (optional)

Date

For children 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



Optional Consent to Contact Primary Care Physician

As a part of this project, The Pediatric Genetic Sequencing Project, the study researchers are interested in speaking with pediatricians or other health care providers about whole exome or genome sequencing test results. We would like your permission to contact a physician or health care provider with whom you plan to share the results. If you give permission, we may make arrangements to interview that provider and audiorecord the interview. We would be asking a few questions about the actual test results, but most of the questions would be about sequencing more generally. We would also be sending a copy of the test results to the health care provider you name before we interview him or her. Your decision to allow us to contact a health care provider about the test results is completely voluntary and your care will not be impacted by whether or not you give permission. You can refuse to allow us to contact your health care provider and still participate in the main study.

By signing this form, you agree to have a member of the research team contact your or your child's health care provider (indicated below) so that the researchers can interview him or her about your child's whole exome or genome sequencing results. You also agree that the researchers may send a copy of the report from your or your child's genetic sequencing to the child's health care provider.

_____ Name of Subject	_____
_____ Signature of Subject (18 years or older)	_____ Date
_____ Name of Authorized Representative (if different than subject)	_____ Relation to subject: <input type="checkbox"/> Parent <input type="checkbox"/> Legal Guardian
_____ Signature of Authorized Representative	_____ Date
_____ Name of Health Care Provider	
_____ Phone number of Health Care Provider	

