



Children's Hospital Boston

Protocol Title: Genetic studies of Strabismus, Congenital Cranial Dysinnervation Disorders (CCDD's) and their associated anomalies.

(Consent F: (Consent F: For research subjects participating via neuro-ophthalmologist referral directed through the North American Neuro-Ophthalmology Society (NANOS))

RESEARCH CONSENT FORM

MRN#:

DOB:

Pt Name:

Gender:

Doctor Directing Research: Elizabeth C. Engle, MD
Phone: 617-919-4030; email: elizabeth.engle@childrens.harvard.edu

About this consent form

Please read this form carefully as it tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. In order to decide whether or not you want to be a part of this research study, you should understand enough about its risks and benefits to make an informed judgment. If you decide to take part in this research study, you will be asked to sign the form to show that you wish to take part.

Why is this research study being done?

We are a group of scientists and doctors at Children's Hospital Boston who are studying the genetic causes of strabismus, congenital cranial dysinnervation disorders (CCDD's) and their associated anomalies.

You have been asked to be a part of this study because you or a member of your family has been diagnosed with one of these disorders. This consent form gives you detailed information about the procedures, risks and benefits of the study so that you can decide whether or not you want to be a part of this research.

Genes are found in the cells of our body and are the instructions that tell our body how to grow and develop. They are passed on to us (inherited) from our parents. The DNA sequence that makes up our genes is remarkably similar from one person to the next, but tiny variations do occur, rendering each of us a unique individual. Most of these changes in our genes are harmless and cause such variation as eye color and height. There can also be changes in genes that cause them not to work properly and lead to health problems or disease. We wish to determine and understand which genes are important for brain development by studying the changes in genes of individuals who have disorders affecting their eye movement, cranial nerve abnormalities and their associated anomalies. We hope that the knowledge we gain from this research will lead to improved diagnosis, management and treatment of these conditions.

Our research is federally funded by the National Institute of Health (NIH). We expect to enroll 1800 patients in this research study per year, and anticipate about 1300 of these will be from Children's Hospital. This research is ongoing and will be undertaken in the Engle Laboratory, located in the Center for Life Science Building of Children's Hospital Boston.

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Procedure:

Medical and family history:

You are being asked to participate in this study because you or a member of your family has strabismus, a CCDD or associated anomaly. We are asking you to participate whether you were born into this family or married a member of this family. If you choose to participate, you will be asked questions about yourself, your children, siblings, grandparents, and possibly other family members. These questions may include age, ethnic background, health status and the biological relationship between individuals. In addition, with your permission, we may review your medical records or contact your health care provider to gain further information about your strabismus, CCDD and associated medical conditions.

Sample collection:

You will be asked to give a sample of saliva or blood, from which we can study your genetic material (DNA). Providing a blood sample will involve our taking approximately 1 to 6 teaspoons of blood from a vein in your arm. If there are costs for your blood draw or transportation to the appointment to have your blood drawn for participation in this research, we will refund these costs to you if you give us the receipt(s) showing the exact cost and date of service.

The sample donation will need to be performed only once unless the laboratory procedures fail, in which case a second sample may be requested. Alternatively, we may take a small swab of cells from your inner cheek, a sample of mouthwash that you have swished in your mouth, or some cut fingernails from which we can isolate a smaller amount of DNA. Finally, if you or your child is scheduled to undergo surgery for the eye movement disorder, we may ask your surgeon if any muscle tissue normally removed during the surgery is available for examination and study.

Research use of samples:

DNA obtained from your sample may be used to search, identify and study genes involved in strabismus, cranial nerve abnormalities and their associated anomalies. We may use techniques that study all of your genes, only some of your genes and/or parts of your genetic material that do not have a currently known purpose or function. We may undertake linkage analysis on your DNA and others to determine the genetic location where a gene associated with your disorder may lie. Once a region has been localized to a chromosomal location, it is possible to identify the causative gene by screening sequences within that region. If a change is identified, then sequencing a subset of the population for this gene will determine whether the change in the normal gene sequence is a polymorphism (non disease causing) or pathogenic (disease causing).

Other techniques may include whole genome analysis in which all or most of your genetic code is studied and used to find the causes of your disorder, or the disorder in your family. In some cases we may use blood that has already been drawn to grow your blood cells in a dish. Blood cells grown in this manner can survive indefinitely, providing a greater source of genetic material. We may also use your blood to examine your chromosomes for abnormalities that may cause the eye movement disorder.

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Confidentiality and storage of research information, samples and data:

Information collected about you during this study will be given a unique code number and will not be put in your medical record. Your sample(s) and research data will be associated with your unique code only and stored without your name, medical record number or other identifying information. The information, samples and data will be accessible to the research study staff only and will be stored within the research laboratory in a secure and locked location and/or on a password-protected database at Children's Hospital Boston. Only the research study staff will be able to identify which sample(s), information and data belong to you and this link to your identity will not be shared with anyone outside of the study.

As part of this research we would like to store any remaining sample for future use. The remaining samples may be stored indefinitely and may be used for future studies on strabismus, congenital cranial dysinnervation disorders (CCDD's) and their associated anomalies. The samples will remain in the possession of Dr. Engle or her successors here at Children's Hospital Boston. If Dr. Engle chooses to share your samples with other investigators, your samples will be made anonymous and distributed without your name, medical record number, or other information linking the sample to you. Your identity will not be shared with outside researchers without explicit consent. If at any time you would like to have your sample removed from storage, please let us know and it will be transferred or destroyed according to your wishes. Results obtained prior to your sample removal will remain part of the study.

In order to allow researchers to share results, the National Institutes of Health (NIH) and other organizations have developed special data/information banks that collect and analyze DNA samples and results of whole genome studies. If provided to them, these central banks would store your genetic information and sample(s) and give them to other researchers to do more studies. Your sample(s) and data would be sent with your unique code number only; no identifiable information about you would ever be given to central banks. We do not think there will be further risks to your privacy and confidentiality by sharing your samples and whole genome information with these banks. There are many safeguards in place to protect your information and sample(s) while they are stored in these banks and used for research.

A copy of this consent form will NOT be placed in you/your child's medical record.

In addition, to provide you with additional protection we have a Certificate of Confidentiality (CC) from the US government. It adds special protection for research information that identifies you. It says we do not have to identify you, even under a court order or subpoena. The government may see your information if it audits us. This Certificate does not mean the government approves or disapproves of our project.

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.

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The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances: if the researchers are concerned that you may be suicidal (thinking about killing yourself) or otherwise at immediate risk for seriously harming yourself or others they will need to notify your primary care provider or counselor and/or involve your parents or guardian according to standard clinic practice or if, during your participation in this study, we learn about serious harm to you or someone else, such as child abuse, we will take steps to protect you or other people, including notifying the Department of Social Services or other authorities.

Cost/time commitment:

Your participation in the study should take no more than an hour. There is no fee for you to participate, as the costs associated with this study are covered by research funds. You will not be paid or otherwise compensated for your participation.

Photographing and videotaping eye movements:

If you agree, we will also photograph and/or video-record your eye movements. These recordings will be used to review your eye movements in the future. Also, with your permission, we may use these recordings in medical teaching and medical publications. These recordings will not be used except as described above, and will not be released to anyone else. Please indicate below whether you agree to this or not.

Yes, I do **No, I do not** agree to have my eye movements photographed and/or videotaped.

Yes, I do **No, I do not** give permission for these photographs and/or videotapes to be used in medical teachings, and/or publications.

Recontact for additional data or participation in future studies:

Over time we may wish to obtain updated information from participants. In addition, other studies may arise as a direct result of this study. Please indicate below whether we are permitted to contact you in the future:

Yes, I do **No, I do not** wish to be contacted in the future in order to provide additional clinical information.

Yes, I do **No, I do not** wish to be contacted if future studies arise.

Risks and Discomforts:

Risks associated with a blood draw are minor discomfort and bruising. When possible we will draw blood at the time of a clinically indicated procedure so that you will not need to have blood drawn only for research purposes. There is no risk associated with providing a saliva sample.

There is a chance that participation in this study could cause psychological distress. Some people involved in genetic studies have felt anxious about the possibility of carrying an altered gene that

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places them at risk or that may be passed on to children. If these feelings arise at any time during the study, you may contact us and we will arrange for you to speak with a genetic counselor.

You should also be aware that there might be social and economic disadvantages, which can be associated with the gathering of genetic information. You should know that our testing might find an inherited defective gene, which puts you at risk for a genetic disorder in the future. Genetic information divulged to the wrong source, could affect you and your family (if an insurance company or employer acquired this genetic information) or socially. We will do our best to keep all information confidential and only with your permission would we make this information available to others. The results of the genetic tests performed for research purposes will not be placed in your medical record. In this manner it will be unlikely that an insurance company or employer would ever learn of such results. You should be aware that we may detect instances of non-paternity (the discovery through the analysis of genetic testing that the father is someone other than who he was thought to be), and such information may interfere with our analysis. This non-paternity information will be kept in the strictest confidence and will not be divulged to anyone.

Potential Benefits:

You and your family may not directly benefit by participating in this research, however we hope that in the future information obtained from this study will help us understand the genetic causes of strabismus, CCDD's and associated anomalies. This may eventually lead to new forms of treatment and diagnosis. An annual newsletter will be mailed to you and will include general information about grouped results although no individual information will be reported in the newsletter.

Research result possibilities and reporting:

This research study is meant to find genes that are important for strabismus and cranial nerve development, although we cannot study all possible diseases and genes. During the course of this research, we might find the gene(s) or a common variant that causes, or is associated with the strabismus, CCDD or associated anomaly in you/your child. Although we do not intend to, we might also find a gene that causes a different disorder or uncovers a risk of developing a disorder or disease in the future that is unrelated to the reason for your/your child's participation in this study.

You have the option of knowing if our study finds a genetic change in the sample collected from you/your child that, based on current scientific data and knowledge, could be (1) the cause of the disorder in you/your child or (2) the cause of another disorder or disease that could significantly affect your/your child's health or medical care. The latter (#2) would only include results that are proven to have a known significant effect on human health. You also have the option of not learning any results from this research.

Results from research genetic testing may take months or years to complete. It is possible that there will be no results from the research on your/your child's sample. If you wish to inquire into the progress of this research, you are welcome to do so at any time.

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Since our research laboratory is not certified for reporting results to patients, we cannot give you results from our research genetic testing. However, if we find a result as described above, we may be able to have these results confirmed by a CLIA-certified clinical laboratory. A CLIA lab is a lab that is authorized to release results from patient tests for clinical and diagnostic purposes. Result confirmation by a CLIA lab would involve the participation of your/your child's health care provider(s) and obtaining a new blood or saliva sample from you/your child. The result would be given to your health care provider and then to you with appropriate medical and genetic counseling. Your result could then be used for clinical and diagnostic purposes and could become part of your/your child's medical record. Testing in a CLIA lab could involve costs not covered by medical insurance.

Please read the statements below and check next to the one that states your current wishes about results from this research study.

1. **do not want to learn about results found out about me/my child. Please do not contact me.**

OR

2. **I want to learn only about results found about me/my child that could explain the condition that was the reason for my/my child's research participation (strabismus, CCDD or associated anomaly).**

OR

3. **I want to learn about results found about me/my child, including results that could (1) explain my/my child's condition (strabismus, CCDD or associate anomaly) and/or (2) be the cause of another disorder or disease that could significantly affect my/my child's health or medical care but is unrelated to the reason for my/my child's research participation.**

You can change your mind about whether or not to receive results from this research at any time by contacting the Study Contacts listed below. The Study Contacts are also available to discuss your options further at your request.

Alternatives:

Participation in the research is completely voluntary. You should not feel any pressure to participate. If you do not want to participate it will not interfere with any future care you or your family receives at this institution.

Research at Children's Hospital

Children's Hospital has recently developed a web-based, interactive educational program for parents called "A Parent's Guide to Medical Research." To find out more about research at Children's Hospital, please visit the program at www.researchchildren.org

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Children's Hospital is interested in hearing your comments, answering your questions and responding to any concerns regarding clinical research at Children's hospital. If you would like further information about the type of clinical research performed at the hospital or have suggestions, questions or concerns regarding clinical research you may send an email to cci@childrens.harvard.edu or call 617 355-7052 between the hours of 8:30 am and 5:00 pm.

What information do I need to know about the Health Insurance Portability and Accountability Act (HIPAA)?

During this research, information about your or your child's health will be collected. In general, under federal law, information about patients is private, but there are exceptions and you should know who will have access to this information and might see it.

Researchers may be collecting information about you or your child from medical records. They may also learn things from procedures that are part of the research itself such as tests, office visits, questionnaires and interviews.

The following people will be able to see this information:

- Medical and research staff at Children's Hospital, including people listed on your informed consent.
- Medical staff who are directly involved in your care that is related to the research or arise from it.
- People who oversee, advise or conduct research at Children's Hospital, and people who oversee or evaluate research and care, including the Committee on Clinical Investigation, staff working on quality improvement, and other clinicians and administrative staff of Children's Hospital.
- People from agencies and organizations that provide independent accreditation and oversight of research
- Sponsors or others involved in funding the research
- Federal agencies that oversee or review research information.
- Government agencies and sponsors.
- If some law or court requires us to share the information, we would have to follow that law or final ruling

You/your child should be aware that the federal privacy rule does not cover all of these possible uses. This means that once some of the above mentioned users receive your/your child's health information they do not have to follow the same rules. Other laws may or may not protect sharing of private health information. If you have a question about this you may contact the Children's Hospital Privacy Officer at 617-355-5502.

There is no set time for destroying this information and no time limit for its use. Researchers continue to analyze data for many years and it is not possible to know when they will be done.

You or your child do not have to sign this form. If the form is not signed, however, you won't be able to participate in the study. Not signing will not affect your care or your child's care at Children's Hospital in any way now or in the future. Also, there will be no penalty or loss of benefits if you choose not to sign and participate.

You or your child also have the right to withdraw from this study at any time. You have the right to end your permission for Children's Hospital to use or share the protected information about you or your child that was collected as part of the research.

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Researchers may also continue to use information already collected to protect the integrity of the study. This means that your withdrawal won't make the whole study useless. Once you remove your permission and you or your child is no longer in the study, no more private health information will be collected. If you wish to withdraw you will need to do so in writing. Your investigator will have a form for you to use. If you or your child decide to share private information with anyone not involved in the study, the federal law designed to protect privacy may no longer apply to this information.

Although there are some legal limitations, you or your child have the right to get protected information resulting from this research that relates to your treatment or to payments. This information is available after the study analysis is done. To request the information, please contact the Hospital's Privacy Officer at 617-355-5502. If you have questions, please be sure to ask for answers.

Research at Children's Hospital: Children's Hospital has recently developed a web-based, interactive educational program for parents called "A Parent's Guide to Medical Research." To find out more about research at Children's Hospital, please visit the program at www.researchchildren.org

Children's Hospital is interested in hearing your comments, answering your questions and responding to any concerns regarding clinical research at Children's Hospital. If you would like further information about the type of clinical research performed at the hospital or have suggestions, questions or concerns regarding clinical research you may send an email to cci@childrens.harvard.edu or call 617 355-7052 between the hours of 8:30 and 5:00.

INVESTIGATOR'S AND/OR ASSOCIATE'S STATEMENT:

I have fully explained to all involved parties (participant/parent/guardian as applicable) the nature and purpose of the above-described procedures and the risks involved in its performance. I have provided the subject/family with the Privacy Rule if requested. I have answered and will answer all questions to the best of my ability. I will inform the participant of any changes in the procedures or the risks and benefits if any should occur during or after the course of the study. I have given a copy of the consent/ authorization form to the subject/family.

Date (MM/DD/YEAR) Signature of **Investigator or Associate**

CONSENT/AUTHORIZATION:

***If the child to be involved in this research study is a foster child or a ward of the state please notify the researcher or their staff who is obtaining your consent.**

I understand that I may use the following contact information to reach the appropriate person/office to address any questions or concerns I may have about this study. I know:

