STUDY TITLE: PRE-EMPTIVE GENOTYPING OF CHILDREN AND ADOLESCENTS AT RISK FOR SURGERY AND SUBSEQUENT PAIN MANAGEMENT

STUDY NUMBER: 2013-0853

FUNDING ORGANIZATION: The National Institutes of Health and the Department of Anesthesia

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INTRODUCTION

We are asking for your permission for your child to be in a research study so that we can learn new information that may help others. If you decide not to give your permission for your child to be in this study, we will still take good care of him/her. If you decide to allow your child to be in this study, you may change your mind at any time during the study and your child 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 allow your child 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 about the safety and usefulness of genetic testing before surgery to predict your child's response to pain medicines. Pain medicines affect children differently. We believe genes are responsible for some of those differences. Testing genes before a child needs pain medicine is called pre-emptive genetic testing. We expect that placing results from pre-emptive testing in the electronic medical record could help doctors make decisions about the best pain medicine and best dose for your child after surgery. We expect this will increase the chances that pain medicine will help. We also expect this will lower the chances of side effects. We are asking your child and other children that are being seen in clinic for possible surgery to be in a research study. Oxycodone is a pain medicine given in pill or liquid form after many surgeries. The pre-emptive genetic test will give doctors suggestions about how best to use oxycodone as well as codeine, hydrocodone, and tramadol. We believe genetic testing will improve how pain medicines work when a child is healing after surgery. We hope this study will improve clinical practices.

WHO IS IN CHARGE OF THE RESEARCH?

Senthilkumar Sadhasivam, MD, MPH is the researcher at Cincinnati Children's Hospital Medical Center (CCHMC) that is in charge of this study.

CCHMC is being funded by the National Institutes of Health and the Department of Anesthesia, to do this study.

WHO SHOULD NOT BE IN THE STUDY?

Your child cannot be in this study if he/she:

1. Is younger than 2 or 22 years old or older
2. Have significant comorbidities (ASA 4 and 5)
3. Has liver or kidney failure
4. Has a substance abuse problem
5. Has a neurodegenerative disease
6. Has a severe pulmonary disease (e.g. cystic fibrosis)
7. Is taking other medicines that affect how well certain pain medicines work. Be sure to ask the study doctors if you think your child is taking a pain medicine

WHAT WILL HAPPEN IN THE STUDY?

The research staff will explain the study to you and you will be able to ask questions to make sure that you understand what it is involved in the study.

If your child can be in the study and you and your child decide to be in the study, your child will be asked to come in for up to two study visits. While in the study, your child will be asked to do the following:

1. The first visit (in person or by the phone) is to explain the details of the study. If you give us permission, we will collect a blood sample for DNA and test your child's genes. If your child is afraid of needles, we will collect spit instead of blood. At this time, your child will be given a study I.D number to keep your child's information a secret to study team members. If your child's genetic test result is placed in his/her medical record as part of the study, the result will be linked to your child's name and medical record number. If we do not get enough DNA from your child's sample, we may need to ask him/her for another sample.
2. After we receive your child's sample, and test the genes we may or may not place your child's results into his/her medical records.
3. The second visit will happen if your child needs to have inpatient surgery and is over the age of 5. While your child is in the hospital, we will ask your child to fill out a one page questionnaire. This questionnaire must be completed at least 24 hours after your child is given pain medicine in pill or liquid form.. If study staff cannot collect your child's completed questionnaire on day of discharge, a staff member may call your child to complete the questionnaire by phone.
4. If your child requires a surgery that is outpatient, such as a tonsillectomy or wisdom teeth removal, you and your child will fill out a pain diary. You will record your child's reported pain levels using a 0-100 scale beginning on the evening of the surgery date to the end of the second day after surgery. During the same time you will also record the amount and quality of sleep your child is getting, daily food intake, and any problems that may arise due to the medicine.
5. Throughout the study, the study team will collect information from your child's medical records for the study.

Your child may be placed in one of two groups. We are starting the study by placing everyone in the same group. Everyone in the first part of the study will have their genetic test results placed in their medical records. People who join the study during the second part of the study will be placed in one

of two groups. This will be done by randomization, which is a way of choosing by chance, like flipping a coin. One group will have genetic test results placed in their medical records. If children in this group need surgery, we will learn how their doctors use the results to pick pain medicine after surgery. We will learn if children have lower pain and less side effects when doctors use these results. The second group will also have DNA taken from blood or spit during the first study visit. It may take up to 3 years for this group's genes to be tested. The genetic test results will not be placed in the medical record during the study period. If the child needs surgery, the doctors will use standard practice for choosing pain medicines. Your child's doctors can order the genetic test if they think it will be helpful when your child has surgery. Neither you nor your child will know what group your child is in.

The study will last for 6 years, however, researchers may spend an additional 2 years analyzing data and publishing the results.

By signing this form, you are giving permission for us to store your child's sample and data for future research in human health.

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

Participating in the study may not directly help your child right now. However, children whose genetic results are placed in the medical records may benefit by better pain management.

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

- If blood is drawn, your child may feel brief pain from the needle. Your child may have some bruising or swelling. Infection, light-headedness and fainting are also possible but unlikely.
- Travel and time required for the visits may be inconvenient.
- What we understand about genetic test results may change as more studies are done. This may cause confusion, emotional distress, or possible clinical, behavioral, and economical consequences.
- The identity of you and/or your child may be accidently discovered even though we try our best to keep the information private.
- Your insurance company may find out about your child's genetic test results if we place them in his/her medical record as a part of this study.
- There may be unknown or unforeseen risks associated with the study participation.

WHAT OTHER CHOICES ARE THERE?

Instead of being in this study, you can choose not to have your child be in it.

HOW WILL INFORMATION ABOUT YOUR CHILD BE KEPT PRIVATE?

Making sure that information about your child remains private is important to us. To protect your child's privacy in this research study we will:

- Use a study ID number unique for your child. The study ID number will be used for study forms and electronic data storage.
- Keep your child's study number secret so that only study staff will know it.
- Use a barcode for the DNA sample that is unique to your child when we store the DNA. We will also use a barcode when we send a portion of your child's DNA to a laboratory outside of CCHMC for genetic testing that is needed for this study.
- Keep the barcode number linked to your child's study number in a password protected file in a secured network drive.
- Use your child's study ID number to identify your child's demographic and clinical data. The data will be maintained in a password protected file on a secured hospital network.
- Keep your child's paper study records and data in a locked office or file within the Department of Anesthesiology or The Center for Autoimmune Genomics and Etiology

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify your child. At most, the website will include a summary of the research study results. You can search this website at any time.

CERTIFICATE OF CONFIDENTIALITY

We will do everything we can to keep others from learning about your child's participation in this study. To further help protect your child's privacy, we have obtained a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS).

With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify your child in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify your child, except to prevent serious harm to your child or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, your child, or your involvement in this study.

A Certificate of Confidentiality cannot be used to refuse to disclose identifiable research information about a minor if a parent or legal guardian requests it. The researchers may use other basis for a refusal to disclose information after checking with their IRB about waivers of parental permission and other issues.

If an insurer or employer learns about your or your child's participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Disclosure will be necessary, however, upon request from personnel of the United States federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency 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 we will in all cases, take the necessary action, including reporting to authorities, to prevent serious harm to yourself, children, or others. For example, in the case of child abuse or neglect researcher will take necessary actions to protect the child.

WHAT IF WE LEARN NEW INFORMATION DURING THE RESEARCH?

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

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

Your insurance company will be billed for usual costs of your child's medical care, but **will not** and **should not** be charged for participation in the study. Tests done specifically for the study will be paid for by the study.

WILL YOU/YOUR CHILD BE PAID TO BE IN THIS RESEARCH STUDY?

You (your child) will be reimbursed for your time and effort while you are in this research study.

If your child needs surgery, your child will receive $20 after completing a study survey or returning the completed diary.

Reimbursement for participating will be paid on the following schedule:
$20 for completing visit 2

We will give you your payment in the form of a reloadable debit card (Clincard) and you will receive a handout that will explain how to use the card. We will provide you with a card and we will load money onto your card after each visit that you complete based on the schedule listed above.

Because this research study involves payment for participation, we are required by Internal Revenue Service (IRS) rules to collect and use your social security number (SSN) or taxpayer identification number (TIN) in order to track the amount of money that we pay you. Unless you have given specific permission for another use of your SSN or TIN related to this research study, we will only use your SSN or TIN to keep track of how much money we pay you and your SSN or TIN will not be used as part of this research study.

WHAT HAPPENS IF YOUR CHILD IS INJURED FROM BEING IN THIS STUDY?

If you believe that your child has been injured as a result of this research you should contact Senthilkumar Sadhasivam as soon as possible to discuss the concerns. Treatment for injuries is available at CCHMC. If your child goes to the Emergency Room or to another hospital or doctor it is important that you tell them that your child is in a research study. If possible, you should give them a copy of this parental permission 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 staff listed on page 1.

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.

WHAT ELSE SHOULD YOU KNOW ABOUT THE RESEARCH?

During the study period, researchers may find changed genes different from the ones we are interested in as part of this study (called incidental findings). If experts believe the incidental findings are important to your child's health, we want to contact you. The study member who contacts you will ask you if you want to learn the results. If you say yes, the results will be explained during a genetic counseling visit or will be given to your doctor. Your insurance will be billed for a genetic counseling visit. Any incidental results we tell you about will be placed in your medical record.
Is this ok? _____ (initial) Yes -or- _____ (initial) No

As part of this study, your child's de-identified data and sample may be shared with other researchers or data warehouses for studies in human health.

Do you want to be re-contacted in the future about other studies you or your child might be able to participate in? _____ (initial) Yes -or- _____ (initial) No

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 child's "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 child's PHI as part of this study. This PHI will come from:

- Your child's CCHMC medical records
- Your child's research records

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

- Laboratory test results, diagnosis, and medicines
- 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 child's protected health information in this study?

- Staff at all the research study sites (including CCHMC)
- Personnel who provide services to your child as part of this study
- Other individuals and organizations that need to use your child's 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 child's PHI is not misused?

People that receive your child's PHI as part of the research are generally limited in how they can use your child's PHI. In addition, most people who receive your child's 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 child's PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share your child's 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 your child 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 child's other medical care be impacted?

By signing this document you agree for child to participate in this research study and give permission to CCHMC to use and share your child's PHI for the purpose of this research study. If you refuse to sign this document your child will not be able to participate in the study. However, your child's rights concerning treatment <u>not</u> related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

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 your child should participate in this research you will document your permission by signature below.

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

_____
Printed Name of Parent or Legally Authorized Representative

_____ _____
Signature of Parent or Legally Authorized Representative* Date

_____ _____
Signature of Individual Obtaining Consent Date