Consent Form to Participate in a Research Study

STUDY TITLE: GENOMIC BASIS OF NEURODEVELOPMENTAL AND BRAIN OUTCOMES IN CONGENITAL HEART DISEASE

STUDY NUMBER: 2016-6315

SPONSOR: Pediatric Cardiac Genomics Consortium (PCGC**)**

FUNDING ORGANIZATION: National Heart, Lung , and Blood Institute (NHLBI), NIH/DHHS and Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), NIH/DHHS

_____
Name of Principal Investigator

_____
Telephone Number

INTRODUCTION

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

WHY ARE WE DOING THIS RESEARCH?

Congenital heart defects (CHD) are the most common major birth defect. Doctors know little about the causes of these defects but would like to learn more. For this reason, a group of doctors and specialists have come together to search for genes that cause these heart defects or that influence how people with these defects do over time. Genes are the blueprint for how we look, how our bodies work, and how our bodies respond to disease.

In this research study we want to learn more about the relationship between CHD and the presence or absence of certain genes and/or gene mutations (changes in the gene), and how those might affect development and behavior.

We are asking you and other people with CHD to be in the research because you have CHD and you have genetic results from a prior research study that we would like to use in this research. We will not be collecting any blood or saliva samples for new gene (genetic) testing, but we would like to use genetic results from a prior study in which you took part.

Multiple centers in the United States will take part in this study. We expect to enroll a total of about 400 participants in this study.

WHO IS IN CHARGE OF THE RESEARCH?

is the researcher at that is in charge of this study. The study is being coordinated through Cincinnati Children's Hospital Medical Center (CCHMC).

The NHLBI and NICHD are providing funds to do this study.

WHO SHOULD NOT BE IN THE STUDY

You cannot be in this study if you have any of the following:

- Have had a heart transplant
- Have had surgery on your heart within the last 6 months

There are also other reasons that might prevent you from being in the study. The study staff will discuss these with you.

WHAT WILL HAPPEN IN THE STUDY?

The research staff will explain the study visit(s) to you. You will be able to ask questions to make sure that you understand what will happen.

If you qualify for the study and decide that you want to take part, you will come to for 1 or more visits over the next 6 months. We may also contact you by phone or letter once a year for 5 years after you finish the study to see how you are doing and to collect updated medical information.

These are the things that will happen if you agree to take part in the study.

- Data Collection – we will collect the following data from you:
  - Demographic data (for example your date of birth, race, ethnicity, etc.),
  - Review of your medical records
  - Review of your current medications
  - We will measure your height and weight
  - We will also access the genetic and other related CHD data that was collected from the previous study you took part in.
  - Physician information- If you wish to have your neurocognitive and behavioral assessment results of this study shared with your physician, we will ask you for your physician's contact information.
- Neurocognitive and Behavioral Health Assessments
  - We will test your ability, academic achievement (reading, math), use of language, memory, attention, ability to organize, and other skills related to learning and behavior. Altogether, the testing and questionnaires will take approximately 3 ½ to 4 ½ hours to complete, with ample breaks between parts of the testing. We may mail one or more of the questionnaires to your

home, if possible.
    - In addition we want to learn how you are doing from your parent's perspective, if you have a parent that would be willing to complete some questionnaires about you. The parent questionnaires will require approximately an hour to complete. We will collect your parent name and address from you and we will mail the forms directly to him/her.
    - Parent questionnaires may be mailed to your parent before your visit in most cases and can be returned to the study center via a self-addressed stamped envelope that will be provided.
        - If you have a legally appointed representative caring for you, we will mail the forms to him/her instead of a parent.
        - If a parent or legally appointed representative is unavailable to complete the forms, we will ask you if there is an alternate person that best knows you such as a spouse, significant other, or close friend to complete the forms.
    - If you are still in school, we will also ask that you contact one of your academic subject teachers and ask that they complete two questionnaires about how you are doing in school.
    - The teacher assessments will take about 40 minutes to complete.
    - If you have already had some of the same neurocognitive and behavioral assessments as part of your regular medical care within the last 6 months, we will ask for your permission to obtain these results from your physician and to use those results in this study. We will ask you to sign a separate form to allow your physician to send us those records.
- <u>Brain Magnetic Resonance Imaging (MRI)</u>
    - You will have an MRI scan of the brain.
    - The MRI does not use X-rays or radiation. The MRI scanner uses magnetic fields to create pictures of the brain.
    - The MRI is a way to take pictures of the brain using a large magnet, radio waves, and a computer.
    - The MRI scanner has a circle-shaped opening, like a tunnel.
    - The scan will involve lying very still in the MRI scanner for about 45 – 60 minutes.
    - You will lie on a table (bed) that moves into the opening of scanner. The scanner will not touch or hurt you. To help take the MRI pictures, a special device like a hat, cap, or helmet will be placed over your head. This is called a coil. It will not hurt you.
    - The scanner makes a series of loud noises such as knocking, buzzing, and/or chirping. These are normal sounds of the scanner. Your ears will be protected with earplugs and/or headphones so that the noises are less bothersome.
    - A series of images will be made by the MRI scanner, each lasting about 3-8 minutes. You will need to lie very still while the images are being made. You may be able to move a little between these imaging periods. The technologist will tell you when to be still and when you can move slightly. We will not use any sedation for the scan. Parents are allowed in the scan room.

- You should not have the MRI if you are pregnant; We will do a pregnancy test in females who are of childbearing potential to make sure you are not pregnant.

If scheduling allows, then all of the study procedures may be done in one visit. However, you may need more than 1 visit (scheduled within 6 months or less of the first visit) to complete all of the study procedures. The study staff will work with you to figure out the best schedule for your study visit(s). If any of the assessments or the MRI images are found to be incomplete, we may ask you to come back for repeat testing. The need to redo the testing is not likely and will only be done if you agree to have the tests repeated.

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

You may not receive direct benefit from the study tests. However, the possible benefits of participation are as follows:

1. You will learn about how you are learning and developing. If there are areas in which you are having difficulty, these can be identified and recommendations for further evaluation or intervention provided, as appropriate. A letter summarizing the neurodevelopmental assessment will be provided to you.

2. The brain MRI will be reviewed by a neuroradiologist (a doctor who specializes in reading brain MRIs). We will let you know about any abnormal findings and give the results to your primary care physician with your permission. Further referrals to other specialists will be made as appropriate.

3. There might be an indirect benefit of knowing that by taking part in this study, you may help to improve the care of patients with similar problems in the future.

At your request, we will give you copies of your MRI images for your records. You will be able to share these results with anyone you choose.

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

Risks from data collection: There is a small chance that your data could be shared with people who are not approved to see it. We will do everything that we can to keep this from happening. We have procedures in place to limit who can see your data (see below 'How Will Information About You Be Kept Private').

Risks from neurocognitive assessments: You may be asked questions that make you uncomfortable or cause you to remember situations that were upsetting to you. You may become frustrated if you are asked questions during testing that you do not know how to answer. All people are going to be asked questions that they cannot answer. You do not need to answer any questions that you do not wish to answer and you can stop the testing at any time. If you become very upset during the testing at any time, we will end the testing. We will also offer to have you speak to someone about what you are feeling. If we discover during the testing that you have feelings of wanting to harm yourself or others, we

will refer you to a specialist. If the study physician determines the risk of harm is great, you may be referred for immediate counseling and/or other treatment regarding the risk to self or others.

Risks from brain MRI:
MRI is generally considered to be harmless because it does not involve radiation (x-rays). There are some risks with MRI that are easy to avoid but which you should be aware of. These potential risks are very rare, particularly when MRI is performed within established guidelines by people who are trained.

MRI uses a powerful magnet to make images. Therefore, persons with certain metal implants, such as certain types of surgical clips or pacemakers should not have an MRI. Other metal objects such as keys, pocketknives, or some types of jewelry must be removed prior to entrance to the magnet room. These objects can be pulled towards the magnet at very high speeds and can cause serious injury. The MRI staff will ask you questions about possible metal objects that you may have. In addition to a large magnet, the MRI scanner also uses radio frequency waves that can, on rare occasions, cause a mild warming sensation similar to what you feel on a warm day at the beach. The MRI scanner makes loud banging noises during the scanning session, therefore you will be provided with earplugs to reduce the noise heard from the scanner. It is also possible that the magnetic fields in the scanner can cause mild nerve and muscle twitching in the arms and legs. Such effects are extremely rare but possible. Some people simply find it uncomfortable and/or claustrophobic to lie in the close space of the MRI scanner. If during the MRI, you get nervous or upset, the procedure will be stopped. Although there are no known long-term harmful effects from having an MRI scan performed, it is always possible that there are long-term effects that are not presently known.

During the MRI procedure, wires may be attached to you to monitor breathing and heart rate. On very rare occasions the presence of such wires has resulted in burns at the site of skin contact. Proper placement and use of the wires greatly minimizes this risk and the technologists have been trained in this procedure so that the probability of a skin burn from the wire contacts is very small.

The MRI staff will do their best to make the scan as comfortable as possible. This may include using pillows to keep your head still and comfortable and headphones and a microphone so you can speak with the MRI technologist during the scan. An attendant will be nearby throughout the scan. We will not perform this test on you if sedation is necessary for you to stay still. If you do not want to have the MRI, you can still take part in the other parts of this study.

Risks from allowing us to use genetic results: We will not be doing any new genetic testing as part of this research study. Rather, we will use the results of previous genetic testing from the earlier research study in which you took part. This information will help us to analyze the relationship between genes and development. The overall results of this research will be made publicly available and will identify if any genes were found to be related to neurodevelopmental functioning and brain structure. Any results made available

to the public will not contain anything that will identify you. Some people in genetic studies feel anxious if they think they might have a gene that puts them at risk or that may be passed on to children. If you have these feelings at any time during the study, you may contact us and we will arrange for you to speak with someone who can help you.

OPTIONAL: You may choose to receive your genetic results from the prior research study in which you took part. We will only share genetic test results if a genetic change or mutation was found that is likely to have caused your congenital heart disease and/or affect your development and behavior. This is called a "pathogenic change." If you would like to receive those results, they will be given to you at the end of this study. You will have the option to let us know your choice by checking yes or no at the end of this form. Because the prior study used a research lab to obtain the genetic results, if you have a genetic mutation that is likely to cause congenital heart disease and/or affect brain function or behavior, we will need to confirm the results in a clinical lab before giving the results to you. To do this, we will ask you for an additional blood or saliva sample. The blood sample will be obtained by using a needle to withdraw some blood (about 1 tablespoon) from a vein, most likely in your arm. The risks of taking a blood sample are minor, such as bruising or bleeding at the site of the blood draw and, rarely, infection or fainting. If you choose to receive your genetic results and you have a pathogenic genetic change, we will also offer you the option of speaking with a geneticist or genetic counselor about the results. The costs for the additional blood/saliva test and genetic counseling will be paid for by the research study and will not be charged to you.

There may be other risks from taking part in this study that we do not know about yet.

WHAT OTHER CHOICES ARE THERE?

Instead of being in this study, you can choose not to be in it. This study does not involve any treatments or medications.

HOW WILL INFORMATION ABOUT YOU BE KEPT PRIVATE?

Making sure that information about you remains private is important to us. To protect your privacy in this research study we will use a unique ID number instead of your name on any of the data/assessments/MRI images that we use for the study. We will store all study information in confidential files that are password protected and accessible only to the study staff that are approved to see the study data. Any paper records for the study will be stored in locked storage cabinets. If any publications are made from this study, we will not use your name or anything else that would identify you.

To further help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health (NIH). The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. 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 federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency funded projects. 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, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information. The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities regarding child abuse and neglect, or harm to self or others.

The medical information and test results collected for this study will be kept in special study databases and collection facilities (repositories) that will be available to the study researchers, other persons with permission for related research, and the study sponsor. It is very unlikely that the study information will be seen by others within the hospital, an insurance company or employer. The genetic content of the stored data could theoretically be used (though with enormous difficulty) to identify you. If you believe you will be bothered by this, talk with the study doctor/staff before you sign this form.

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 you. At most, the website will include a summary of the study results. You can search this website at any time.

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 health, safety or willingness to stay in this study. If the study assessments reveal signs of abuse or potential for harm to self or others, we will follow local and state regulations for reporting this information.

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

You will not be charged for the data collection, brain MRI, or neurocognitive assessments that are part of this research study. However if you are referred for further clinical follow up or testing, you or your insurance company will be responsible for those charges.

WILL YOU BE PAID TO BE IN THIS RESEARCH STUDY?

You will be paid $200 for taking part in this study in return for your time and effort. Payment will be made once all study procedures have been completed. If you are unable to have the brain MRI, you will still be paid the full amount for your participation. You will also receive reimbursement for parking fees, meals, mileage, and/or ground transportation for the study visit. If you have to travel from far away for your study visit, reimbursement for travel expenses (hotel and airfare and/or train for example) are available and will need prior approval from the study doctor and the study sponsor.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

For questions, concerns, or complaints about this research study you can contact the study person listed on page 1 of this document.
If you would like to talk to someone that is not part of the research staff or if you have general questions about your research study rights or questions, concerns, or complaints about the research, you can call the CCHMC Institutional Review Board (IRB) at 513-636-8039. .

WHAT ELSE SHOULD YOU KNOW ABOUT THE RESEARCH?

Long term storage of study data:

The information collected from this research study will be available indefinitely in a secure storage site such as the National Center for Biotechnology Information (NCBI) repository.

As part of your participation in the study, a unique subject number (called a GUID) maybe assigned to you that will allow researchers to see if you have been involved in more than one research study or database for patients with congenital heart disease. If you have participated in more than one CHD study or database, this unique subject number may prevent any incorrect duplication of findings. This subject number will also allow your de-identified data to be combined with data from other research studies to increase the likelihood of meaningful analysis. Only this subject number and not your personal identifiable information will be accessible to other investigators.

Data from these storage sites will be available to other, future researchers for study of cardiovascular and other diseases. Before a researcher can get any study data, they must get NIH approval. The researchers will not have access to any identifying information such as your name or medical record number. With this security measure, researchers will not be able to link information back to you. Knowing that this information may be used by a research team in the future to study the heart or other conditions may cause stress to some people. If you believe you will be bothered by this, talk with the study doctor/staff before you sign this form.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

(Site to insert Institution language regarding use of PHI for research).

SIGNATURES

Results and Future Research

Please check the box below to indicate if you would like results from the neurocognitive testing and brain MRI shared with your physician.

- ☐ No, do not share results with my doctor.
- ☐ Yes, please share results with my doctor. If yes, list doctor's name, address, and phone number below.

DoctorName: _____

Address: _____

Phone: _____

Please check the box below to indicate if you would like to learn your genetic results from the prior research study. If you check yes, and you have a pathogenic (disease causing) genetic change in a gene for congenital heart disease and/or brain function or behavior, the results will be provided to you at the end of this research study. Because the prior study used a research lab and not a clinical lab to obtain your genetic results, any results that we provide to you will first need to be confirmed in a certified laboratory with a new blood or saliva sample to be taken from you.

- ☐ No, I do not want to receive my genetic results.
- ☐ Yes, I would like to receive my genetic results if researchers suspect that I have a genetic variation that could be important to my care ("pathogenic genetic change"). I understand that if I have a pathogenic genetic change in a gene for congenital heart disease and/or brain function or behavior, a new blood or saliva sample will be obtained from me and tested at no cost to me. I understand that genetic counseling will be provided at no cost to me.

Are you willing to be contacted in the future about new research opportunities or findings:

- ☐ No
- ☐ Yes

SIGNATURES

The purpose of this study, what will happen, risks and benefits have been explained to me. I have been allowed to ask questions and my questions have been answered to my satisfaction. I have been told who to contact if I have more questions. I understand that I am free to withdraw this consent and stop from being in this study at any time, even after signing this form, and it will not affect my care. By signing this form, I agree to take

part in this research study and to follow the instructions given by the research staff during the study. I have been told that I will be given a signed copy of this consent form.

_____
Printed Name of Research Participant

_____ _____
Signature of Research Participant Indicating Consent Date

_____ _____
Signature of Legally Authorized Representative* Date

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

_____ _____
Signature of Individual Obtaining Consent Date