University of California, Los Angeles

PARENT PERMISSION FOR MINOR TO PARTICIPATE IN RESEARCH

GENOMIC ANALYSIS IN CHILDREN WITH MENTAL RETARDATION, AUTISM, MACROCEPHALY, MACROSOMIA, ASYMMETRY, CONGENITAL ANOMALIES, AND DYSMORPHISM

Julian A. Martinez-Agosto MD PhD from the **Department of Human Genetics and Medical Genetics/Pediatrics** at the University of California, Los Angeles (UCLA) is conducting a research study.

Your child was selected as a possible participant in this study because your child has symptoms of a genetic disorder that may include mental retardation/developmental delay, autism, macrocephaly, macrosomia, asymmetry, or birth defects, or these findings may have already been published in a medical journal. Your child's participation in this research study is voluntary.

Why is this study being done?

The study will be utilizing blood cells looking for mutations (changes in genes) that might cause people to have mental retardation/developmental delay, autism, macrocephaly, macrosomia, asymmetry, or birth defects. Every cell in the body contains a chemical called deoxyribonucleic acid (DNA). DNA is similar to an instruction book that tells your body how to grow an develop. These DNA instructions are inherited from each parent in the form of genes. When DNA is copied from parents to children, it some times isn't copied exactly the same. These changes, called mutations, can be negative and cause birth defects or other problems. This study is designed to find mutations in genes that may cause mental retardation/developmental delay, autism, macrocephaly, macrosomia, asymmetry, or birth defects.

What will happen if my child takes part in this research study?

If you agree to allow your child to participate in this study, we would ask him/her to:

- MEDICAL EVALUATION: Your child will undergo a medical evaluation that will include name, date of birth, height, weight, and head circumference, body measurements, family medical history, physical findings, vital signs and results of clinical testing taken by a member of the study team or a collaborator. We may also obtain past information from your child's medical record. We will ask you to sign a separate consent form to give us permission to obtain photographs of your child and how to use them. Photographs will be obtained using a digital camera and will include your child's full face and whole body. The photographs will be stored in a secure location and no personal information will be included with the photograph. You may choose not to allow us to take or use photographs and still participate in the study. Your initial participation will take about 90 minutes.
- BLOOD DRAW: DNA will be removed from your child's blood sample in the laboratory. DNA is present in your child's genes. Genes are the material passed

from parent to child that influences the make-up of the body and mind, such as how someone looks and if someone is more likely to get a disease. Some of the DNA may be saved for future testing, and some of the cells from your child's blood may be kept alive and growing in the laboratory as a "cell line". The amount of blood collected depends on your child's age:

- five milliliters (5 ml) for infant
- fifteen milliliters (15 ml) for toddler/child

We will also collect 15 ml of blood from each parent. Blood will be drawn from a vein in your child's arm by a phlebotomist at UCLA or your Medical Center. Your child's blood sample will be sent to the UCLA Orphan Disease Laboratory core for DNA extraction and to Cedars-Sinai Clinical Research Center Lymphoblastoid Cell Line Facility for establishment and maintenance of a cell line. It is possible that if we need more DNA we may re-contact you to collect another blood sample from your child.

- GENETIC ANALYSIS: The method used to analyze your child's DNA is called whole exome sequencing. The portion of the genetic code that contains all the genes is called the exome. Because exome sequencing reads very large amounts of genes in the genome, there is a much greater chance that we may find changes in genes that cause other diseases besides mental retardation/developmental delay, autism, macrocephaly, macrosomia, asymmetry, or birth defects. We could identify changes in genes that cause these conditions, normal variations, that cause other diseases, or changes of unknown clinical significance.

  In addition, we would like you to know the limitations of the research testing and exome sequencing and what we will NOT be able to tell you about the changes that we find:

  1. Not all gene changes that cause disease will be detected
  2. Some changes that are not currently known to cause health problems will be found to cause health problems in the future. We cannot promise to be able to tell you about those changes in the future. However, we will attempt to contact you if we learn about something that is of urgent and actionable medical significance during the course of this study.
  3. We will not tell you about gene changes that are not known to have health implications.
  4. This research genetic analysis cannot be substituted for diagnostic testing recommended by another physician.

- ADDITIONAL DATA: You are under no obligation to receive study notices or participate after providing the initial blood sample and exchange of the above information. However, additional imaging and measures as well as updates to your child's evaluation can be voluntarily submitted at later dates at your initiative or may be requested by the principal investigator as frequently as three times per year.

How long will my child be in the research study?

Participation will take a total of about one to two hours for a medical evaluation and blood draw. Your child will be in the research study for the duration of the project.

However, you will not be contacted unless you consent that you would like to be contacted in the future.

Are there any potential risks or discomforts that my child can expect from this study?

- *Risks of sample collection*
  BLOOD DRAW: Puncture of a vein may lead to:
  -Some discomfort, swelling, or bruising near the puncture site
  -Feeling dizzy or faint
  -Infection or possible nerve damage at the site, which is a rare event
  -The procedure may involve risks that are currently unforeseeable.

- *Risks associated with genetic findings:* Identification of gene changes could cause emotional and psychological problems. Learning about disease risk, that you passed on a gene to your child that does not work, or of finding out your own risk for a new disease can be distressing. Your child's privacy is very important to us and we will use many safety measures to protect your child's privacy. However, in spite of all of the safety measures that we will use, we cannot guarantee that your child's identity will never become known. Although your child's genetic information is unique to your child, your child shares some genetic information with parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify your child. Despite this possible limitation, every precaution will be taken to maintain your confidentiality now and in the future. While this project will not use information that is traditionally used to identify, such as your child's address, telephone number, or social security number, people may develop ways in the future that would allow someone to link your child's genetic or medical information in our study back to your child. It also is possible that there could be violations to the security of the computer systems used to store your genetic and medical information to you.

We have learned from past research that we will not always be able to predict future research findings and new technologies. You should be aware that unforeseeable problems may arise from new developments.

Sometimes genetic information suggesting different parentage is obtained during research. We do not plan to report such findings to participants.

Within the limits imposed by technology and the law, every effort will be made to maintain the privacy of your genetic information.

There also may be other privacy risks that we have not foreseen.

GENETIC DISCRIMINATION

There are state and federal laws that protect against genetic discrimination.

There is a new federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans,

and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long term care insurance.

Are there any potential benefits to my child if he or she participates?

You should not expect your condition to improve as a result of participating in this research. You have the right to refuse to participate in this study. If a specific mutation (change in the cell's genetic information that causes your disease) can be identified in your cells, then your parents can be tested to see if they carry the same mutation. Therefore, this may help with genetic counseling for your parents for any future pregnancies, as well as for yourself in the future.

The information obtained from this study will contribute to medical knowledge and diagnosis of mental retardation/developmental delay, autism, macrocephaly, macrosomia, asymmetry, and birth defects.

What other choices do I/my child have if my child does not participate?

The alternative to participation is to NOT participate in this study.

Will my child be paid for participating?

There will be no payment to participate in this study., The study will cover the costs of drawing and shipping the blood sample and you will not be responsible for the costs associated with the blood draw or medical evaluation. Neither you nor your insurance company will be billed for your participation in this research.

Will information about my child's participation be kept confidential?

Any information that is obtained in connection with this study and that can identify your child will remain confidential. It will be disclosed only with your permission or as required by law. Our laboratory will keep research records that contain identifiable information, including name, medical record number, and contact information. The identifiable information is kept in a locked file and stored separately from the research data. The only people who will know that you and/or your child are a research subject are members of the research team and, if appropriate, your physicians and nurses. No information about you and/or your child, or provided by you during the research, will be disclosed to others without your written permission, except:

- if necessary to protect your and/or your child's rights or welfare (for example, if you are injured and need emergency care); or
- if required by law.

Authorized representatives of the UCLA Office for Protection of Research subjects may need to review records of individual subjects. As a result, they may see your name; but they are bound by rules of confidentiality not to reveal your identity to others. When the results of the research are published or discussed in conferences, no information will be

included that would reveal your identity. The blood samples obtained from you will be coded so they will not have any linking identification to you.

Storage and Release of Samples and Medical Information: Anonymous information from the analyses will be put in a completely public database, available to anyone on the Internet. Your coded medical information and information from more detailed analyses of your coded samples will be put in a controlled-access database. The information in this database will be available only to researchers who have received approval from a National Institutes of Health Data Access Committee. Note that traditional identifying information about you, such as your name, address, telephone number, or social security number, will NOT be put into either the public or controlled-access databases for this project.

What are my and my child's rights if he or she takes part in this study?

- You can choose whether or not you want your child to be in this study, and you may withdraw your permission and discontinue your child's participation at any time.
- Whatever decision you make, there will be no penalty to you or your child, and no loss of benefits to which you or your child were otherwise entitled.
- Your child may refuse to answer any questions that he/she does not want to answer and still remain in the study.
- Your health care provider may be an investigator of this research protocol, and as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way associated with this project. You are not under any obligation to participate in any research project offered by your physician.

Who can I contact if I have questions about this study?

- **The research team:**
  If you have any questions, comments or concerns about the research, you can talk to the one of the researchers. Please contact:

Principal Investigator:
Julian A. Martinez-Agosto MD, PhD
Division of Medical Genetics
Department of Pediatrics
10833 LeConte Avenue, CHS 32-231
Los Angeles, CA 90095
Phone: 310-206-6581
If not immediately available, please call (310) 825-6301 and page Dr. Julian Martinez

- **UCLA Office of the Human Research Protection Program (OHRPP):**
  If you have questions about your child's rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, please call the OHRPP at (310) 825-7122 or write to:

  UCLA Office of the Human Research Protection Program

11000 Kinross Avenue, Suite 211, Box 951694
Los Angeles, CA 90095-1694

You will be given a copy of this information to keep for your records.

Please indicate by initialing the category below what type of information you want to receive. It is your responsibility to let the investigator know if your address and/or telephone number changes. The contact information is in this informed consent form under "The research team".

- **INFORMATION ABOUT MY SAMPLE**

_____I would like to receive general Information about what the study found

_____ I would like to receive specific Information about what the study found about me

_____I **do not want** to receive any information about my sample

- **ACTIONABLE FINDINGS**

_____ I understand that the research team will/may contact me to find out if I want to learn about genetic changes that they feel have urgent medical significance for my health if the results are actionable. I will not be told about all genetic changes, even though they could have health or reproductive problems.

- **FUTURE USE OF DATA AND SAMPLES**

Please check the appropriate box below and initial ONE option:

_____I would like to allow my blood/cells/DNA sample and associated data to be used for future research

_____I **would not like** to allow my blood/cells/DNA sample and associated data to be used for future research

- **SHARING OF SAMPLES**

Please initial ONE option:

_____ I agree to have my blood/cells/DNA sample and associated data shared with other researchers.

_____ I **do not want** my blood/cells/DNA sample and associated data shared with other researchers.

SIGNATURE OF PARENT OR LEGAL GUARDIAN

Name of Child

Name of Parent or Legal Guardian

Signature of Parent or Legal Guardian | Date

SIGNATURE OF PERSON OBTAINING CONSENT

Name of Person Obtaining Consent | Contact Number

Signature of Person Obtaining Consent | Date