UNIVERSITY OF WISCONSIN-MADISON

Subject CONSENT to Participate in Research
And
AUTHORIZATION to Use and/or Disclose Identifiable Health information for Research

Title of the Study: GFAP Mutations and Alexander Disease

Principal Investigator: Albee Messing
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INVITATION

If you are being asked to consent to participation in this research study on behalf of your child, please read “you” as “your child” throughout this document.

You are invited to participate in this research study about the genetic causes of Alexander disease. You are invited to take part because you or a member of your family has been diagnosed with Alexander disease, or with an Alexander disease-type illness. We expect that eventually 300 individuals will participate in this study, but because this is a rare disorder we do not have a fixed target number of participants.

Your participation in this research study is voluntary. If you decide not to participate, the health care provided to you by the University of Wisconsin-Madison (UW-Madison) and its affiliates (the University of Wisconsin Hospital and Clinics and the University of Wisconsin Medical Foundation), if any, or by your local health care provider, will not be affected in any way.
A. WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of the research is to find out what types of changes in the GFAP gene lead to Alexander disease, how the changes in this protein cause the disease, and whether changes in other genes also contribute to the disease.

B. WHAT WILL MY PARTICIPATION INVOLVE?

If you decide to participate in this research you will be asked to release information about your health history and current condition, and provide tissue samples such as cheek swabs or blood for molecular studies. In most cases cheek swabs will be suitable, and can be collected by you using a kit provided by us. The procedure consists of gently twirling a small brush on the inside of your cheek for about 30 sec. (firmly, but not so hard that your cheek bleeds), and then placing the tip of the brush in a small tube containing a preservative solution. The same procedure is done on the other cheek using a second brush and tube. The collection of cheek samples should take no more than 15 min. If blood samples are necessary, we require approximately 10 cc (2 tsp) that will have to be collected by medical personnel.

We will also collect the following information about you for this research study:

1. From you:

   name, birth date, gender, home address, phone number, email address, history of nervous system-related diseases, history of nervous system-related diseases in immediate family members, ancestors, or first-degree relatives (aunts, uncles, cousins)

2. From your medical records and/or health records (such as MRI's), kept by local health care provider:

   report from your doctor (usually neurologist or pediatrician) about your health history and examination findings; report from your radiologist about MRI images; MRI images themselves (as films or CD's); report from pathologist about biopsy samples (if taken), glass slides of pathology samples (if taken)

If you wish to take part in this study, we will need to have experts look at MRI results (in the form of images or films) and pathology results (in the form of tissue samples placed on glass slides) to ensure that the diagnosis of Alexander disease is accurate. The MRIs will be sent to Dr. Marjo van der Knaap (Free University Hospital, Amsterdam), and the tissue samples to Dr. James E. Goldman (Columbia University, NY) for their review. In the event Drs. van der Knaap or Goldman disagree with the diagnosis of Alexander disease, this information will be given to your physician for further discussion with you.
C. ARE THERE ANY BENEFITS TO ME?

You are not expected to benefit directly from participating in this study. Your participation in this research study may benefit other people in the future by helping us learn more about Alexander disease.

D. WILL I BE PAID FOR MY PARTICIPATION?  no

E. ARE THERE ANY SIDE EFFECTS OR RISks TO ME?

The main risk of taking part in this study is that your study information could become known to someone who is not involved in performing or monitoring this study. For instance, insurance companies have been known to use information on genetic testing to deny coverage to applicants. However, our research studies are not a "genetic test" as this term is commonly used by insurance companies or employers, and you should NOT answer "yes" to a question about whether you have had "genetic testing" because of your participation in this study. It is only in the circumstance that you decide to obtain repeat testing by a certified diagnostic laboratory that you should answer "yes" to such a question about genetic testing.

Learning the results of the test may be upsetting to you or your family members, especially in the case of Alexander disease for which there are currently no cures or treatments.

Collection of the tissue samples presents no serious risk. There may be some brief discomfort, and on occasion when blood is collected the vein may become red and sore.

F. HOW WILL MY PRIVACY BE PROTECTED AND WHO WILL USE MY HEALTH INFORMATION?

The identities of all participants in this study will be kept confidential to the extent possible. All blood or tissue samples, or DNA samples, will be identified by code numbers only. Dr. Messing will maintain a list of the sample donors in a locked file cabinet at the University of Wisconsin-Madison, and only Dr. Messing will have access to this information.

The results of this study may be published in a medical journal. For hereditary disorders, pedigrees (family trees) are an essential means of communicating patterns of inheritance to the scientific community. Hence, as part of such a publication we may include a pedigree describing your family, with symbols representing all individuals we think are relevant (that is, we typically leave out lots of children who might exist but who are not participants in our study). In the standard format for pedigrees, square symbols indicate males, and circles indicate females. A filled symbol indicates a person who is affected by the disease under study, and a shaded symbol indicates a person we are not certain about, but who might be affected. A diagonal line in a symbol indicates that
a person has died. For those who are affected, we show approximate age of onset. For those who have died, we show the age of onset as well as the age when they died. In addition, the written portion of the manuscript might include some description of the health problems you have experienced (only ones we think are relevant to Alexander disease though), and we are may include a few of the MRI images you have allowed us to see. Most importantly, we want to assure you that in all cases names, addresses, telephone numbers, birth dates, medical record numbers – in short, anything that would make you readily identifiable - will NOT be part of these publications. Members of your family who are not enrolled as participants in our research (that is, have not signed the consent forms) might be illustrated in the pedigree, but only showing their gender and place in a particular generation (that is, without any information about their health).

However, because Alexander disease is such a rare disorder, it is true that some close friends or family members who are already familiar with your health history might read this publication and think they know who you are. If so, it is important to understand that they would be doing so based on incomplete information and by making assumptions.

The information collected from you during this study and from your medical records will be used by the researchers and research staff of the UW-Madison. It may also be shared with others at the UW-Madison and outside the UW-Madison, as follows:

**Others at UW-Madison and its affiliates who may need to use your health information in the course of this research:**

- UW-Madison regulatory and research oversight boards and offices (although tissue samples and information provided to such boards and offices are generally coded, and do not contain any identifying information)
- UW-Madison Waisman Center genetic counselors who may be called upon to assist in reporting of results as explained below in Section I.

**Others outside of UW-Madison and its affiliates who may receive your health information in the course of this research:**

- The investigators and research staff at Columbia University and the University of Alabama-Birmingham (although tissue samples and information are coded, and do not contain any identifying information)
- Dr. James Goldman at Columbia University. You should understand that Dr. Goldman is responsible for reviewing pathology specimens when available. Hence he may be made aware of identifying information such as names and birth dates as part of routine clinical practice. Subsequently he may also learn genetic results so that we can learn whether particular mutations lead to unique forms of pathology. Dr. Goldman is bound by the same confidentiality guidelines as Dr. Messing.
• Dr. Marjo van der Knaap at the Free University Medical Center, Amsterdam, The Netherlands. You should understand that Dr. van der Knaap is responsible for reviewing all MRI’s of participants in our research, and hence is made aware of identifying information such as names and birth dates as part of routine clinical practice. After our studies are completed we then share genetic information with Dr. van der Knaap so that she can determine whether particular mutations lead to specific types of changes visible in MRI. Although Dr. van der Knaap is located outside the United States, and is not subject to the same privacy laws that exist here, she utilizes similar practices for guarding confidentiality as we do (such as keeping all records in a locked office, and keeping all documentation relating to our research on private computers that are not part of the hospital record-keeping system).

• Occasionally your genetic results may be shared with others outside the UW-Madison and its affiliates, but it is not shared in a way that can identify an individual.

Certificate of Confidentiality
To help us protect your privacy, we have obtained 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. 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.

G. IS MY PERMISSION VOLUNTARY AND MAY I CHANGE MY MIND?

Your permission is voluntary. You do not have to sign this form and you may refuse to do so. If you refuse to sign this form, however, you cannot take part in this research study.

You may completely withdraw from the study at any time.

IF YOU DECIDE NOT TO PARTICIPATE IN THIS STUDY OR IF YOU STOP WHILE THE STUDY IS UNDERWAY, THE HEALTH CARE YOU RECEIVE FROM THE UW-MADISON AND ITS AFFILIATES WILL NOT BE AFFECTED IN ANY WAY.
H. HOW LONG WILL MY PERMISSION TO USE MY HEALTH INFORMATION LAST?

By signing this form you are giving permission for your health information to be used by and shared with the individuals or institutions described in this form. Unless you withdraw your permission in writing to stop the use of your health information, there is no end date for its use for this research study. You may withdraw your permission at any time by writing to the person whose name is listed below:

Dr. Albee Messing, 1500 Highland Ave, Rm 713, University of Wisconsin-Madison, Madison, WI 53705-2280

Beginning on the date you withdraw your permission, no new information about you will be used. Any information that was shared before you withdrew your permission will continue to be used. If you withdraw your permission, you can no longer actively take part in this research study.

I. REPORTING RESULTS TO SUBJECTS, PHYSICIANS, OR FAMILY MEMBERS

It is possible that our analysis indicates alterations in the DNA sample that could be of interest to you. If you wish, and only if you initial below, we can provide these results to you through a physician and/or genetic counselor of your choosing. However, the laboratories where we conduct our analyses are not certified under the Clinical Laboratory Improvement Act (CLIA). The results of the genetic testing are for research purposes only, and are not intended to be used for diagnosis, prevention or treatment of any disease, or for the assessment of the health of any subjects. If you wish to have genetic testing results for those purposes, you should have the testing repeated by a diagnostic laboratory that is CLIA certified for clinical testing.

_____ Initial here if you wish to have results reported to a physician or genetic counselor.

If you already know the name of this individual, please provide it here:

Name __________________________ phone number __________________________

If results are being reported only to a physician, a genetic counselor associated with our research program will contact you shortly after you receive these results to answer any questions you may have and, if you wish, provide names of genetic counselors in your area.
J. FUTURE USE OF TISSUE OR DNA SAMPLE

Let us know whether Dr. Messing or others may use your tissue or DNA for other research by putting your initials by one of the following choices:

_____ we may use your DNA or tissue for other research or share it with other researchers (as coded samples, without any identifying information)

_____ we may NOT use your DNA or tissue for any future research or share it with other investigators

In the event that Dr. Messing ceases to be involved with this research project, another investigator would be identified to assume custody of these samples and you would be contacted to be informed of the change in investigators.

K. WHO SHOULD I CONTACT IF I HAVE QUESTIONS?

Please take as much time as you need to think over whether or not you wish to participate. If you have any questions about this study at any time, contact the Principal Investigator, Albee Messing, at 608-263-9191. For information on the rights of research subjects, you may contact the UW Hospital and Clinics Patient Relations Representative at (608) 263-8009.
AGREEMENT TO PARTICIPATE IN THIS STUDY
AND
PERMISSION TO USE AND/OR DISCLOSE MY HEALTH INFORMATION

I have read this consent and authorization form describing the research study procedures, risks, and benefits, what health information will be used, and how my health information will be used. I have had a chance to ask questions about the research study, including the use of my health information, and I have received answers to my questions. I agree to participate in this research study, and permit the researcher to use and share my health information as described above.

Name of Participant (please print): ________________________________

________________________________________
Signature of Participant Date

Name of Parent or Guardian (please print): ________________________________

________________________________________
Signature of Parent or Guardian Date

Relationship to Subject: ________________________________________________

Address: ________________________________________________

________________________________

Phone No.: ________________________________

YOU WILL RECEIVE A COPY OF THIS FORM AFTER SIGNING IT.

Signature of person obtaining consent and authorization:

________________________________________
Signature Date