

## CONSENT FORM

**TITLE: Translational Research in the Dystrophinopathies**

**PRINCIPAL INVESTIGATOR:** Kevin Flanigan, M.D.

**CO-INVESTIGATORS:** Robert Weiss, Ph.D., John Atkins, Ph.D., Lynne Kerr, M.D., Ph.D., Mark Bromberg, M.D., Ph.D., Jacinda Sampson, M.D., Ph.D.

### **Background**

This study is aimed at understanding how mutations in the dystrophin gene determine the symptoms and severity of muscular dystrophy. Because your physician has determined that the form of muscle weakness which affects you or some members of your family is likely due to muscular dystrophy, we are inviting you to participate in this study.

Types of muscle disease which are due to mutations in the dystrophin gene include Duchenne Muscular Dystrophy, Becker Muscular Dystrophy, and isolated cardiomyopathy. In this document we will use the term “dystrophinopathies” to mean any syndrome caused by alterations in the dystrophin gene. A dystrophinopathy is often an inherited illness, transmitted from a parent to a child in their genes. Genes are fragments of inherited material (DNA) which direct the body to make a particular protein, and proteins are the machinery of cells. The dystrophin gene is located on the X chromosome. Because women have two copies of the X chromosome, they have two copies of the dystrophin gene. Some women who carry a mutation in one copy of their dystrophin gene have symptoms, and others do not. Some women who currently do not have symptoms may have evidence for muscle disease when we examine them.

Some families or patients with dystrophinopathy have deletions of the dystrophin gene; that is, they are missing a portion of their DNA. Others have smaller rearrangements of the gene. How these different mutations influence disease severity is not fully understood. This study is aimed at understanding how different mutations in the dystrophin gene determine the symptoms and severity of muscular dystrophy. A second goal of our study is to establish a registry of patients with dystrophinopathies. Although this consent form does not ask your consent to participate in any clinical trial, we will notify you of clinical trials for which you might be a candidate, if you give us permission to do so.

### **Study procedure**

There are several parts to the study:

- (1.) You will be examined about once a year. The examination will be essentially the same as the examination you probably have had in a muscle clinic or neurologist’s office. For example, your strength will be tested by the examiner pushing against your limbs. You will be timed performing tests such as getting up off of the floor walking about thirty feet down a hall. You will have a breathing test to measure the volume of air you can inhale. The examiner will score your performance on these tests, and record it.
- (2.) You will be asked to help the study coordinator fill out a questionnaire each year. The questionnaire will ask about your medical history. As examples, the



questionnaire will ask about your level of function at home, as well as about what sort of medications you have taken in the past year or what sort of surgeries you have had. The study coordinator will also use information from your clinic record to fill out the questionnaire. For example, if you have had an echocardiogram to measure heart muscle function, the results of that study will be included in your questionnaire.

- (3.) You may be asked for a sample of blood for analysis of the dystrophin gene. If you agree to have blood drawn, we will draw 3-4 tablespoons of blood from which we will extract DNA for study. The blood draw will only require 5-10 minutes of your time.
- (4.) If you have had a muscle biopsy as part of your clinical evaluation, a leftover piece of muscle is probably archived at this or another hospital. We would like to obtain that muscle biopsy specimen in order to perform special studies with it. These studies include evaluation of the size and amount of the dystrophin protein, as well as the size and amount of the molecules which direct the assembly of the protein (the DNA and RNA).
- (5.) Information regarding your clinical course and your gene mutations will be stored in a database maintained by Dr. Flanigan and his colleagues. Without identifying you, this information may be made available to researchers who are investigating muscular dystrophy. For example, researchers may be interested in figuring out whether patients with heart muscle weakness (cardiomyopathy) have particular variations in the dystrophin gene, and may request a list of dystrophin gene variations associated with cardiomyopathy or other clinical features. Any such information shared with other researchers will not include your name or other identifying information.

### **Risks**

Foreseeable risks of this study include the possible complications of drawing blood and include bruising, infection, and slight discomfort. These risks are extremely small when performed by experienced health care providers.

Discrimination for health insurance sometimes occurs when patients have genetic disorders. However, in this case, you already have a clinical diagnosis of muscular dystrophy, so allowing us to gather together clinical information does not add significant risk. All clinical records will be kept in a locked file and will be accessed only by the investigators to minimize this risk.

### **Benefits**

There are several ways in which you may benefit from this study. For each of these following, please check and initial next to one of the boxes below it:

- (1.) If you request that we do so, we will return the results of the genetic testing of your dystrophin gene to you. We will return the results in a letter. In addition, we will also have a certified genetic counselor available to you, either in person or by telephone, so that you



may be certain to have any questions about the testing answered. For example, if you request it, the genetic counselor may speak to you and your family about how your dystrophin gene mutation may be inherited or carried by other family members.

a.  \_\_\_ Please return the results of the dystrophin gene analysis to me

b.  \_\_\_ Please do not return the results of the dystrophin gene analysis to me.

(2.) \*If you request it, we will return the same results of the genetic testing to your physician.

a.  \_\_\_ Please return the results of the dystrophin gene analysis to my physician

b.  \_\_\_ Please do not return the results of the dystrophin gene analysis to my physician.

(3.) \*If you request it, we will return the results of the clinical testing to your physician, so that they may use it for clinical purposes.

a.  \_\_\_ Please return a summary of the results of the clinical testing to my physician.

b.  \_\_\_ Please do not return a summary of the results of the clinical testing to my physician.

**\*Please note:** You were enrolled in this study because of your clinical diagnosis of dystrophinopathy, so this diagnosis is already present in your clinical medical record. Please see the discussion below about the Certificate of Confidentiality from the National Institutes of Health. If your referring physician puts the result of genetic or strength testing in your medical record, the Certificate of Confidentiality will not protect this specific information (just as it will not protect any information in your clinical medical records). However, the Certificate will protect all of the other information in the database and registry which is not included in your clinical record.

(4.) From muscular dystrophy researchers around the country (or world) we may receive notifications of clinical trials. We will review the criteria by which they select patients. We will also confirm that they have approval from their own institution's Research Review Board. **We will not give your name or any personal information to these researchers.** If you request it, we will notify you in writing about the existence of studies for which you **may** be appropriate for inclusion. We will provide you with any contact information that we have been given, and if you wish to have more information, you will need to contact those other researchers directly.

**Please be sure to note that if we tell you about the existence of a study at another institution, it does not mean that we are endorsing it. It also does not mean that Dr. Flanigan or the University of Utah's Institutional Review Board can verify that the study is safe and reasonable. You need to review and sign a separate consent form for any research study in which you choose to participate.**



a.  \_\_\_\_\_ Please notify me of any research studies for which I may be a candidate. I understand that if you notify me it does not guarantee that I will be enrolled in that study. I also understand that if you notify me, I will need to contact those researchers myself, and determine for myself whether I wish to consent to participate in their study.

b.  \_\_\_\_\_ Please do not notify me of any research studies for which I may be a candidate.

We cannot guarantee any benefits to you from participating in this study. Your participation may be of benefit to others, and to society. Any significant new findings discovered during the course of the study which might relate to your willingness to continue the study will be shared with you.

### **Alternative procedures**

No alternative procedures are available for comparing disease severity to gene mutations. You can choose not to participate in this study.

### **Confidentiality**

All data will be kept confidential, unless you request that we return information to your physician or physicians. Only investigators and coordinators will have access to the names of participants. Research records will be kept behind locked doors and information on computers will be protected by passwords.

### **Person to contact**

If you have questions, complaints or concerns about this study, you can contact the Research Coordinator at 801-585-1299. If you think you may have been injured from being in this study, please call Dr. Flanigan at 801-587-9540.

### **Institutional Review Board**

Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at [irb@hsc.utah.edu](mailto:irb@hsc.utah.edu).

### **University's Liability Statement:**

If you are injured from being in this study, medical care is available to you at the University of Utah, as it is to all sick or injured people. The University of Utah does not have a program to pay you if you are hurt or have other bad results from being in the study. The costs for any treatment or hospital care would be charged to you or your insurance company (if you have insurance), to the study sponsor or other third party (if applicable), to the extent those parties are responsible for paying for medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs.

The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Utah Governmental Immunity Act is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See Section 63-30d-101 through 63-30d-904 of the Utah Code.



**Voluntary participation**

It is up to you to decide whether or not to take part in this study. If you decide to take part you are still free to withdraw at any time and without giving a reason. Refusal to participate or the decision to withdraw from this study will involve no penalty or loss of benefits to which you are otherwise entitled. If you don't take part, you can still receive all standard care that is available to you. This will not affect the relationship you have with your doctor or other staff, nor decrease the standard of care that you receive as a patient.

**Unforeseeable Risks**

Unforeseeable risks may also be associated with this study.

**Right of Investigator to withdraw subject**

The Investigator has the right to withdraw you from the study at any time. Reasons for the Investigator to withdraw you from the study might include if he determines that you do not have a dystrophinopathy, or that you are unable to provide an adequate medical history.

**Costs to the subject**

There will be no cost or compensation to you for taking part in this study.

**New information**

Any new information developing during the course of the study that may relate to your willingness to continue participation will be provided to you.

**Number of subjects**

We expect that about 1700 people will be enrolled in this study at one of the participating sites, about 300 of those patients will be enrolled at the University of Utah.

**Stored specimens**

Please read each sentence below, think about your choice, and mark "YES" or "NO". No matter what you decide to do, your decision will not affect your medical care.

May the University of Utah retain your blood and/or tissue sample(s) after the end of this research project for use in future research?

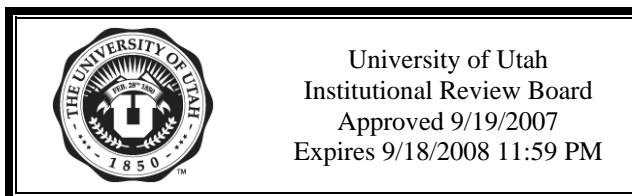
**YES, my sample(s) may be saved for future neurological/neuromuscular research**

**NO, my sample(s) must be destroyed at the end of this research project**

If yes, may the University of Utah keep your name and other identifying information with your sample(s)?

**YES, my personal identifiers and medical information can be kept with my sample(s). All information will be kept secure and confidential.**

**NO, my name and identifiers must be removed from my sample(s). My sample(s) cannot be linked back to me.**



If the above stated sample(s) are used in any future research by the University of Utah or its research partners, the Institutional Review Board may require that you be contacted for your permission prior to the use of the sample(s) in a new project if it determines new consent is required for your protection.

I understand that I reserve the right to withdraw my consent in the future and that I would need to notify the investigator of my decision. If you decide to have your identifiers removed from your sample(s), you will not be able to withdraw your sample later because it cannot be linked back to you.

**Authorization to use and disclose protected health information for research**

Signing this document means you allow us, the researchers in this study, and others working with us to use information about your health for this research study. You can choose whether or not you will participate in this research study. However in order to participate you must sign this consent, including this authorization to use the following protected health information:

- a) Name
- b) Address
- c) Phone Number
- d) Birth date
- e) Contact Person's name, address, phone number, and birth date.
- f) Family medical history
- g) Allergies
- h) Current or past medications or therapies
- i) Prior medical history
- j) Results of laboratory, radiologic or pathologic tests
- k) Results of physical examination
- l) Results from outside previous clinical evaluations
- m) Medical Record Number(s)

In addition to your protected health information located at the University of Utah, we may want to request the above listed test results previously performed at another institution. In order to request this information, we would have you sign a separate consent called "Medical Release of Information".

Others who will have access to your information for this research project are the University's Institutional Review Board (the committee that oversees research studying people and authorized members of the University's workforce who need the information to perform their duties (for example: to provide treatment, to ensure integrity of the research, and for accounting or billing matters).

In conducting this study, we may share your information with groups outside the University of Utah Health Sciences Center. The information we share may include information that directly identifies you. These are the groups:

- Other local hospital(s) that we are working with, including Primary Children's Medical Center, or Shiner's Hospital. Co-investigators who are University of Utah faculty also see and enroll patients from these sites, and are working with the investigators in these



- studies;
- Other academic research centers we are working with: Ohio State University, Washington University (St. Louis), University of Iowa, Cincinnati Children's Hospital, Children's Hospital of Philadelphia, and University of Minnesota who are working with the investigators in studying the mechanisms of disease due to dystrophin mutations;
  - The National Institute of Neurologic Disorders and Stroke, part of the National Institutes of Health, a federal agency that needs to confirm the accuracy of the results submitted to the government.

Information disclosed to groups outside the **University of Utah Health Sciences Center, Primary Children's Medical Center, Shriners Hospital** may no longer be covered by the federal privacy protections.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health (NIH). 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 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 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. No voluntary disclosure of your information will be made.

You may revoke this authorization. **This must be done in writing.** You must either give your revocation in person to the Principal Investigator or the Principal Investigator's staff, or mail it to: Kevin Flanigan, MD, University of Utah Health Sciences Center, Department of Neurology, 3R210 SOM, 30 N 1900 E, Salt Lake City, UT 84132-2305.

If you revoke this authorization, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

You have a right to information used to make decisions about your health care. However, your information from this study will not be available during the study; it will be available after the study is finished. This authorization does not have an expiration date. After you sign this, you will be given a copy with your signature.

**Consent**

I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I will be given a signed copy of the consent and authorization form to keep.

**I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.**

\_\_\_\_\_  
Participant's Name

\_\_\_\_\_  
Participant's Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of Person Obtaining  
Authorization and Consent

\_\_\_\_\_  
Signature of Person Obtaining  
Authorization and Consent

\_\_\_\_\_  
Date

**If the participant is unable to give consent and authorization, consent and authorization is given by the following authorized personal representative of the individual:**

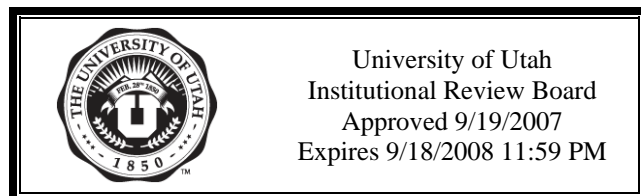
\_\_\_\_\_  
Name of Authorized Personal  
Representative

\_\_\_\_\_  
Signature of Authorized Personal  
Representative

\_\_\_\_\_  
Date

If the participant is unable to give authorization and consent, indicate the legal representative's authority to act for the individual:

- Spouse
- Adult (18 years of age or over) for his or her parent
- Individual with power of attorney
- Guardian appointed to make medical decisions for individuals who are incapacitated



\_\_\_\_\_  
Birth date of the Participant

\_\_\_\_\_  
Sex (M or F)

Ethnic Background (please check one):

Caucasian

American Indian /Alaska Native

Asian or Pacific Islander

Hispanic

African American

I do not wish to provide this information.

