UNIVERSITY OF WASHINGTON
Adult CONSENT FORM
Investigations of FSHD and Other Neuromuscular Disorders Study

Researchers:

Joel Chamberlain, PhD	Research Assistant Prof.	Medical Genetics	206-221-4579
Leo H. Wang, MD, PhD	Assistant Professor	Dept. of Neurology	206-598-6190
Susan Strom, MPH	Research Coordinator	Dept of Neurology	206-685-2028

24-hour emergency Telephone Number: call paging operator at 206-598-6190

and ask to have Dr. Wang paged.

Researchers' statement

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called "informed consent." We will give you a copy of this form for your records.

We are asking you to take part in the study because (check one):

☐ You have been diagnosed genetically with facioscapulohumeral dystrophy (FSHD) or other muscle dystrophy.

☐ You are enrolling as a comparison participant who does not have FSHD.

PURPOSE OF THE STUDY

Facioscapulohumeral dystrophy is the third most common muscular dystrophy after Duchenne muscular dystrophy and Myotonic dystrophy. FSHD occurs in about 1 out of every 15,000-20,000 people. The age at which FSHD begins varies from at birth to late life with 95% of patients manifesting weakness by age 20. The disease typically begins with weakness of muscles of face and upper arm with protrusion of shoulder blade, followed by weakness of upward movement of foot and hip muscles. FSHD may involve each side of the body differently. The muscles responsible for speech, swallowing, eye movements and respiration tend to be spared. The disease leaves about 20% of affected patients wheelchair bound and 1% with respiratory weakness. Unfortunately, at the present time there is no effective treatment for FSHD.

We know that genetics play a role in FSHD and a number of gene variants (changes) have been identified that affect muscles disorders. Genes are part of your DNA that mostly control the production of proteins. RNA (a molecule similar to DNA) carries the instructions on how to make the proteins. In this research we will be looking at the proteins that cause FSHD and other muscle disorders and how the proteins are made by genes. To move forward with research concerning this disease, we want to identify and develop diagnostic biomarkers and understand how inheritance contributes to disease. Biomarkers are observable, objective, and measurable

characteristics of biological products, such as proteins, that can function as predictors of disease. Identifying these predictors of disease is an aim of this study.

This is an observational study only; there is no drug being tested. We expect to enroll up to 20 total participants both with ("cases") and without ("controls") muscle disorders. The muscle sample will be frozen and transferred to Dr. Joel Chamberlain's Laboratory at the University of Washington, and blood samples will be collected for use in this study and in future studies.

STUDY PROCEDURES

Consent Process

The consent process will be done either by mail or in person. Please take some time to carefully read this consent form. When you are done, and all questions have been answered to your satisfaction and you wish to proceed with the study, we will ask you to sign this consent form. Then mail or give it to the research coordinator. The consent form will also be signed by one of the researchers, and you will receive a copy that is mailed/given to you. No study procedures will take place until the consent form is signed by both you and the research coordinator. You are free to refuse anything asked of you and can stop participation at any time.

Allow the Review of Your Medical Records

You will be asked to sign a release of your medical records form at the time of consent, in compliance with HIPAA standards. We will do a thorough review of your records to ensure you meet all qualifications for this study. If you enroll in the study, we will keep a copy of your medical records filed with your research documents. If you do not meet study criteria, those records will be destroyed, We may need to ask you to sign a new Release of Medical Records form.

Once you are determined to be eligible to join this study, and you want to continue, we will make an appointment with you to conduct the following study visit procedures at the University of Washington Medical Center (UWMC) Clinical Research Center (CRC) on 7 South. Directions to the CRC will be given to you.

Clinical Assessments The following procedures will take about 2 to 3 hours to complete.

At the initial study visit we will perform the following clinical assessments:
Clinical Severity Score (CSS): This is a standard clinical severity scale that assesses the extent of weakness in various body regions that can describe the level and progression of muscle weakness.
Quantitative strength testing: You will be asked to squeeze a hand-held myometer; an instrument that measures muscle contraction strength.
Manual muscle testing: You will be asked to use specific muscles to resist against manual pressure or gravity as a measure of muscle strength.

Data Collection: We will ask you for contact and demographic information, create a family tree (pedigree) focusing on relatives that also have muscle disorders and/or inherited disorders, and your medical history information. You are free to decline answering any question we ask.

Sample Collection:
We will collect no more than 90 ml (about 6 tablespoons) of blood from a vein in your arm. The blood will be used for the following tests:

- PT/PTT: to check that your blood is clotting normally
- CBC: complete blood cell count to check the numbers of blood cells as a general indication of health
- Blood sample for serum extraction to look for proteins and other biomarkers, and plasma extraction to bank (store) for future genetic testing.

Muscle Biopsy
At the initial study visit you will undergo one needle muscle biopsy performed by Dr. Leo Wang, MD. Muscle biopsies will be obtained from FSHD subjects as well as from unaffected control subjects. We will evaluate several possible areas for the biopsy, but muscle sample will only be taken from one area in your upper arm or leg. It will take about 15-20 minutes to complete the muscle biopsy. The chosen area will be cleaned and draped and Lidocaine (a local anesthetic) will be injected to numb the skin and muscle. Lidocaine will sting briefly when it is injected. About a ¼ inch incision will made to allow a hollow needle to withdraw small pieces of muscle about the size of the letter "o" in this sentence. After the procedure, pressure will be applied for about 10 minutes to minimize bleeding. We will use Derma bond (skin glue) instead of stitches to close the wound and wrap the area with an Ace bandage. Dr. Wang may ask you to remain lying down for up to 20 minutes before leaving. Some pain or discomfort may occur after the Lidocaine wears off that can be treated with an over-the-counter pain reliever. A small scar may be visible. We will extract biomarkers (proteins) from your muscle tissue and study how proteins affect weakness in the muscle.

Safety Assessments
Your medical history will be reviewed, as well as your vital signs taken at the study visit. Blood tests (as described above) will be obtained prior to the biopsy to reduce the risk of bleeding. Following the muscle biopsy procedure, Dr. Wang may ask you to remain in lying position with leg/arm elevated for about 20 minutes to avoid bleeding. The research coordinator will call you the following day to check and make sure that there are no problems or concerns with the biopsy site.

Genetic Testing Now and In The Future
For this study we want to understand how improper "gene expression" can lead to an inherited disease. When a gene "expresses" properly, it makes a useful product (usually proteins) to keep the body healthy. When an "expression" is flawed it can cause a disease or defect. We want to investigate the genetic mechanism (RNA expression) and the protein produced associated with FSDH and other inherited diseases.
We also want to be able to use your sample and data in future genetic research that we cannot fully describe today. Future research may include broad sharing of your samples and data. It is possible research samples and data collected today will be important for productive discovery for any inherited conditions. No direct benefit can be promised from any future research, though some people might find satisfaction in contributing to scientific knowledge about genetic problems and medical conditions. We will ask you at the end of the consent if we can use your coded samples and data in the future for broad sharing with other qualified researchers for inherited disease research. Future genetic studies may include the exome; all the protein coding

regions of your DNA or the whole genome; the entire portion of the DNA that includes all genes (and also areas that are not genes).

dbGaP (database for Genotype and Phenotype) and other Health Databases
In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that collect the results of whole genome studies. The NIH and other data banks will store your genetic information and give it to other qualified researchers to do more studies. Qualified researchers that can access the national databases can be from the government, academic, or commercial institutions. We do not think that there will be further risks to your privacy and confidentiality by sharing your whole genome analysis with these databanks; however, we cannot predict how genetic information will be used in the future. Your information may be submitted to unrestricted databases. The information will be sent with only a code number attached. Your name and other identifiable information will never be given to them. There are many safeguards in place to protect your information while it is stored in repositories and used for research.

There is a small chance that your genetic information could be shared with others by mistake. In the unlikely event that your information was mistakenly shared and if it were linked with a medical condition, this could affect your ability to get or keep some kinds of insurance. There is also the risk that data could be released to the public, employers, or law enforcement agencies. If family members were to see this information it could also affect them. This could hurt family relationships. It is possible that you could be identified from the sample if someone has another sample from you. The two samples could be matched to identify you from the sample given for this study.

You will not receive any results from allowing your data to be placed in the national databases unless it is considered medically relevant.
You can withdraw your consent at any time you don't want your data in the national databases. There will be no consequences for withdrawing consent. However, data that has already been sent to researchers cannot be retrieved from those researchers.

RISKS, STRESS, OR DISCOMFORT

Blood Draw: minor pain, bruising and/or infection may occur at the site of the blood draw. The blood draw may cause light-headedness.

Muscle Strength Testing: muscle soreness may last one or two days.

Muscle Biopsy: Lidocaine sting at injection, bruising and transient pain in the area of the biopsy are expected. You may experience bleeding, infection and numbness if the nerve is touched by the needle. If numbness occurs, it usually resolves within several weeks. Rarely, a person might be allergic to Lidocaine with reactions ranging from mild skin rash to anaphylactic shock. Pain or discomfort at the biopsy site may persist for several days.

Precautions: You should avoid getting the biopsy site wet. Cover wound with plastic when taking a shower and do not immerse the area in a tub for 24 hours. Avoid swimming in a pool for about 7 days after the procedure.

Risk of breach of confidentiality: It is possible for a privacy breach if it becomes known of your participation in this research or if your identity is discovered in future research.

Return of Research Results. We will not return any research results in this study to you as they are not informative to your medical care. If we should discover information that is medically important to you, we will do our best to contact you.

Protection Against Risks

We will make every effort to keep your research and medical records secured against unauthorized access, but this cannot be guaranteed. All subject data will be de-identified and coded with a unique study subject number. The link between study subject number and identifying information will be kept separate from data in a locked file and/or password protected computer file. Sharing databases only use coded IDs and have strict data security measures in place.

Procedures will be performed according to standard accepted techniques. All subjects will be monitored closely by staff during and after the procedure. You will be asked to report any continuing discomfort caused by the blood draw and muscle biopsy procedures. We will call you within 24 hours after the muscle biopsy procedure to inquire about any concerns related to the muscle biopsy site. You should call us if the area appears to be infected or painful. The researcher will treat patients having adverse experiences appropriately and observe them at suitable intervals until the experiences resolve. You may contact Dr. Wang if you experience any study-related injury, illness or distress by calling 206-598-6190 and asking to have Dr. Wang paged.

Blood and Tissue Storage

Your blood, tissues and collected information will be used for investigations to understand the mechanisms that cause FSHD and other inherited disorders for an indefinite amount of time. With your permission, we may share your samples and information with other qualified investigators studying FSHD and a wide variety of inherited disorders.

ALTERNATIVES TO TAKING PART IN THIS STUDY

You may elect not to participate in this study without risking the loss of present or future care available at the University of Washington.

BENEFITS OF THE STUDY

There are no direct benefits to you for participating in this study. The potential benefit to the population of individuals with FSHD is that a successful investigation may result in the development of disease specific biomarkers that can be used to monitor a patient's status, disease progression and response to interventions over time. These tools could be used to measure effectiveness of investigational agents used in future clinical trials.

SOURCE OF FUNDING

The study team and/or the University of Washington are receiving financial support for this study from Friends of FSH Research, a local non-profit charity.

CONFIDENTIALITY OF RESEARCH INFORMATION

Your research information collected for this study will be kept confidentially, meaning that study information will be labeled with a coded number only. Your name and other identifying information will not be associated with your data or sample. The code linking your identity to

your study information will be kept locked in a file and stored in a password protected computer file. It will be kept indefinitely.

All of the information you provide will be confidential. However, if we learn that you intend to harm yourself or others, we must report that to the authorities.

Government or university staff sometimes review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

Your participation in this study will be noted in your UW medical record. If you do not already have a UW medical record, one will be created for you.

OTHER INFORMATION

Taking part in this study is voluntary. You may refuse to participate and you are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. You can remove your samples and data from this study by contacting Dr. Joel Chamberlain, PhD at 206-221-4579. However, any samples or data that have already been shared cannot be retrieved.

If you do not already have one, a UWMC medical record will be created for you. Your participation in this research study will be noted in your medical record. The CRC staff will record the muscle biopsy procedures in your medical record. They will also record any event that happens on the CRC that requires treatment (such as fainting during a blood draw).

You will be provided a stipend of $200 for participating in this research biopsy. The University of Washington requires us to record your social security number for all stipends over $50.

Results of this research may lead to the development of a commercial product. You will not have any financial ownership or claim to the product as a result of your research participation.

RESEARCH-RELATED INJURY

If you think you have a medical problem or illness related to this research, contact Dr. Wang right away. You may reach Dr. Wang by calling 206-685-2028 and asking the operator to have him paged. You may call this number 24 hours per day. He will treat you or refer you for treatment.

You may also contact the research coordinator, Susan Strom, at 206-685-2028 during regular business hours. If you reach a recording, please leave a message. It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study.

If you are injured as a result of being in this study, necessary medical treatment will be offered at a UW Medicine facility. The costs of the treatment may be billed to you or your health insurance just like other medical costs, or it may be covered by the UW's discretionary Human Subjects Assistance Program (HSAP), depending on a number of factors. The researcher may request HSAP coverage by following established procedures. If you wish to request HSAP coverage yourself, contact the researcher or the UW Human Subjects Division at hsdinfo@uw.edu or 206-543-0098. Ask the researcher if you would like information about the limits and conditions of the HSAP. The UW does not normally provide any other form of compensation for injury. However,

the law may allow you to seek payment for injury-related expenses if they are caused by malpractice or the fault of the researchers. You do not waive any right to seek payment by signing this consent form. We will bill your health insurance for treating problems that result from your *muscle disorder* or from standard clinical care. If you have no health insurance or your insurance refuses to pay, we will bill you.
A medical record will be created for your subjects at UW Medicine and CRC staff may need to access those medical records for you. This may be because they are performing procedures or collecting data for you. It may also be required if an event happens on the CRC that requires treatment (such as fainting during a blood draw).

Printed name of study staff obtaining consent Signature Date

Subject's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research subject, I can call the Human Subjects Division at (206) 543-0098. I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

Printed name of subject Signature of subject Date

Please put your ***initials*** in the boxes below to indicate your agreement.

- ☐ You may use my coded samples and data for future research on inherited muscle disorders.
- ☐ You may use or share my coded samples and data with researchers working on future investigations on any inherited disorder.
- ☐ You may share by coded data in health databases such as dbGaP.
- ☐ In general, participants do not receive any individual results from future research conducted with information placed in the NIH data banks, but in rare circumstances researchers may find something that may be of medical importance. If this happens, I want to receive these results.
- ☐ You may contact me regarding on future research projects which may include asking my permission to contact my relatives. I am under no obligation to participate or agree to any request.
- ☐ You may **NOT use my data or sample** for any other research.

Copies to: Researcher
Subject