UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM to Participate in Research, and AUTHORIZATION to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position:_____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant:

_____

2. What is the title of this research study?

Measurement of Frataxin mRNA in NHP and Human Biofluids

3. Whom do you call if you have questions about this Research Study?

Principal Investigator: S H Subramony M.D.
Office phone number: 352 733 3032

Research Coordinator: Deborah Morrison
Office phone number: 352-273-5189

4. Who is paying for this Research Study?

The sponsors of this study are **the UF Center for NeuroGenetics** and the Friedreich's Ataxia Research Alliance (FARA).

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research? How long will you be involved?

The purpose of this research study is to determine a way to measure frataxin messenger RNA (mRNA) in fluids such as blood and cerebrospinal fluid (CSF) from patients like you with Friedreich's ataxia (FRDA). FRDA is caused by abnormality (mutation) in the frataxin gene. Genes function by producing a copy of itself called messenger RNA (mRNA) which then directs the production of the related protein. The mutation in FRDA decreases its ability to make enough of its mRNA and in turn, its ability to make enough of the protein frataxin, thus leading to the disease. Treatments being developed for FRDA have the ability increase frataxin levels including in brain where it is needed. Currently, there is no accepted way to measure frataxin protein or the messenger RNA (from which the protein is made) in the spinal fluid that surrounds the brain and this will be important to do so when a therapy is expected to increase frataxin in the brain. In our study, we aim to measure frataxin mRNA in both the blood and CSF. We have developed new methods to measure frataxin mRNA produced in brain tissue by using both spinal fluid and blood. Our method relies on the idea that mRNA from the brain, such as the frataxin mRNA, is packed into small bubbles or vesicles that then enter the spinal fluid and blood. We are able to detect frataxin mRNA in these bubbles in CSF from patients with other illnesses and from healthy participants. The current project will measure frataxin mRNA from spinal fluid and blood of FRDA patients and assess whether the frataxin mRNA in the CSF or blood of FRDA patients can serve as a measure of frataxin production in the brain. If successful, this will provide an important tool to monitor treatments for FRDA that aim to increase frataxin production.

Your participation will include 2 visits.

b) What is involved with your participation, and what are the procedures to be followed in the research?

Your participation will involve 2 visits. Visit one can happen during a routine clinic visit or visit for another study, and will be used to get informed consent for this study. This visit may also be arranged remotely via Zoom in which case we will email you copy of the informed consent beforehand via DocuSign. We will explain the consent document during visit 1 and if you agree to participate, ask you to sign the consent. We will provide a copy of the consent to you. If this is done via Zoom, you will email the signed consent back to us and we will then provide a copy to you after we have signed . Once the consent has been obtained, we will ask you to obtain blood tests here at the Shands Medical Lab lab to make sure that you have a good blood clotting mechanism. Visit 2 will be scheduled and you will have your procedures done at that visit. During visit 2, we will collect brief clinical data such as your medical history and basic demographic information. We will assess the severity of your Friedreich's Ataxia. We will perform a physical and neurological examination. This information will be used to examine the relationship of findings from your spinal fluid and blood to the status of your disease.

A pregnancy test will be administered if you are a woman of childbearing potential before continuing the visit. A negative test is required to continue with the study procedures.

To collect CSF, a spinal tap will be done on you in the "interventional radiology (IR) suite" in the Shands (Neuromedicine) hospital. This procedure will be done by trained medical staff. Local anesthesia will be used to numb the site of injection on your back. We plan to collect about 15 milliliters or 1 tablespoon of

spinal fluid. In addition to CSF, a sample of blood (approximately 5-10 milliliters or 1-2 teaspoonfuls) will be collected.

c) What are the likely risks or discomforts to you?

Collection of the clinical data poses minimal risk such as the discomfort of a physical and neurological examination, and the risk for falls during the examination. Blood sample collection is associated with pain in the region. Rarely, some excessive bleeding may occur including blood collection under the skin (hematoma) that may need compression and local pain relief. There is a remote possibility of an infection being introduced into your blood.

Spinal tap and spinal fluid collection can be associated with some discomfort in your back both during the procedure and for a few hours afterward. This will lessen over a day or so. Some persons experience a “spinal headache” for a day to two after the procedure. This can be a bad head and neck pain, aggravated by sitting or standing and may be associated with nausea and rarely vomiting and dizziness. The investigators will ask you to rest as much as possible in bed for a day and be well hydrated, procedures that lessen the chances of a spinal headache.

Rare risks of spinal tap include bleeding at the site or around the spinal sac and introduction of an infection into the spinal fluid. These are extremely rare.

The study investigator is an experienced neurologist who can provide care if any side effects happen.

Study team members will take appropriate steps to protect any medical, genetic, and private health information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you. This consent form outlines the information that will be collected, used, protected, and shared.

d) What are the likely benefits to you or to others from the research?

There is no direct benefit to you for participating in this study. Our goal is to increase knowledge that may be helpful to people with Friedreich’s ataxia in the future.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

There are no alternative procedures or courses of treatment for this study except to continue your regularly scheduled clinical visits to the ataxia clinic.

Additional and more detailed information is provided within the remainder of this Informed Consent form. Please read before deciding if you wish to participate in this study.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

You will continue to receive routine medical care for your medical condition from your regular physician(s) while you are in the study. If you decide not to participate in this study, it will not affect your clinical care.

7. What will be done only because you are in this Research Study?

Overview of the Study

Participants will complete the study during 2 visits (visit 1 and 2). Visit 1 can be combined with a routine clinic visit for care or research but also may be done remotely via Zoom. During visit 1, the investigators will fully explain the study and obtain your informed consent. For remote visits, a copy of the consent will be emailed to you before the visit and the study team will schedule a time to discuss the consent. The informed consent will be reviewed in detail with you and you will have an opportunity to ask any questions before signing the document and agreeing to the study. In either case, once you agree to the study after being fully informed, you will sign the consent document and a copy of it will be provided to you after the investigator signs it.

Once informed consent has been obtained, you will be asked to obtain lab work to test your blood for its ability to clot well. This lab work will be reviewed before visit 2. Visit 2 will take several hours (less than 6 to 8 hours) and will involve collection of clinical data, collection of a blood sample and then collection of spinal fluid.

Description of Study Procedures

Blood Work prior to scheduled visit (~30 minutes)

- You will need to go to one of the UF Health's local labs in Gainesville, FL to have blood work done before the scheduled visit. This blood work will ensure you meet the inclusion criteria before the spinal tap.

Overall health and safety assessment (~30 minutes)

- Your birthdate, gender, contact information, health history, current medications, and allergies will be obtained. The information will be stored in your study file.
- If you are a woman of childbearing potential, your urine sample will be tested to see if you are pregnant. If the test is positive, you will not be able to continue in the study.
- Your FRDA DNA test from your medical record will be assessed and a copy placed in the research folder. No additional genetic testing will be performed.
- Measurements such as your height, weight, blood pressure, pulse, respiratory rate, and temperature will be obtained.
- A general physical examination will be done by the study physician.

Neurological examination, mFARS, and blood sample (~30 minutes)

- The study physician will perform a neurological examination and use this to rate your ataxia severity in the mFARS scale.
- This will include examining your eye movements, speech, strength of your muscles, sensation, coordination in your arms and legs and ability to stand and walk among other things.
- We will ask you questions regarding your activities of daily living for a questionnaire called FRDA activities of daily living scale (FARS ADL).
- A blood sample of approximately 5-10 milliliters (or 1-2 teaspoonfuls) will be obtained.

Spinal Tap (~3 hours)

- About 15 milliliters or 1 tablespoon of cerebrospinal fluid (CSF) will be collected though a test called a spinal tap.
- The spinal tap will be performed in the interventional radiology suite at the Neuromuscular hospital via x-ray fluoroscopy.
- This procedure uses X-ray (fluoroscopy) to visualize your low back spine so that the spinal tap needle can be placed in the spinal sac in your low back under visual guidance. This can minimize discomfort and can help increase the success of the procedure in one attempt.
- You will be given local anesthesia to numb the area before collection.
- You will be asked to relax while laying down following the procedure for 1 to 2 hours before leaving.

If any identifiable information was collected as part of this research, it is possible that your research information, **with all personally identifiable information removed**, could be used for future research studies, or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 3 of this form.

8. What identifiable health information will be collected about you and how will it be used?

The research team will collect demographic information, medical history, physical examination findings, neurological clinical information, and genetic test results.

The research team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals, or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The research team listed in question 3 above will use or share your health information as described below to carry out this research study.

9. With whom will this health information be shared?

This health information may be shared with:

- The study sponsors (listed in Question 4 of this form);
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- Government agencies which are responsible for overseeing public health concerns, such as the Centers for Disease Control and federal, state, and local health departments;
- The IRB that reviewed this Research Study and who ensures your rights as a study participant are protected.

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

Your total duration in this study is approximately 2 separate days. This will include visit 1 for obtaining informed consent and visit 2 for performing all the research tests.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

Up to 14 participants will be screened to allow for failed screening, but only 10 people are expected to complete this study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

- Some of the clinical examination tasks you will be asked to complete may be uncomfortable and may carry the risk of falling due to your illness.
- The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure.
- Spinal tap and spinal fluid collection can be associated with some discomfort in your back both during the procedure and for a few hours afterward. This will lessen over a day or so. Some persons experience a “spinal headache” for a day to two after the procedure. This can be a bad head and neck pain, aggravated by sitting or standing and may be associated with nausea and rarely vomiting and dizziness. The investigators will ask you to rest as much as possible in bed for a day and be well hydrated, procedures that lessen the chances of a spinal headache.

- Rare risks of spinal tap include bleeding at the site or around the spinal sac and introduction of an infection into the spinal fluid. These are extremely rare.
- If you take part in this research, you will have one medical imaging study which use radiation. The tests you will have include one fluoroscopic spinal tap. The estimated effective dose equivalent from this procedure is 0.3 mSv. To give you an idea about how much radiation you will get, we will make a comparison with an everyday situation. Everyone receives a small amount of unavoidable radiation each year. Some of this radiation comes from space and some from naturally occurring radioactive forms of water and minerals. This research would give your body the equivalent of approximately 1 extra month worth of this natural radiation. The radiation dose we have discussed is what you will receive from this study only and does not include any exposure you may have received or will receive from other tests. Collection of your personal medical history may produce some discomfort. There is a slight risk that information about you could be revealed inappropriately or accidentally during the study.
- Release of medical information could result in a potential loss of privacy. There is a small chance that some research may yield results that will have a negative impact on participants, family members, other individuals, or groups. This impact may include the ability to be insured or employed or changes in family relationships. A Federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer.
- There are also risks related to invasion of privacy and breach of confidentiality. We will remove your name and any other identifying information that could directly identify you from your study information and/or blood sample and replace it with a participant code. Only a few study team members at the University of Florida will have access to the link between your code number and your study and personal information. Other investigators and study team members will only have access to coded information. When the results of the study are announced, they will not include information that can personally identify you.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

There are no direct benefits that you can expect to receive as a result of participating in this study.

13b. How could others possibly benefit from this Research Study?

While you will not benefit directly from participating in this study, your participation will help researchers identify a possible method for measuring frataxin released from the brain which can be useful in future treatment trials.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

14. What other choices do you have if you do not want to be in this study?

Taking part in this study is voluntary. You are free not to take part for any reason. If you decide not to be part of this study, tell the Principal Investigator and do not sign this consent form.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- If you do not keep appointments for the study visits or fail to complete study activities.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

No, there will be no additional costs to you or your health plan as a result of your participation in this study. The sponsor will pay for all protocol-required health care costs related to your participation. There may be costs associated with the healthcare you receive while you are participating in this study, but these services are considered to be conventional care that you would have received even if you chose not to participate in this study. There will be no additional costs to your or your health plan just because you are in this study.

If you receive any healthcare at UF Health that is not related to this study, this care will be billed as usual. If you feel you have received a bill related to this study in error, please contact the Principal Investigator.

17. Will you be paid for taking part in this Research Study?

You will be compensated with a pre-paid debit card in the amount of $200.00 for your completion in this study. For participants that may require an overnight stay, hotel accommodations will be provided at the discretion of the PI. We will reimburse hotel costs up to $300.00. You will be required to send the hotel receipt, and these funds will be added to the debit card. Payment will be managed through the UF Research Participant Program.

If you are paid more than $199 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. Payments to nonresident aliens must be processed through the University of Florida Payroll and Tax Services department. If the payments total $600 or more in a calendar year, the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

Your payment for participation in this research study is handled through the University of Florida's Research Participant Payments (RPP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (RPP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

If you have any problems regarding your payment contact the study coordinator.

18. What if you are injured while in this Research Study?

It is important that you promptly tell any member of the research team if you experience an injury or have questions about any discomforts that you experience while participating in this study.

If you are injured while you are participating in this study, the cost of the diagnosis and/or treatment may be covered by the University of Florida or the study sponsor or billed to you or your insurer just like other medical cost, depending on a number of factors, such as if the injury was the result of the study intervention, or the way in which the study was conducted.

The University of Florida and the study sponsor do not normally provide any other form of compensation for injury. The principal investigator and others involved in the study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact Dr. Subramony at (352)-733-3032 if you experience an injury or have questions about any discomforts that you experience while participating in this study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing Date