Research Consent Form

Title of Study: Nonalcoholic steatohepatitis liver disease genome atlas
Principal Investigator: Joseph Grzymski, PhD
Co-Investigators: Gai Elhanan, MD; Karen Schlauch, PhD; Jim Metcalf; Robert Read
Study contact: Shaun Dabe; Toni Curreri
Study ID Number: 2002004220
Sponsor: Gilead Sciences

Introduction

You are being invited to participate in a research study conducted by the Renown Institute for Health Innovation (RIHI) and its partner Desert Research Institute (DRI) in conjunction with participation in the Healthy Nevada Project. This is an observational study trying to understand genetic links to Nonalcoholic steatohepatitis or NASH. Before you agree to be in the study, please read this form carefully. It explains why we are performing the study; what you must do to participate in the study; what personal information, including genetic information and protected healthcare information, you agree to share as a participant in the study, and other important information you need to know.

At any time, you may ask us to explain anything about the study that you do not understand.

You do not have to participate in this study; your participation is voluntary. If you agree now but change your mind, you will need to contact us to withdraw and we can explain to you what happens with the information you agreed to share when you withdraw.

Why are we performing this study?

We are performing this study to understand the relationship between genes and a liver disease Nonalcoholic steatohepatitis or NASH; for which there is no current FDA approved therapy. Specifically, we want to understand whether specific germline mutations in genes are more prevalent in people with NASH. We also want to understand whether specific germline mutations in genes are more prevalent in people who are possibly resistant to NASH. We hypothesize that certain germline mutations are more prevalent in NASH cases and perhaps this knowledge can be used in developing better therapies or in risk mitigation of the disease. In other words, we believe that participants with specific mutations (differences) in liver-related-genes may have increased risk for disease. We want to test this hypothesis. For this study, we want to understand the relationships between germline mutations and NASH.

We will ask you to participate by granting us access to your medical information which will be used in a de-identified study. De-identified information in your medical record, such as blood tests or imaging tests, will be used to study NASH, along with your de-identified genetic information from the Healthy Nevada Project. Some participants may be asked to provide a blood sample or undergo imaging tests so that information can be used for this research. All of

the information we collect will be stored in a database as de-identified information. This means that the information and data you supply to this study will be separated from your name, and anything else that can associate the data to you. Your data will appear as a random participant number. The data will be used to look for patterns and other statistically relevant information that may be beneficial in predicting, planning for, and possibly developing therapies for NASH.

In addition, the de-identified information in the joint genetic and health information database will be made available for other research projects and to researchers outside of the Renown Institute for Health Innovation as approved by the investigators, including for commercial or for-profit purposes. For example, the information will be available for any research question, such as research to understand health outcomes based on exposures, development of new scientific methods, and development of new treatments for certain diseases. Your identity, nor any ways of associating you with your data, will never be shared.

Why are we asking you to be in this study?

A. We are asking you to consider being a part of this study because you participated in the Healthy Nevada Project (HNP), agreed to be contacted for other studies resulting from the HNP, and meet certain criteria for the Nonalcoholic steatohepatitis liver disease genome atlas study.

B. We are asking you to consider being a part of this study because you meet certain criteria for the Nonalcoholic steatohepatitis (NASH) liver disease genome atlas study. There are currently no accepted FDA approved drugs to treat NASH and we need volunteers at various risk for the disease to develop new treatments.

How many people will be in this study?

We expect to enroll approximately 55,000 participants across the geographic area of Northern Nevada.

What will you be asked to do if you agree to be in the study?

If you have not participated in the Healthy Nevada Project, you will be asked to join as an inclusion criteria for participation in this study. The Healthy Nevada Project is a clinical research study that provides de-identified genetic data that can be used for research using a small saliva sample. You will be asked to go through the consent process for the Healthy Nevada Project if you are not already enrolled in the project.

As a participant in this study, you will be asked to allow us access to your medical information to be used in a de-identified data set for research and development, and associate that information with your de-identified genetic information in our joint genetic and health information database. You may be periodically contacted via email or web survey by RIHI and asked to answer questions or surveys that will provide important additional data points that will be used as part of the research. You may also be periodically contacted via email with important

information, such as new research developments, insights or opportunities being offered to participants.

You may also be asked to provide a blood sample which will be used in an enhanced liver fibrosis (ELF) test or similar diagnostic test. Not all participants will be asked to provide a blood sample. If you are asked to provide a blood sample, that can be done at your convenience or when you have a regularly scheduled blood draw during your normal course of care. You will need to have your blood drawn by a certified phlebotomist, which will only take a few minutes to collect, and allow the sample to be shipped to a certified laboratory for analysis and the results from the test to be entered into your medical record.

Some participants may also be asked to have an imaging test performed, such as elastography or liver elastography, that checks the liver for fibrosis. This test is performed using ultrasound, and is a completely non-invasive, painless procedure that takes approximately 10 minutes to complete. Not all participants will be asked to have this test, and if one is completed, the information will be entered into your medical record.

How long will you be in the study?

The study enrollment will take about 30 minutes of your time which includes the education, consent and registration process. The anticipated observation period of this study is approximately 7 years, but may vary depending on research goals. Once enrolled in this study, your participation will not take a lot of time. For the duration of this research study, you will be periodically contacted via email and asked to answer several questions providing additional relevant data, which will not take much time. You may also be periodically contacted via email with important information, such as new research developments, insights or opportunities being offered to participants. If you are asked to provide a blood sample, the sample collection can be done at your convenience and will not take a lot of time. Your de-identified genetic and health information will be stored indefinitely in a database for research use, as described under “Why are we performing this study?”.

What happens if you choose not to be in this research study?

If you decide not to be in the study, there is no other obligation.

What if you agree to be in the study now, but change your mind later?

You may withdraw from the study at any time by notifying the Principal Investigator of the study. The result of withdrawing from the study is that you will no longer receive any emails and have no obligation to answer those emails; your genetic results will be completely de-identified and we will have no way of contacting you if medical knowledge changes. However, any data collected will continue to be a part of the entire study genetic and health information database and will continue to be used by the researchers and may be used for future research. As the data are de-identified, the researchers will have no way to tie the data they are reviewing to you or any other individual study participant.

Is there any way being in this study could be bad for you?

Your participation in this study is voluntary and the risk is minimal. If you are asked to provide a blood sample, venipuncture has some risks. 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.

Risks from participating in the Healthy Nevada Project do not change by participating in this study.

Although the Renown Institute for Health Innovation nor the Desert Research Institute cannot provide a 100% guarantee that your data will be safe, they have strong policies and procedures in place to minimize the possibility of a data breach. In addition to the risks noted above, there may be additional risks to participation that are currently unforeseeable.

Will being in this study benefit you in any way?

Overall participation in this study is not intended to personally benefit you or your health. Aspects of the study regarding hypothesis-driven investigations will have no direct clinical benefit to you. If you are asked to provide a blood sample or have imaging performed, you will be provided with clinical diagnostic information from these tests. The results of the tests will be put in your medical record and will be available to your doctor to help direct your care.
The ELF test is a laboratory diagnostic test specific to liver function and the prediction of advanced fibrosis.

This study is designed to attempt to understand a disease for which there is no current FDA approved therapy. If this research helps lead to new approved therapies, it is possible you may benefit from those advancements.

Who will pay for the costs of your participation in this research study?

There is no cost to you associated with participation in this study. You will not receive a bill for any procedures, such as venipuncture, diagnostic or imaging tests, performed specifically for this study.

Will you be paid for being in this study?

You will not receive any cash payment for being this study.

If your information is used as part of or to create valuable products or services, there are no plans to pay you or give any compensation to you and your family.

Who will know that you are in in this study and who will have access to the information we collect about you?

The researchers who conduct the laboratory and statistical analyses do not have access to Registration Information (name, address, email address, user ID, and password) of participants.

Employees who interact with research participants have access to names and contact information of participants, but have no access to laboratory and statistical analyses. All employees are trained to work with human research participants. In addition, all researchers are trained to conduct research responsibly. This information will be used for research purposes and will be analyzed as de-identified data. We may also provide your de-identified data to other researchers conducting research projects in the future, as described under "Why are we performing this study?". Your doctor will have access to your diagnostic test results as described under "Will being in this study benefit you in any way".

How will we protect your private information and the information we collect about you?

We will treat your identity with professional standards of confidentiality and protect your private information to the extent allowed by law. The Renown Institute for Health Innovation and DRI have strong data privacy and security policies and procedures in place to protect your information and minimize the possibility of a data breach.

During the initial phases of the study, your de-identified genetic data and the results of your blood analysis will be provided to researchers. We will not provide the researchers with your name or other information that could identify you. Your name will not be used in any publications or reports that result from the study.

If other researchers request access to your data for use in future research, we will only provide your de-identified data.

Do the researchers have monetary interests tied to this study?

The researchers and/or their families have no direct financial interest in the study sponsor or its outcome.

Who can you contact if you have questions about the study?

At any time, if you have questions about this study, contact Joseph Grzymski, PhD (PI) 775-673-7478; Shaun Dabe (study contact) 775-982-6916 or Toni Curreri (study contact) 775-982-6914.

Agreement to be in study

We will give you a copy of this form to keep.

By signing your name below, you agree to be in this study and acknowledge and agree to the following:

1. You acknowledge that you have been given the opportunity to fully read this form and ask any questions.
2. You agree to fully participate in the registration, consent and education process to participate in the study.
3. You acknowledge that not all participants will be asked to provide a blood sample, and if asked, you authorize us to schedule an appointment for a blood draw to be collected by a certified phlebotomist and to ship the blood sample to a certified laboratory for an enhanced liver fibrosis (ELF) test or similar diagnostic test for liver function.
4. You agree that the results of this test, if performed, will be made available in your medical record to help guide your normal course of care.
5. You acknowledge that not all participants will be asked to have an imaging test performed, and if asked, you authorize us to schedule an appointment for the test to be completed and the results of that test to be entered into your medical record.
6. You authorize that your age, ethnicity, email, zip code and phone number may be used as part of the database for the study, which will be maintained and used for future research by DRI and other researchers with the approval of the study PI.
7. You agree to participate in the study by reasonably responding to email requests for additional data and allow such additional data to be used in the study.
8. You agree that the study team may contact you regarding future research opportunities.
9. All right and obligations herein may be transferred by DRI or RIHI to any successor organization.

_____
Participant's Name Printed

_____ _____
Signature of Participant Date

CONTACT INFORMATION

Email Address: _____

Date of Birth: _____

Home Phone: _____

Mobile Phone: _____

Zip Code: _____

Ethnicity: _____

Birth Gender: _____

Kit ID (use barcode scanner to enter): _____

☐ **I am at least 18 years old**