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: Alexa Anderson and Savanna Grime
Study ID Number: 2002004220
Sponsor: Gilead Sciences Inc.

Study Summary

You are invited to participate in a research sub-study of the Healthy Nevada Project (HNP), being conducted by Renown Institute for Health Innovation (RIHI) and sponsored by Gilead Sciences Inc. Please read our study summary and detailed study information carefully to learn what will be asked of you in the event you choose to participate in this study.

Eligibility: To be in this study, you must be a Renown Health patient who is already enrolled or enrolling in the Healthy Nevada Project (HNP). If you are unsure whether you meet these criteria, please contact the study team during normal business hours Monday – Friday by calling 775-982-6914.

Voluntary Participation: This research study is completely voluntary, and you may take as much time as needed in making a decision on whether to participate. Please feel free to consult with your health care providers or family before participating. You may consent to this study without the presence of our research staff and if you have any questions or concerns while reviewing this consent form, you may talk to a member of the study team anytime M-F during normal business hours by calling 775-982-6914. You may withdraw your consent at any time during the study and declining or stopping your participation will have no negative effects on you.

Study Purpose: We are conducting this research study to learn more about a type of liver disease called Non-Alcoholic Steatohepatitis (NASH) and how it relates to your human genetic data obtained through participation in the Healthy Nevada Project. This is an observational study trying to understand why some people develop NASH and some people do not.

Study Procedures: If you choose to participate in this study, you may be asked to volunteer for various clinical tests, such as an Enhanced Liver Fibrosis (ELF) test or imaging tests. These tests will be provided at no-cost to you and may be performed either along with your routine blood work, clinical procedures, or at dedicated research labs operated by Renown Health. Occasionally, it may be necessary to schedule a separate appointment with our research team

to complete the tests. The results of the tests will be placed into your medical record and available for you and your health care providers to review and use for your clinical care.

Study Data: Once a part of your medical record, test results may be used to drive clinical care and contribute to the study aims of understanding the influence genetics has on liver disease. All information gathered from your participation in this study, and the Healthy Nevada Project Study (7701703417) will be maintained in private databases and shared among approved researchers both internally, externally, and across the Helix Research Network (HRN) to perform studies over time. Your personal identifying information, such as name, birthdate, or contact information, will be removed from any data that is shared with researchers to protect your information and maintain your privacy. These data are studied in aggregate to help advance our understanding of NASH.

Benefits of Participating: This observational study is not designed to directly benefit you, however, if you are asked to volunteer for clinical tests, results of the tests offered by this study may benefit you through early detection of risks for liver fibrosis or liver disease. For example, the Enhanced Liver Fibrosis (ELF) test is an FDA approved blood test that returns a risk score for liver fibrosis or scarring of the liver. You would receive a risk score of low, moderate, or high risk for liver fibrosis and liver related problems. Knowing your risk score may help you and your provider take steps to lower your risk of liver disease if needed. Additionally, you may help contribute to our overall understanding of liver disease that could lead to the development of future tests, treatments and tools to improve how we care for patients in the future.

Risks of Participating: This study is considered to be minimal risk of harm. This means the risks of your participation in the research are similar in type or intensity to what you encounter during your daily activities or routine clinical care. Potential risks include the following:

- If chosen to provide a blood sample, there are risks associated with venipuncture.
- There are potential risks to your privacy. Despite RIHI and Helix having extensive policies and procedures in place to prevent a data breach, in the event of a breach, there is a chance that research data and health information could be compromised.
- If you receive results from any voluntary tests offered by the study, and those results indicate increased risk for disease, it may be important to follow up with your healthcare providers. You would be responsible for any follow up care following these tests, including the cost of additional testing or clinical visits that may not always be covered by insurance.

Rights and Confidentiality: The researchers and the University of Nevada, Reno will treat your identity and the information collected about you with professional standards of confidentiality and protect it to the extent allowed by law. You will not be personally identified in any reports or publications that may result from this study. The US Department of Health and Human Services, the University of Nevada, Reno Research Integrity Office, and the Institutional Review may look at your study records.

You may ask about your rights as a research participant. If you have questions, concerns, or complaints about this research, you may report them (anonymously if you so choose) by calling the University of Nevada, Reno Research Integrity Office at 775-327-2368.

You may also ask questions of the researchers by calling the study team at 775-982-6914 or by sending an email to RenownIHI@renown.org.

Thank you for your interest in participating in research. Please see below for detailed information regarding this study.

DETAILED CONSENT FORM AND STUDY INFORMATION

Introduction

You are being invited to participate in a research study conducted by the Renown Institute for Health Innovation (RIHI) 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 type of liver disease called Nonalcoholic steatohepatitis or NASH; for which there is no current FDA approved therapy. Specifically, we want to understand whether specific germline mutations (differences) 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 in liver-related-genes may have increased risk for disease. We want to test this hypothesis by examining the relationships between germline mutations and NASH.

How will my data be used and shared if I participate in this study?

For this study, our research study enrollment team is able to identify who has participated in the study. This enables us to recontact you for surveys and other study opportunities in the future. We share limited, identifiable information with our testing partners in order to connect you to your samples/tests. This enables us to return your testing results back to you and/or your healthcare providers as a clinical benefit and contact you if needed. Examples of information sent to our testing partners include:

- First name
- Last name
- Medical record number
- Date of birth
- Order date
- Other order-related information

Once your data is part of the medical record (such as results from genetic testing), it remains part of your record. It is subject to Renown's Medical Record policies and HIPAA.

If you choose to participate, your information will then be added to a private research database consisting of information from multiple sources and from thousands of participants. This data includes, but is not limited to, genetic information, medical record information, survey data, public health records, geologic data and environmental data. This research database will be protected by multiple layers of information security, including limiting who can access the data and maintaining encryption of the data. The database will be maintained indefinitely or until it no longer offers scientific value to the research community.

When a research dataset is created to be shared with researchers, we remove certain identifiable information from the data set and assign a random participant ID. Researchers examining the data do not have access to personally identifiable information. The study will always ensure your personal privacy.

Research data from the joint genetic and health information database, used by the research community at Renown Health, DRI and UNR, may be shared with one or more of the below entities to facilitate the goals of the research study.

- As approved by RIHI and for the purposes of this study on NASH or other similar liver conditions, research data will be shared with our sponsor Gilead Sciences Inc and other approved researchers. For example, the data will be available to researchers at Gilead who are seeking to understand what causes NASH or other similar liver conditions, for the development of new scientific methods, and development of new treatments for NASH or other similar liver conditions. No information that can identify you such as your name, date of birth, or contact information will be used or shared with researchers. RIHI will vet and approve all requests from outside researchers before providing them with access to data.

The information that RIHI uses to contact you, which is collected and validated during enrollment, is **NOT** shared with outside partners. That means that researchers outside of RIHI will **NOT** have access to your contact information and provides an added layer of protection.

If you withdraw from the study, your data used in previous datasets will remain and cannot be revoked. You will be removed from the research database, and any newly formulated datasets will not contain your data or information.

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) and agreed to be contacted for other studies resulting from the HNP.

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 go through the consent process and join as a requirement for participating in this study. The Healthy Nevada Project is a research study that sequences your DNA, shares genetic results with participants, and provides researchers with access to genetic data that can be used for research.

If you choose to participate in this sub-study, you may occasionally be contacted throughout the study to volunteer for various clinical tests, such as an Enhanced Liver Fibrosis (ELF) test, imaging tests, or similar diagnostic tests. These tests will be provided at no-cost to you and may be performed either along with your routine blood work, clinical procedures, or at designated labs or clinics operated by Renown Health. **Not all participants will be asked to undergo additional tests and enrollment in this study does not guarantee access to additional testing.**

If you are invited to have testing performed that requires a blood sample, you will need to have your blood drawn by certified phlebotomists or study coordinators with Renown Health, which will only take a few minutes to collect and can be performed at your convenience. Your samples will be shipped to certified laboratories for analysis and the results will be entered into your medical record. These results can then be used by you and your healthcare providers to help with your clinical care. The results of any such test would be used as part of the dataset for this study.

As the study progresses, 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. The results of any such test would be entered into your medical record and used as part of the dataset for this study.

As a part of your participation in the Healthy Nevada Project and this study, you affirm that your health record data (including results from this study) and genetic data obtained through the Healthy Nevada Project may be stored in a combined research database with the intent of generating research datasets to be used by researchers.

Lastly, 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 or other approved methods with important information, such as new research developments, insights or opportunities being offered to participants.

How long will you be in the study?

The anticipated observation period of this study is approximately 7 years and may vary depending on research goals. Your genetic and health information will be stored indefinitely in a database for future research use, as described under “How will my data be used and shared if I participate in 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 or other communication as part of the study. Any clinical results that have been entered into your medical record from participating in voluntary tests will remain a part of your health record per Renown’s Medical Record policies and HIPAA. Any information already converted to a research record that has been used and shared in previous datasets will remain, however, any newly formulated datasets will not contain your data or information.

What are the risks associated with being in this research study?

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 associated with drawing blood from a vein include discomfort, possible bruising and swelling, infection, or faintness.

If you volunteer for any clinical tests offered by this study, the results of those tests will be entered into your medical record to help with your overall healthcare. Some test results may indicate you could be at higher risk for disease, and you may choose to seek additional follow

up visits with your healthcare providers. Any follow up medical care resulting from tests offered by this study, but outside of the scope of the study, will be your responsibility, including the cost of additional testing or clinical visits that may not always be covered by insurance.

If you receive information that you may be at higher chance of developing a health problem due to something we discover from your sample, these results may be stressful for you and your family.

Risks from participating in the Healthy Nevada Project do not change by participating in this study, which includes the risks of having your genetic information analyzed and shared for research.

Renown Institute for Health Innovation and its partners cannot provide a 100% guarantee that your data will be safe, however, they have strong policies and procedures in place to minimize the possibility of a breach. In addition to the risks noted above, there may be additional risks to participation that are currently unforeseeable.

What are the possible benefits from participating in this research study?

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 blood samples or have imaging performed, you will be provided with clinical diagnostic information from these tests at no cost to you. For example, the ELF test is a laboratory diagnostic test specific to liver function and the prediction of advanced fibrosis. The results of this test or other tests will be put in your medical record and will be available to your doctor to help direct your care and identify potential health risks.

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?

We share limited, identifiable information with our testing partners in order to connect you to your samples/tests. This enables us to return your testing results back to you and/or your healthcare providers as a clinical benefit. Examples of information sent to our testing partners include:

- First name
- Last name
- Medical record number
- Date of birth
- Order date
- Other order-related information

The researchers who conduct the laboratory or statistical analyses do not have access to Registration Information (name, address, email address, user ID, and password) of participants. Researchers only have access to your information in the research database, which is assigned a unique code in order to protect your identity.

Employees who interact with research participants have access to names and contact information of participants but have no access to the research database. All employees are trained on how to work with human research participants. In addition, all researchers are trained on how to conduct research responsibly. RIHI may provide data to other researchers involved in this research study, including researchers at Gilead Sciences. Again, no information that can identify you such as your name, date of birth, or contact information will be provided to these researchers.

RIHI will use your registration information to contact you about future research opportunities or to provide you with information that we find is important for your health, and RIHI needs to contact you for those reasons. Your registration information will never be associated with the joint genetic and health information database that will be used for research purposes.

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. We have strong data privacy and security policies and procedures in place to protect your information and minimize the possibility of a data breach.

If other researchers request access to your data for use in future research, we will provide no information that can identify you such as your name, date of birth, or contact information. Your

name, date of birth, or any contact information will not be used in any publications or reports that result from the study.

Your identity will be kept as confidential as possible as permitted within the law.

Note, for example, that regulatory authorities (including the United States Food and Drug Administration), and the Institutional Review Board (who protects the rights of research participants) have the right to inspect all records regarding this study to monitor, audit, or review your identifiable record for verification of study procedures and/or 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 or would like to withdraw?

At any time, if you have questions about this study, contact Joseph Grzymski, PhD (PI) 775-673-7478(Joseph.Grzymski@renown.org); Alexa Anderson (study contact) 775-982-2797 (Alexa.Anderson@renown.org) or the study team at 775-982-6914 (RenownIHI@renown.org).

To withdraw, please email: RenownIHI@renown.org

Participant Contact Information

Name:

Email Address:

Date of Birth:

Home Phone:

Mobile Phone:

Mailing Address:

Ethnicity:

Birth Gender:

Agreement to be in study

We will give you an electronic copy of this form to keep, either through email or stored within the document center of your Renown MyChart.

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 enroll in Healthy Nevada Project or are already enrolled in the study.
3. You agree to fully participate in the consent and education process to participate in the study.
4. 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.
5. You agree that any results from various clinical tests, if performed, will be made available in your medical record to help guide your normal course of care.
6. 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 and shared with your healthcare providers.
7. You authorize that your age, gender, ethnicity, address, email, phone number and genetic and health information may be used as part of the databases established for the study, which will be maintained and used for future research by RIHI and other researchers with the approval of RIHI. No information that can identify you, such as your name, date of birth, or contact information, will be used for research purposes.
8. 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.
9. You agree that the study team may contact you regarding future research opportunities.
10. All rights and obligations herein may be transferred by RIHI to any successor organization.

_____
Participant's Name Printed

_____ _____
Signature of Participant Date