



**University of California, San Diego**  
**Heritability of fatty liver as measured by MRI: a cross-sectional study of**  
**twins and family members**  
**Informed Consent Statement**

Drs. Rohit Loomba and Thuy-Anh Le are conducting a research study to investigate the heritability of fatty liver in twin pairs and first degree relatives. This study is being funded by the National Institute of Diabetes and Digestive and Kidney diseases (NIDDK).

We are asking you to participate in this research study. Before you consent to join this study, we must explain the purpose of the study, any risks to you, your rights as a study participant, and what is expected of you during the study. If any part of this consent statement is unclear, please ask the study doctor or other study staff to explain it to you so that you understand. You are entitled to have any questions about the study answered to your satisfaction. Before making your decision, we ask you to think about it at home and to discuss it with your family or friends. If you decide to join the study, we ask you to give your consent by signing in the space provided below. The study staff will also sign the statement. We will give you a copy of the signed statement. We will also give you instructions for contacting the study staff if you need to contact them during the study or after the study has ended.

**WHY IS THIS STUDY BEING DONE?**

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease in the United States. The cause of NAFLD is poorly defined but is thought to involve complex interactions of genetic and environmental factors. NAFLD is often associated with the traits of the metabolic syndrome including diabetes, high cholesterol or elevated blood pressure. Currently, there are no accurate noninvasive means of evaluating NAFLD and its more serious form which includes inflammation that may lead to severe scarring in the liver. The goal of this study is to evaluate shared genetic factors that underlie NAFLD and features of the metabolic syndrome as determined by blood work and radiographic studies (including magnetic resonance imaging (MRI) and ultrasound) in a cohort of twins and first degree relatives.

**TYPE OF STUDY**

This is a cross-sectional study consisting of a one-time visit by twin pairs or first-degree relatives.

**SELECTION OF PATIENTS**

In order to participate in this portion of the study, you must carefully read and sign the informed consent. To be eligible for this study, you must be at least 18 years old and be willing and able to complete all procedures. If you are a female who is pregnant or nursing, you will not be allowed to participate. If you are a female, you will be asked to complete a urine pregnancy test prior to study procedures.

If you have any contraindications to magnetic resonance imaging (MRI), have a history or extreme claustrophobia or cannot fit comfortably in the MR scanner, you will not be allowed to participate. Contraindications to MRI include patients with pacemakers, metallic cardiac valves, magnetic material such as surgical clips, implanted electronic infusion pumps or other conditions that would preclude proximity to a strong magnetic field.

**HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?**

We plan to recruit a total sample of 500 subjects, of which 240 will be twins (120 twin pairs) and 260 will be sibling-sibling or offspring-parent or two (or more) first degree relatives.

**HOW LONG WILL I BE IN THE STUDY?**

The study consists of a single visit. For each subject, the study visit will be for 1.5 hours, the magnetic resonance techniques will total 20-30 minutes, and ultrasound (ARFI) will be 10 minutes in duration.

**WHAT IS INVOLVED IN THE STUDY?**

Following an information session during which the consent and the UCSD HIPPA forms are reviewed, discussed and signed, the following tests and procedures will be done.

We will ask you to come in a fasting state (nothing but water for 12 hours before the visit). We will interview you and give you a physical examination. We will also take your blood pressure, temperature, pulse, height, weight, waist and hip measurements. We will ask you about alcohol consumption and about any medicines that you are taking or that you have taken in the past.

We will draw 30 mL (~2 tablespoon) of your blood for laboratory testing and serum and plasma banking. You will also be asked to provide about 3 ml of urine for laboratory testing and specimen banking. The specimens that we will bank will include your urine, blood serum and plasma - a clear yellowish fluid after separation of blood cells. You will be given the stool sample collection kit at time of the visit and will be asked to return the kit with fresh stool sample by mail.

A urine pregnancy test will be performed for all women of childbearing age. Women who have had hysterectomies are excluded from pregnancy testing. If the test is positive or if it is negative but you are trying to conceive you will not be enrolled in the study.

**Magnetic Resonance Imaging (MRI) and Magnetic Resonance Elastography (MRE):** During this visit you will undergo a magnetic resonance imaging (MRI) scan, which takes about 20-30 minutes. During the MRI scan you will lie down on a narrow bed. The bed will be rolled slowly into a tunnel that is 6 feet long, 22 inches wide, and open at each end. You will lie on your back on a table and be asked to remain still while the scanner takes images of the inside of your body. At times during the scan, you will be asked to hold your breath and keep still. During these times you will hear a loud tapping noise and you may feel warm during this procedure. In addition, a new technique call elastography will be performed whereby a vibrating paddle will be placed over your abdomen while images are obtained.

**Ultrasound and Acoustic Radiation Force Impulse Exam (ARFI):** ARFI is a new ultrasound technique that is being studied in fatty liver disease. This technique builds upon the traditional ultrasound techniques and does NOT involve any radiation or contrast agent. You will be asked to lie on the examination table while images of your liver are obtained using the ultrasound machine by well-trained staff and lasts about 10 minutes long.

**SPECIMEN BANKING AND DATA REPOSITORY**

Your specimens (serum, plasma, stool and urine) collected as part of this study will be stored and kept locked in a UCSD facility and only Dr. Loomba or his research associates will have access to them. At the end of the study, the data collected on you will be maintained at NARF building GI offices in a locked computer file with access available to the principal and study investigators only.

The purpose of this collection is to analyze markers of heritability of fat in the liver in twin pairs and first degree relatives. Your samples and data will be used by the researchers



carrying out this study, but they also may be used by other researchers, both during the study and after it ends for health research. Your samples and data may be stored for 50 years.

Your samples and data will be labeled with a code number. Your name, address, social security number, date of birth and other personal identifiers will not be available on the sample, and we not will give out your name or other information that identifies you to the researchers who use your samples and data.

If you do not agree to have your samples and data stored, you may not participate in this study. If you agree now but change your mind later about having your samples, you may withdraw unused samples during the study. No additional samples will be stored and no further data will be collected on you, but samples and data already collected will continue to be used. If you decide later that you do not want the specimens collected from you to be used for future research, you may tell this to Dr. Loomba, who will use his best efforts to stop any additional studies. However, in some cases, such as if your cells are grown up and are found to be generally useful, it may be impossible to located and stop future research once the materials have been widely shared with other researchers

Because researchers will not have access to your identity, you will not get the results of any studies that might be performed on your samples. The specimens collected from you and the DNA that they contain may also be used in additional research to be conducted by the University of California personnel collaborating in this research. These specimens, DNA, and their derivatives may have significant therapeutic or commercial value. You consent to such uses.

**Genetic study:**

There is a separate optional component of the study where you will be asked to donate a blood sample for genetic research. If you give us permission, a sample of your blood will be used as a source of DNA to study the genetic component of NASH in twin pairs and first degree relatives. Also, some of your sample will be saved for future genetic research related to NAFLD and also for future liver research that may not be related to NAFLD. Because DNA or genetic analysis can be used for research on many diseases and because DNA can reveal much information about you, consent for DNA research is requested separately. This separation allows you to refuse this part of the research program and still participate in the ‘Heritability of fatty liver as measured by MRI: a cross-sectional study of twins and family members’ study. If you decide to donate your blood, we will draw 5 mL (approximately 1/2 teaspoon) from your forearm veins. Your blood sample will be stored in Dr. Loomba’s locked research freezer at the Clinical Teaching Facility (CTF-building A).

Your DNA or the information from it may be used by other scientists for additional research in the future. Because researchers will not have access to your identity, you will not get the results of any future studies that might be performed on your DNA. . These specimens, DNA, and their derivatives may have significant therapeutic or commercial value. You consent to such uses.

You agree to participate in the genetic component of the study.

Yes:  Study participant initials: \_\_\_\_\_

No:  Study participant initials: \_\_\_\_\_



## **WHAT ARE THE RISKS OF THE STUDY?**

**Blood drawing:** Taking blood may cause some pain, discomfort, bleeding or bruising/swelling where the needle enters the body, and, in rare cases, dizziness, lightheadedness, fainting or infection.

**MRI:** The magnetic resonance scanner is a long narrow tube that is open on both ends. A small number of individuals experience claustrophobia once inside. You will be able to signal the investigators with a squeeze ball device at any time to pause or stop the study or simply to ask questions.

The scanner produces loud banging noises while acquiring images. You will be given a set of earplugs to help with the noise.

There are no known effects from exposure to the magnetic fields. However, some patients might become anxious during scanning. If this happens to you, you can stop the procedure at any time. You can also experience some discomfort and fatigue from lying in a confined space during the imaging.

If you have any metal clips, plates or a pacemaker in your body, you should tell the investigator. MRI may not be appropriate under some of these conditions: a cardiac pacemaker; metal fragments in the eyes, skin or body; heart valve replacement, brain clips, venous filter, history of sheet metal work or welding, aneurysm surgery, intracranial bypass, renal or aortic vascular clips; prosthetic devices such as middle ear, eye, penile implants or joint replacements; hearing aide, neurostimulator, insulin pump, IUD, pregnancy; vascular shunts or stents; metallic implants, plates, pins, wires or screws; permanent eyeliner or eyebrows, or tattoos.

**MRE:** MRE imaging involves placing a vibrating paddle over the abdomen while images are being obtained. The vibrating paddle may cause discomfort to you. You are able to tell the MR technologist if the vibrations become uncomfortable, and the MRE part of the examination will be discontinued.

**Ultrasound (ARFI):** The ARFI ultrasound imaging method to be used for this study is investigational, but is considered to be of minimal (i.e., non-significant) risk. Possible effects of ultrasound imaging on nursing mothers have not been examined. Therefore, nursing mothers will be excluded.

**Unforeseeable risks:** Although serious injury to organs or death have never been attributed to ultrasound imaging or MRI, it is possible that currently unforeseen side effects, including serious injury to organs or death may occur. Also, because this is an investigational study, there may be some other unknown risks that are currently unforeseeable. The subject will be informed of any significant new findings.

### **Testing for hepatitis B and C and HIV:**

**Risk of testing for infectious illnesses:** You will be tested for hepatitis B and C, if you have not received these tests in the past or when clinically indicated. Patients who are found to have either hepatitis B or C would be given a referral to the UCSD liver clinic and counseled appropriately by Dr. Loomba. HIV testing would only be performed when it is clinically indicated. These tests are necessary to make sure that these study procedures would be appropriate for you. Testing for HIV and hepatitis viruses may result in a diagnosis of infection with these viruses. You will be informed of the results of these tests; if you do not wish to know the results, you should refuse to participate in this study. In the event that you are diagnosed with HIV, your doctor will give you the results in a face-to face discussion (not by telephone or mail), counseling will be offered to you, and the results will be entered in your medical record and reported with accordance with California state law. In the event that you are diagnosed with hepatitis or HIV, you may be referred to a doctor who specializes in these illnesses. The diagnosis of HIV or hepatitis may result in earlier treatment and/or prevention of many complications from the illnesses. Efforts will be made to keep your personal information



confidential. Awareness of a diagnosis of these illnesses may have serious personal or social consequences. Some of these consequences include possible difficulty obtaining health/life/disability insurance or employment, and difficulty traveling to some foreign countries.

**Confidentiality:** While every effort will be made to maintain your privacy, it is possible that others may learn about your health information and such a breach might lead to problems with getting insurance or a job. Your medical records will be kept private but research staff will look at this information. This information will be included in computer programs kept private by password protection. Written information will be stored in locked areas. Research records will be kept confidential to the extent provided by law. It is however, always possible that the information in the research records could become known outside of the research setting.

**ARE THERE BENEFITS TO TAKING PART IN THE STUDY?**

You may or may not benefit from participation in the study. However, you will help future patients by helping doctors and other scientists learn more about genetic contributions to fatty liver disease and traits of the metabolic syndrome. Additionally, you will have a free comprehensive physical exam visits with blood work.

At your direction, we will provide the results of any procedures done to screen you for this study to your primary care doctor or liver care provider.

**WHAT OTHER OPTIONS ARE THERE?**

You can choose to not participate.

**WHAT ABOUT CONFIDENTIALITY?**

Every reasonable effort will be made to keep your records confidential. However, while you are in this study all research records may be made available to:

- The UCSD Institutional Review Board (for the protection of human subjects in research)
- Other regulatory entities responsible for overseeing research, such as the Federal Office for Human Research Protections and National Institute of Diabetes and Digestive and Kidney diseases (NIDDK).

Your records will not be released without your consent to the extent the law allows. The study doctors can use the study results as long as you cannot be identified. This information will be included in computer programs kept private by password protection and encryption. Written information will be stored in locked areas accessible to study staff only.

Your participation in this study will be kept confidential and your name, address, and other personal identifying information will not be made known to anyone other than study personnel at this site. The information will be labeled with only an identifying number and code that cannot be linked to your name or other personal identifiers except at the clinical center where you complete visits. When results from this study are published in medical literature, you will not be identified by name. Representatives from the United States Food and Drug Administration (FDA) or the Institutional Review Board at this clinic may review your records, including your medical records.

We will protect your confidentiality and resist any demand to disclose information that may identify you. However, we cannot resist a demand from the U.S. Government that is used for auditing or evaluation of or for information that must be disclosed in order to meet the requirements of the U.S. Food and Drug Administration. You or a member of your family may



voluntarily release information about you or your involvement in the research. If an insurer, employer, or other person obtains your written consent to receive research information, then we may not withhold that information. If the study staff learns of possible child abuse or neglect or a risk of harm to yourself or others, we are required to notify the proper authorities.

The study doctor or staff may contact you in the future for other research studies. Please check the box if you agree.

Study participant initials: \_\_\_\_\_

**WHAT ARE THE COSTS?**

You will not be billed for any part of this study and there are no costs to you.

**WHAT IF I AM INJURED IN THE STUDY?**

If you are injured as a direct result of participation in this research, the University of California will provide any medical care needed to treat those injuries. The University will not provide any other form of compensation to you if you are injured.

You may call the UCSD Human Research Protections Program office to inquire about your rights as a research subject or to report research-related problems at (858) 455-5050.

**WILL I GET COMPENSATED TO BE IN THIS STUDY?**

You will be compensated \$100 for your participation in this study.

**WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?**

Drs. Rohit Loomba, Thuy Anh Le, or \_\_\_\_\_ have explained this study to you and answered your questions. If you have other questions or research-related problems, please call: Rohit Loomba at 619-543-6222 or 858-534-2624.

After Hours:

UCSD Hospital Operator at 619-543-6737 – Ask the operator to page Drs. Rohit Loomba, or Thuy Anh Le. Let the operator know that you are a research participant.

**WHAT ARE MY RIGHTS AS A RESEARCH SUBJECT?**

Participation in research is entirely voluntary. You may refuse to participate or decide to stop participating at any time without jeopardy to the medical care you receive. If you do participate, you may freely withdraw from the study at any time. Your decision will not change your future medical care at this site or institution. The study doctor or the sponsor may stop your participation in this study at any time without your consent. The reasons may include: the study doctor thinks it is necessary for your health and safety, you have not followed study instructions, the sponsor has stopped the study, or administrative reasons require your withdrawal. We will tell you about new information that may affect your health, welfare, or willingness to stay in this study. If you are found to be ineligible to continue with this study, we will keep the data that has already been obtained during prior visits in a locked computer file. We may contact you for future studies.

If you have questions about your rights, or to report research related problems, please contact:

University of California, San Diego  
Human Research Protections Program  
(858) 455-5050



**SIGNATURE AND CONSENT TO BE IN THE STUDY**

Your signature below means that you have read the above information about this study and have had a chance to ask questions to help you be informed about what you will do in this study. Your signature also means that you have been told that you can change your mind later if you want to. You will be given a copy of this consent form and a copy of the "Subject's Bill of Rights" to keep. By signing this consent form you are not giving up any of your legal rights.

You agree to participate.

\_\_\_\_\_  
NAME OF SUBJECT

\_\_\_\_\_  
SIGNATURE OF SUBJECT

\_\_\_\_\_  
DATE

\_\_\_\_\_  
SIGNATURE OF PERSON WHO EXPLAINED THIS FORM

\_\_\_\_\_  
DATE

\_\_\_\_\_  
Legally Authorized Representative's Name  
or Witness to the "X" (print)

\_\_\_\_\_  
Relationship to the Subject

\_\_\_\_\_  
Representative or Witness Signature

\_\_\_\_\_  
Date



## SUBJECT BILL OF RIGHTS

As a subject in a research study or as someone who is asked to give consent on behalf of another person for such participation, you have certain rights and responsibilities. It is important that you fully understand the nature and purpose of the research and that your consent be offered willingly and with complete understanding. To help you understand, you have the following specific rights:

1. To be informed of the nature and purpose of the research in which you are participating.
2. To be given an explanation of all procedures to be followed and of any drug or device to be used.
3. To be given a description of any risks or discomforts, which can be reasonably, expected to occur.
4. To be given an explanation of any benefits which may be expected to the subject as a result of this research.
5. To be informed of any appropriate alternative procedures, drugs, or devices that may be advantageous and of their relative risks and discomforts.
6. To be informed of any medical treatment which will be made available to the subject if complications should arise from this research.
7. To be given an opportunity and encouraged to ask any questions concerning the study or the procedures involved in this research.
8. To be made aware that consent to participate in the research may be withdrawn and that participation may be discontinued at any time without affecting continuity or quality of your medical care.
9. To be given a copy of the signed and dated written consent form.
10. To not be subjected to any element of force, fraud, deceit, duress, coercion, or any influence in reaching your decision to consent or to not consent to participate in the research.

If you have any further questions or concerns about your rights as a research subject, please contact the research doctor or the UCSD Human Research Protections Program at 858-455-5050 during normal working hours.

