Regulation of Muscle Protein Phenotype in Humans with Obesity

NCT04700800

June 14, 2024

MAYO CLINIC

Name and Clinic Number

Approval Date: **June 14, 2024**
Not to be used after: **June 13, 2025**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: Regulation of Muscle Protein Phenotype in Humans with Obesity

IRB#: 20-003294

Principal Investigator: Dr. Roust and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	Information that results from this research will help us to better understand the effects of being overweight on the metabolism of proteins in muscle. You have been asked to take part in this research because you meet the inclusion criteria, we are currently seeking in this research study.
What's Involved	The study includes 2 screening visits and one main study visit, which are outlined in more detail in this document. The number of visits you will need to complete will be determined by which research group you are assigned to. The entire time you spend in this study could be up to 3 months. Procedures include: • Electrocardiogram (ECG) • DEXA Scan • Urinalysis

	• Physical Exam performed at your screening visit • Glucose Tolerance Test • Labs which include: CBC, lipids, liver function tests, electrolytes • Infusion of Amino Acids • Infusion/ingestion of Stable Isotopes • Muscle Biopsies • Urine pregnancy test • Exercise
Key Information	There may be parts of this study you find uncomfortable or unpleasant. You will have to have needle sticks for blood drawing, IV catheters, and muscle biopsies. The biopsy procedure can cause an unpleasant feeling in your muscle for a few minutes. Also, unless you are performing exercise, you have to remain in bed during the entire duration of the study (approximately 9 hours, you will likely be onsite for 11-12 hours) and will not be allowed to walk around. You will have to use a bedside commode, bedpan, or urinal instead of the restroom. The risks associated with study participation are completely described later in this form, be sure to review them carefully. There are no costs to you for being in the study. The goal of the study is to gather information; you will not directly benefit from participation.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Lori Roust, MD **Phone:** (480) 301-8000 **Institution Name and Address:** Mayo Clinic Arizona 13400 E. Shea Blvd Scottsdale, AZ 85259
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you are either an overweight individual, which is the main population that this study is focused on, or a lean individual that is studied as a control to compare responses to those of the overweight individuals.

Why is this research study being done?

Information that results from this research will help us to better understand the effects of being overweight on the metabolism of proteins in muscle. Metabolism is the chemical reaction in the body's cells that change food into energy. Understanding the protein metabolism within muscles is important because muscles are made primarily of proteins that are responsible for determining the muscle phenotype (physical characteristics of an organism). Muscle phenotype in humans with obesity is characterized by decrease in the content of what are called "slow" type muscle fibers, a condition linked to the pre-diabetic/diabetic state.

Better understanding in protein metabolism in the overweight individuals can alleviate metabolic reactions that contribute to the pre-diabetic state in these individuals, ultimately preventing diabetes.

Information you should know

Who is Funding the Study?
The National Institutes of Health through Arizona State University and Mayo Clinic in Arizona are funding this study. They will pay the Principal Investigator, Co-Investigators, your study doctors and the institutions to cover costs related to running the study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team

for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

You will participate in this study for approximately 3 months.

What will happen to you while you are in this research study?

If you agree to be in the study, you will first be contacted over the phone and if you meet the initial criteria for the study you will be ask to complete day 1 screening visit at the Ambulatory Infusion Center (AIC) at Mayo Clinic in Scottsdale, Arizona, we will also ask you to record your diet and complete a physical activity survey at that time. If you still meet the criteria, you will be scheduled for day 2 screening visit at the Ambulatory Infusion Center (AIC) at Mayo Clinic in Scottsdale, Arizona.

There will be two different subject groups in this study. The first group will consist of 72 subjects. This group will be referred to as group A in this document. The second group of subjects will consist of 18 subjects and will be referred to as group B in this document. The study team will let you know which group you will be assigned to. Enrollment in the study and assignment in study group will be based on screening results and answers to dietary and exercise questions.

Both Groups A&B will complete the following Screening procedures:

Remote Consenting:
If you meet the initial criteria for the study during the phone screening, you will have the option to either review the consent form, medical history, and medications over the phone with a member of the study staff or you may choose to do so in person at your screening visit day 1. The pre-screening will take approximately 1 hour and if you choose to participate, an electronic signature will be obtained.

Screening Visit Day 1(may be conducted over several days):
This screening visit will take about 6 hours, during which time you will talk to the research staff about the study, read the consent form, and have your questions answered. If you are interested in participating, you will sign the consent form if not already done so remotely. You will be

asked to come to the AIC around 7:00-8:00 AM for the screening tests. You will not eat breakfast on this morning and have nothing to eat or drink (except water) after 10 PM the night before.

During this visit, we will do some tests and procedures to see if you are eligible to take part in this research study. The Principal Investigator and the study team will review the results of these tests and procedures. If you aren't eligible, the Principal Investigator or a member of the study team will tell you why.

At this visit we will:

- Ask you about your medical history
- Ask you about the amount of physical activity you participate in
- Give you a physical exam, including height, weight, and "vital signs" (blood pressure, temperature, heart and breathing rates), and measure your waist and hip circumferences
- Ask you for a urine sample, for urinalysis
- Test your urine for pregnancy if you are a female able to become pregnant; if this test is negative, we will proceed with screening
- Perform an electrocardiogram (ECG) to measure the electrical activity of your heart; the ECG is performed by attaching sticky electrode patches on your chest
- Draw a blood sample for laboratory tests to measure chemicals in your blood, including blood cell count, lipids (fats), HgbA1c (a way of measuring your blood sugar), thyroid hormone, liver function tests, blood glucose and clotting ability
- Oral glucose (sugar) tolerance test (the procedures of this test are described below)

Oral Glucose Tolerance Test

A needle with a soft plastic tube over it, called a catheter (also called an IV), will be inserted into a vein in your arm. The needle is removed, and the catheter stays in your vein. This catheter will stay in place so that only one stick with a needle is required and we can draw blood from the catheter. You will be asked to drink a flavored drink called glucola and blood will be drawn every 30 minutes for 2 hours from the catheter in your arm to see how your body uses sugar. The total amount of blood drawn will be about 1/3rd cup or 4-5 tablespoons.

Screening visit Day 2

This screening visit will take about 6 hours. At this visit we will perform:

- Maximal oxygen uptake test
- Dual-energy X-ray absorptiometry (DEXA) scan
- Give you a physical exam (if not already done on screening visit Day 1)

Maximal Oxygen Uptake Test

It is a strenuous cycling exercise test designed to measure your cardiovascular (commonly called "aerobic") fitness. If this test is performed on a day separate from the day of the screening visit of Day 1, we will ask you to come back to the AIC after not having eaten for between 3-4 hours to do this test.

To monitor your heart rate, we will connect you to an electrocardiogram (ECG) by putting some sticky electrode patches on your chest or we will have you wear a special belt around your chest. You will breathe into a mouthpiece so that we can collect the air that you breathe out while you ride a stationary bicycle. We will start you off easy on the bicycle and increase the difficulty of the pedaling until you tell us to stop. We will take your blood pressure several times using a cuff around your arm in the standard way. The total bicycling time will be about 15 minutes, and the total time from set up to finish will be about one hour. If at any time you feel you need to stop the exercise test because you feel you cannot continue, be sure to tell the staff immediately and we will stop the test. In addition, the test will be stopped if any cardiac abnormalities are observed during the test or abnormal changes in blood pressure occur.

Dual-energy X-ray absorptiometry (DEXA)

This procedure is done to evaluate your body composition and specifically the amount of body mass that is composed of lean (that is, fat-free) and fat tissues. It will be performed within the Radiology Department in Mayo Clinic Arizona.

3-Day Dietary Record:

As part of your participation in this research, you will be responsible to collect a 3-day dietary record over the course of your screening visits with the purpose of evaluating your typical diet. You will fill out the online form by using the Automated Self-Administered 24-hr dietary recall (ASA-24) software https://asa24.nci.nih.gov/researchersite/

Stanford Brief Activity Survey (SBAS)

Your habitual physical activity will be evaluated using the Stanford Brief Activity Survey (SBAS). This is a very short 2 item self-reported physical activity assessment tool, which likely will take under 5 minutes to complete.

Monitor Physical Activity

Through the course of your screening visits, we will measure your physical activity using a small wearable device. We will ask you to wear a small device/monitor (brand name: activPAL^{TM}) on your thigh to monitor your physical activity for a week. The physical activity monitor will be attached by using a self-adherent elastic wrap to the skin, in the midline of the front part of your thigh. This is a tiny device that you wear throughout the 24-hour day (that is day and night).

After completing all the screening procedures, we ask that you do not participate in any other research studies while you are participating in this study. In addition, while you are a participant in this study, we ask that you do not donate blood, change your physical activity and nutrition habits or start a weight loss program.

During the 3-day period leading to the main study visits we will ask you to consume foods of your typical diet, as reported by you on the online 3-day dietary record. During the 3-day period leading to the main study you will also be asked to avoid any beverages with alcohol and avoid any exercise that is beyond your normal daily physical activities.

MAIN STUDY VISITS:
Medical personnel will be in charge of supervising and performing tests that are described in the main study infusion visits.

With the exception of water, you will not be allowed to consume any food or snacks until the end of the study at approximately 4:30 pm. At that time (end of the study) you will be provided with a meal.

Group A will be asked to return to the Mayo Clinic AIC in a few days after screening visits to complete either *an amino acid infusion/ingestion* visit or *amino acid infusion/ingestion+exercise* visit. During either of these visits you will receive stable isotope infusion/ingestion.

Group B will be asked to return to the AIC in a few days after your screening visits to complete one exercise and stable isotopes infusion/ingestion visit. The study visit will differ from group A as it will not include the amino acid infusion.

Main Study Visit (Group B)
Study visit will take about *11-12 hours*. At this visit you will have:

- Infusion/ingestion of Stable Isotopes
- Infusion of Saline + Exercise
- 4 Muscle biopsies
- Drawing of blood samples
- Cycling exercise

EXERCISE+INFUSION/INGESTION OF STABLE ISOTOPES of AMINO ACIDS and Saline:
Infusion/ingestion of stable isotopes will be started soon after arriving to the AIC and following the insertion of the IVs. You will exercise for 45 mins and starting at approximately 5 hours after the initiation of the study visit. All infusions will be continued until the end of the study while continuously resting in bed.

In case of ingestion of the stable isotopes, these will be provided as small boluses dissolved in water (~10-20 ml), and you will be asked to ingest those boluses of stable isotope-water mixture every 10-15 minutes during the course of the study visit.

These are stable isotopes of amino acids. Stable isotopes are naturally occurring and are not radioactive. The stable isotopes are already present in your body in small amounts and the infusion/ingestion will help to increase them in amounts that are detected in sufficient quantity for the purpose of our experiments.

Main Study Visit (Group A)
Study visit will take about *11-12 hours*. At this visit you will have:

- Infusion/ingestion of Stable Isotopes
- Either infusion of Amino Acids *or* infusion of Amino Acids+Exercise
- 4 Muscle biopsies
- Drawing of blood samples
- Cycling exercise, if participating in the Amino Acids+Exercise visit

INFUSION/INGESTION OF STABLE ISOTOPES/AMINO ACIDS: Infusion/ingestion of stable isotopes will be started soon after arriving to the AIC and following the insertion of the IVs (one of the IVs, placed halfway in your arm will be used for the infusions, while the other, placed on the top part of your hand, will be used for drawing blood). Infusion of the amino acids will be started approximately at 5.5 hours after the start of the stable isotopes infusion/ingestion. All infusions/ingestions will be continued until the end of the study while continuously resting in bed.

Details of the procedures to be followed are described below:

Muscle biopsies
You will have four muscle biopsies taken from your legs during the main study visit. These muscle biopsies will be taken from the thigh muscles of your legs. The first muscle biopsy will be taken about 2 hours after the initiation of the stable isotope infusion/ingestion. The procedure involves the taking of a small piece of muscle tissue from your leg. To do this, we will clean your thigh and use a local anesthetic (numbing medicine like your dentist uses) to numb a small area in your skin. Next, we will make a small cut in your skin (about ¼ inch). A special needle will then be passed through this cut into the muscle and a piece of muscle tissue about the size of a pea will be obtained. The place where we make the cut will be closed with "steri-strips," which are like small band aids. The second muscle biopsy will be taken at 4.5 hours, the third biopsy will be taken at 6 hours, and the fourth biopsy will be taken at 9 hours, after the start of the study.

Blood Draws

We will draw blood samples several times during the course of the 11-12 hours study visit from the IV in your hand. This hand will be placed in a heated pad or box with a temperature of about 140 degrees Fahrenheit.

This temperature is similar to very warm bath water. The purpose of the heated pad is to increase the blood flow to your hand in order to allow us to draw blood moving fast from your lower arm artery to your lower arm vein. Your hand will remain in this pad or box while you are remaining in the bed for the duration of the study. You should notify the study nurses immediately if your hand feels uncomfortable. The total volume of blood drawn during your 11-12 hours study will be approximately 13 tablespoons.

Stable Isotope Infusion/Ingestion

Small amounts ("tracer dose") of the stable isotopes leucine and phenylalanine (these are amino acids serving as building blocks of proteins in the body) will be infused into your vein through the IV in your arm with the purpose to track their metabolism in the body. Alternatively, the stable isotopes will be ingested as small boluses dissolved in water (~10-20 ml) every 10-15 minutes during the course of the visit. By making small elevations in the concentration of these substances in the blood, and by monitoring their changes over time in blood and measuring their incorporation into muscle proteins we will be able to determine their metabolism, which is representative of the metabolism of proteins in muscle. You may be administered both the leucine and phenylalanine stable isotopes, or only the leucine stable isotope and depending on the goals of the specific infusion study you are assigned to.

Amino Acid Infusion

If participating in Group A, you will receive a continuous infusion of an amino acid solution containing the amino acids found in your body. This amino acid solution is known with the prescription name “Clinisol, 15%”. The amino acid infusion is expected to increase the average amino acid concentrations in your body approximately twofold.

Cycling Exercise

You will perform exercise on a stationary bicycle for 2-5 minutes at very easy rate to warm up. You will then exercise on the bike for 45 minutes at 65% of your best effort. Your best effort means the hardest you can exercise and is based on the values achieved during the Maximal Oxygen Uptake Test during the screening visit. If you participate in the Amino Acid+Exercise visit (Group A), you will receive an Amino Acid infusion after the completion of the exercise and until the end of the visit.

Physical Activity Monitoring

We will ask you to wear a small device/monitor (brand name: activPAL™) on your thigh to monitor your physical activity for one week during the screening portion of the study. This is a tiny device that you wear throughout the 24-hour day (that is day and night). The activPAL monitor is waterproof, so you do not have to worry if getting wet during shower or in the pool. You will be asked to arrive in comfortable clothing that will allow the activPAL device to be attached to your right thigh. Data analyzed after removing the monitor will give us information about your daily moving activities, including sitting, standing, walking, exercising.

The physical activity monitor will be attached by using a self-adherent elastic wrap to the skin, in the midline of the front part of your thigh.

Tests done only for research purposes and are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you unless in the rare event that a finding might affect the health of you or your family. We will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

There may be parts of this study you find uncomfortable or unpleasant. You will have to have multiple needle sticks for blood drawing, IV catheters, and muscle biopsies. The biopsy procedure can cause an unpleasant feeling in your muscle for a few minutes. Also, unless you are in the exercise visit, you have to remain in bed during the entire duration of the study (approximately 11-12 hours) and will not be allowed to walk around. You will have to use a bedside commode, bedpan, or urinal instead of the restroom.

General Discomforts

You will not receive breakfast and may experience hunger symptoms during this study. A snack or lunch will be provided as soon as the study procedures are finished. For the infusion visits you will have to stay in bed and will be attached to infusion/blood drawing lines so that you cannot move much. This may cause some discomfort and perhaps back pain.

Electrocardiogram (ECG)
This test uses small sticky pads that are placed on your chest and limbs to measure the electrical activity of your heart. There may be mild discomfort from the sticky pads and a possibility of the skin being irritated by the adhesive on the sticky pads. Chest hair may need to be shaved prior to the placement of the sticky pads.

Line Placements
The most common problems from the placement of catheters in your arm are:
Pain and bruising, feeling lightheaded, or faint during the procedure; bleeding at the site where the catheters are placed; infection where the catheter enters the skin or inflammation of the vein.

More serious very rare problems include:

- clotting in the veins and blockage of blood flow
- bulging of the vein and pooling of blood in the vein
- fracture or breaking off of a piece of the catheter

These risks are greatly reduced by the use of sterile techniques to avoid infection and having skilled medical staff performing the overall study procedures. On occasion, a catheter may need to be replaced because we cannot draw blood from it or it falls out of the vein.

Blood Drawing
The risks of drawing blood include pain, bruising, or rarely, fainting and infection at the site of the needle stick. The amount of blood taken during the study participation will be no more than approximately 13 tablespoons, which is well below the amount taken during a typical blood donation. Saline will be given as replacement so you will not likely have any noticeable effects.

Oral Glucose (Sugar) Tolerance Test
Some people's blood glucose (sugar) levels drop very low toward the end of the Oral Glucose Tolerance Test. But some people feel like their glucose levels are low, when their levels actually are not low. Symptoms of low blood glucose include weakness, hunger, sweating, and feeling nervous or restless. If you develop these symptoms during the test, you may have your sugar levels checked quickly with a glucose meter. If your sugar level is very low, the test will be stopped.

Exercise Tests
The cycling exercise is expected to result in muscular and respiratory fatigue. There are some risks associated with exercise and exercise testing. There is less than a 1 in 10,000 chance of having a heart attack or stroke during the exercise. Careful screening and monitoring during exercise will minimize these risks. There is also a small risk of pulling a muscle or injuring a tendon or ligament, probably less than 1 in 100. We will use the exercise testing guidelines from

the American Heart Association/American College of Sports Medicine. Therefore, individuals with conditions related to heart disease, respiratory, or orthopedic limitations, and who are at the greatest risk for exercise-associated complications, will not be part of these studies. You may experience muscle fatigue, dizziness and in rare cases nausea and vomiting after the exercise tests because you exercise as hard as you can. If you experience these symptoms the investigators will stop the test at any time you feel you do not want to continue. These symptoms are rarely seen in trained athletes but may occur in un-trained individuals who are not used to strenuous exercise.

Dual-energy X-ray absorptiometry (DEXA)
You will be exposed to radiation from the DEXA scan. The amount of radiation has a low risk of harmful effects.

Stable Isotope Infusion/Ingestion
There is no known risk of infusing or ingesting stable isotopes. Stable isotopes are naturally occurring and *are not radioactive*. The stable isotopes are already present in your body in very small quantities. In regards to the infusion, any adverse reactions during the isotope infusion that suggest allergic reaction or infection will be promptly addressed by the medical personnel. Depending on the seriousness of the reaction, the infusion study will be terminated. Thus, the risk of this procedure is no different than the general risk of infused substances.

Amino Acid Infusion
The infused amino acid solution is a commercially available product regularly used in clinical practice and research and, therefore, there is minimal risk associated with its infusion. Any adverse reactions during the amino acid solution infusion that suggest allergic reaction or infection will be promptly addressed by the medical personnel. Depending on the seriousness of the reaction, the infusion study will be terminated.

Muscle Biopsies
There may be a sensation of "pressure" at the time of the muscle biopsy. About a third of people report feeling cramping or pain. The pain is mild to moderate and lasts 5-10 seconds. The pain usually stops when the needle is removed. Some discomfort, like a sore muscle, may be present for a day or two. The most common problems from the muscle biopsy are:

- pain and bruising
- small scar at the site
- feeling lightheaded or faint during the procedure
- bleeding at the site
- infection at the site

Numbing medication will be used to minimize pain. As with any medication, allergic reactions are possible; allergic reactions to the numbing medicine could cause problems such as a skin sore, swelling, or hives. There is a small risk of infection or bleeding where you have the muscle biopsy. Major bleeding from the biopsy site is highly unlikely since no major artery or vein is located in the area where the biopsy is performed. We will minimize the risk of infection by using strict sterile procedures. Bleeding can also be seen as bruising at the place on your leg where we take the muscle. The swelling or bruising usually goes away with rest within 2-3 days, although sometimes it may take a week. Very rarely some subjects may experience numbness or tingling at the biopsy site. This is usually temporary and goes away in few days.

The tape used for placing the activPAL on your thigh is hypoallergic, so we do not expect any discomfort. However, if for some reason you experience any discomfort/rash or chafing related to the placement of the activPAL, you can contact the study team and have the placement of the monitor evaluated. The actiPAL could be replaced, including placing it in the opposite leg.
Many side effects go away shortly after the infusion study/muscle biopsies are completed, but in some cases side effects can be serious, long lasting, or may never go away. Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

<u>Pregnancy and Birth Control</u>

1) Will women of child-bearing-potential be allowed to participate in this study?
Yes: Women of child-bearing-potential will be able to participate in this study if they have a negative pregnancy test and agree to use acceptable birth control (see #5) since the risks to an unborn child are either unknown or potentially serious.

2) Will pregnant, and/or nursing women be allowed to participate in this study?
No: There is not enough medical information to know what the risks might be to a fetus or infant.

3) Do you need to have a pregnancy test done to be part of the study?
Yes: As part of this study a pregnancy test is required for all women who are able to become pregnant. A urine pregnancy test will be done prior to each study visit.
You will be told the results of the pregnancy test. If the pregnancy test is positive, you will not be able to take part in the study.

4) Will men who are able to father a child be allowed to participate in this study?
Yes: Men who are able to father a child are allowed to take part in this study.

5) What types of birth control are acceptable?

- Surgical sterilization
- Approved hormonal contraceptives (such as birth control pills, Depo-Provera)
- Barrier methods (such as a condom or diaphragm) used with a spermicide
- An intrauterine device (IUD)
- Abstinence

During this study, we will ask you to fill out questionnaires about your diet and exercise. We hope that you will answer all of the questions, but you can skip any questions you don't want to answer.

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator, Arizona State University and Mayo Clinic may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you don't follow the study procedures,
- if the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries:
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

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

You won't benefit from taking part in this research study. It is for the benefit of research.

What alternative do you have if you choose not to participate in this research study?

This study is only being done to gather information. You may choose not to take part in this study.

What tests or procedures will you need to pay for if you take part in this research study?

You will not need to pay for tests and procedures which are done just for this research study.

These tests and procedures are:

- Electrocardiogram (ECG)

- DEXA Scan
- Urinalysis
- Physical Exam performed at your screening visit
- Glucose Tolerance Test
- Labs which include: CBC, lipids, liver function tests, electrolytes
- Infusion of Amino Acids
- Infusion/ingestion of Stable Isotopes
- Muscle Biopsies
- Urine pregnancy test
- Exercise Test

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You will be compensated for taking part in this research study. If you start the study but stop before finishing the study, you will receive part of this money: You will receive $40 for the screening visit on Day 1, and $30 for the exercise test (Maximal Oxygen Uptake Test) and DEXA scan on screening visit on Day 2.

You will receive: $500 for the 11-12 hour Main Study Visit

If you are not able to finish any of the 9 hr. infusion study visit, you will be paid $50 per hour for the time you spend, not to exceed $500. The overall compensation for participation in this research study is $570.

Payment for participation in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end.

Will your information or samples be used for future research?

Your samples will be stored and processed in the Principal Investigator's and Co-Investigators' laboratories in Mayo Clinic Arizona. Part of these samples may also be processed by laboratories at Mayo Clinic in Rochester, Minnesota. Finally, your samples may also be sent to a Mayo-designated laboratory outside of Mayo Clinic. The designated laboratory will use your sample solely for purposes as described in the research study. Your samples will be either returned to Mayo or destroyed by the designated laboratory upon termination or expiration of the research study. Your samples will be sent to the designated laboratory in a coded format, which protects your identity. Mayo has the right to end storage of the sample without telling you. Your information or samples collected for this study will not be used or shared for future research studies even if the identifiable information such as your name, Mayo Clinic number or date of birth is removed.

Participating in Future Research Studies

We would like to contact you in the future to see if you would be interested in participating in another research study. You will not be contacted 5 years after from the date you sign the consent form. Please indicate below if you are willing to be contacted about any future research studies. (this will not prevent you from being contacted by other study teams not related to this study)

I agree to be contacted about future research studies.

☐ Yes ☐ No Please initial here: _____Date: _____

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. Your medical information in electronic format will be stored on a computer that is password protected. Any hard-copy paper records will be stored in locked cabinet.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples

that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- Researchers involved in this study at other institutions.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study. Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
Plummer Building PL 3-02
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

MAYO CLINIC

Name and Clinic Number

Approval Date: **June 14, 2024**
Not to be used after: **June 13, 2025**

Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature