College of Public Health and Human Sciences

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CONSENT FORM

Project Title:	Exercise and Insulin Signaling in Human Skeletal Muscle
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Co-Investigator(s):	Matt Robinson, Ph.D.
Student Researcher(s):	Harrison Stierwalt, M.S., Sarah Ehrlicher, M.S., Ryan Wong
Study Staff:	Craig Graham, M.D., Nicholas Phillips, M.D., Joshua Lenhof, D.O.
Sponsors:	Collins Medical Trust John C. Erkkila, M.D. Endowment for Health and Human Performance National Center for Advancing Translational Sciences (NCATS)
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1. WHAT IS THE PURPOSE OF THIS FORM?

This form contains information you will need to help you decide whether to be in this research study or not. Please read the form carefully and ask the study team member(s) questions about anything that is not clear.

2. WHY IS THIS RESEARCH STUDY BEING DONE?

Insulin is a hormone that is produced after you eat food and has many effects throughout the body. A major effect is causing your muscles to take up sugar. People who gain weight do not respond as well to insulin. Exercise can improve the response of muscle to insulin, but the reasons why this occurs are not fully understood. We are studying the effects of exercise and insulin in people who are lean and people who are overweight.

3. WHY AM I BEING INVITED TO TAKE PART IN THIS STUDY?

You are being asked to take part in this study because you are 18 to 45 years old, do not regularly exercise and are either lean or overweight. You do not smoke or use nicotine products, and do not have any major medical condition such as diabetes or heart disease.

4. WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

This study is for research purposes only. The study will require **4 study visits** to the Samaritan Athletic Medical Center on the campus of Oregon State University. The total estimated time commitment for full participation in this study is ~19 hours, over a period of ~1 month.

Visit 1: General Screening Visit (~2 hours)

The purpose of this visit is to determine whether or not you are eligible to participate in the study. This visit will involve:

- Completing a general medical history questionnaire.
- Measurement of your height, body weight, blood pressure, waist and hip circumference.
- If you are female, you will provide a urine sample to ensure you are not pregnant.
- **Blood Sampling**. This involves briefly inserting a needle into a vein in your arm to collect a sample of your blood. The results of your blood tests will be available to you in a medical record with Samaritan Health Services.
- A low grade, whole-body x-ray scan (**DEXA scan**). This involves resting quietly on a padded table as the scanner passes over your body for about 5 minutes.

You will be provided a light snack before you leave.

Following completion of Visit #1, you will be notified regarding whether or not you are eligible to continue participation in the study. **If you are eligible**, we will schedule your next study visits.

Visit 2: Maximal Exercise Test Visit (~1 hour)

The purpose of this visit is to complete a **Maximal Exercise Test**. This will involve:

- Measuring the activity of your heart using a 12-lead electrocardiogram (an "EKG"). This will involve placing stickers on your skin across your chest.
- Measuring your blood pressure.
- Breathing through a mouthpiece and wearing a nose clip.
- Pedaling on a stationary bike for 10-15 minutes

At the start of the test pedaling the bike should be easy, but it will get progressively harder every minute. We will encourage you to continue pedaling until you voluntarily stop because you can no longer pedal anymore. At that point we will stop the test and you will rest for about 5 minutes. Once you are feeling okay, you will be allowed to leave.

Visits 3 and 4: Metabolic Study Visits (~8 hours each)

The third and fourth visits are longer study visits. A visual overview of the study events is provided in **Figure 1**. You will complete the visits in random order, and the visits will be separated by at least 1 week.

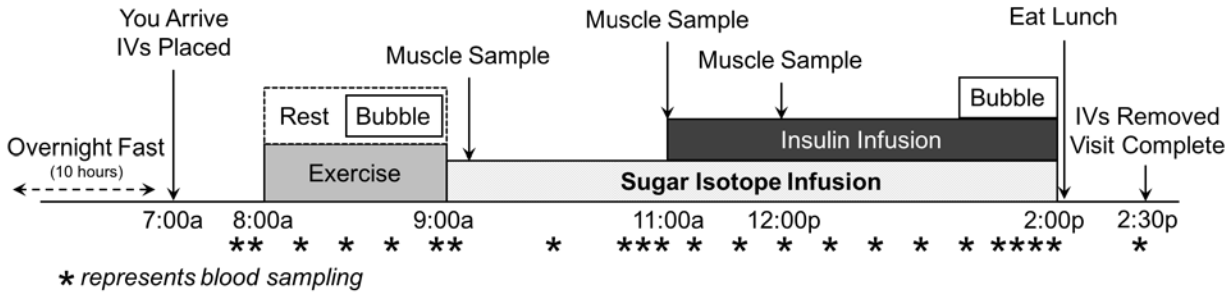

Figure 1. A timeline of events for the metabolic study visits. During these visits you will be asked to rest or perform stationary bike exercise, all of the other events of the study visit will be exactly the same during both visits. Listed times are approximate, and may vary slightly during your participation. Bubble refers to times that we will measure your resting metabolism.

The details of the study visit are provided in a supplemental document that will be provided for you. In general, visits 3 and 4 will each involve:

- Placement of 2 IVs for blood sampling and infusions
- Providing ~200 mL of blood (less than 2 cups)
- Providing 3 small muscle samples (each about the size of a pea) from muscle in your thigh, 2 from 1 leg and 1 from your other leg
- Arriving after an overnight fast (not eating for 10 hours), and remaining fasted for the duration of the visit

The only difference between Visits 3 and 4 will be whether you are asked to perform 1 hour of stationary bike exercise at a moderate intensity, or you remain resting in bed. All other events of these visits will be exactly the same. During both visits you will spend the majority of the time resting in a bed.

5. WHAT WILL HAPPEN TO MY PERSONAL DATA AND SAMPLES?

We may store your information, blood and muscle sample indefinitely. Because it is not possible for us to know what studies may be a part of our future work, we ask that you give permission now for us to use your samples and personal data without being contacted about each future study. Future use of your sample will be limited to studies about metabolism.

We will not pay you for the use of your sample or any products, patents, or licenses that result from these samples.

If you agree now to future use of your samples and personal data, but decide in the future that you would like to have them removed from research tests, please contact either of the researchers:

Sean Newsom, Ph.D (sean.newsom@oregonstate.edu)

Matt Robinson, Ph.D. (matthew.robinson@oregonstate.edu).

_____ You may store my samples and personal data for use in future studies.
Initials

_____ You may <u>not</u> store my samples and personal data for use in future studies.
Initials

Future contact: We may contact you in the future for another similar study. You may ask us to stop contacting you at any time.

Study Results: The information collected from you will be used for research purposes and cannot be used for diagnosing disease. If you are interested, we can discuss your results with you.

6. WHAT ARE THE RISKS AND POSSIBLE DISCOMFORTS OF THIS STUDY?

The possible risks and/or discomforts associated with the being in the study include:

Overnight fast: You will be asked to not eat any food or beverages containing calories or caffeine. You will only be able to drink water during your fasting period. You may feel light-headed, weak, or hungry during the fast.

Blood Sampling and Testing: You will have blood tests, body measurements and blood pressure measurements that are used for research purposes. This includes the potential for findings that may have implications for your health. In this case, you will be advised to visit your doctor. The risks of having blood drawn include some pain when the needle goes in and a small risk of bruising and/or infection at that site. Some people get lightheaded, nauseous, or faint. You are less likely to have these problems if you drink at least 2 glasses of water. The American Red Cross recommends that you do not donate more than 1 pint (32 tablespoons) of blood within a 2-month period. Tell the study team if you have recently had your blood drawn for any reason. The heating pad on your hand may cause discomfort or redness on the skin. This will go away when we remove the heat.

Dual energy x-ray absorptiometry (DEXA scan): You will be exposed to a low dose of x-rays during the DEXA scan. There are no discomforts associated with this procedure. The amount of radiation has a low risk of harmful effects. The maximum radiation dose you will receive in this study is 1.2 mrem, which his less than 1/1000th of the federal and state occupational whole body dose limit allowed to radiation workers (5,000 mrem). The average annual background radiation you already receive is at least 620 mrem/year. The more radiation you receive over the course of your life, the more the risk increases of developing a fatal cancer or inducing changes in genes. The radiation in this scan is not expected to significantly increase these risks, but the exact increase in such risks is not known.

DEXA scan and Pregnancy: The DEXA scan is not safe for pregnant women. The risks associated with radiation to an unborn child are not known. If you are a woman of childbearing potential, we will do a pregnancy test before the DEXA scan. We will be collecting a urine sample. This may be embarrassing. We will provide you privacy to minimize embarrassment. You must use an effective form of pregnancy prevention while you are enrolled in this study. Notify the study team immediately if you think or know that you have become pregnant during the course of this study.

IV Blood Sampling and Infusion: Risks are very similar to the risks provided above for **Blood Sampling** (review these risks listed above). The risks of IVs include fainting, pain, bruising, and

rarely infection at the site of the needle stick. With all infusions there is a risk of infection. To minimize the risk, all IV fluids will be prepared by a pharmacy and we will use sterile technique to administer the infusion. As a final precaution, infusions will be passed through a sterile filter. There is a risk that IV placement may be difficult. We may ask you if we can place an IV up to three times, for any given IV site. There is also a risk that an IV stops working during the study, this may require us to place a new IV.

Sugar Isotope Infusion: With all infusions there is a risk of infection. To minimize the risk, all IV fluids will be prepared by a pharmacy and we will use sterile technique to administer the infusion. As a final precaution, infusions will be passed through a sterile filter.

Insulin Infusion: There is a risk of low blood sugar during the insulin infusion. Low blood sugar can make you dizzy, sweaty, shaky or weak. We will be checking your blood sugar every 10 minutes during the insulin infusion and giving you sugar in your IV to keep your blood sugar at a normal, healthy level. There is a risk of redness and tenderness with IV sugar solutions. We will dilute the sugar with saline to decrease this risk. With all infusions there is a risk of infection. To minimize the risk, all IV fluids will be prepared by a pharmacy and we will use sterile technique to administer the infusion. As a final precaution, infusions will be passed through a sterile filter.

Resting Metabolism: There is a risk for claustrophobia (fear of closed spaces) during the resting metabolic rate when the plastic bubble is over your head. However, the plastic bubble is clear and fresh air will come through the bubble for the entire duration of the test.

Muscle Sample: Possible risks include bleeding and infection. We will minimize bleeding and swelling by applying pressure to the site. We will minimize infection by using strict sterile procedures. You will also be given care instructions to follow for the days following the biopsy to minimize the risk of infection. Pain is unlikely because we are using a local anesthetic (lidocaine) but you may feel pressure in your leg during the biopsy. There is a risk that we may need to enter the biopsy site up to three times to get a good muscle sample. The site may be sore for a few days after the biopsy. In rare instances, some people have residual numbness at the site for a year or longer. There may be a small scar at the biopsy site. There can be a temporary stinging sensation in your skin when we use lidocaine. There is a risk for allergic reaction to lidocaine. You must not be allergic to lidocaine to participate in this study.

Maximal Exercise Testing: The risk of maximal exercise tests ("VO2 max") include:

- Acute exercise may present a risk of sudden death
- Cardiovascular event (i.e., heart attack or cardiac arrhythmia)
- Overall risk of cardiac events is about 6 events per 10,000 tests
- Serious injury
- Falling
- Physical discomfort from the test and equipment
- Fatigue
- Muscle aches, cramps, joint pain

- Muscle strain and/or joint injury
- Delayed muscle soreness
- Abnormal blood pressure/heart rate
- Shortness of breath
- Lightheadedness, fainting
- Dizziness
- Nausea

Importantly, the facility where you will be tested will be equipped to handle these types of emergencies and the staff involved in the testing procedure are well trained. However, you must understand that the stress of exercising at high levels can be dangerous and that you may stop the test at any time.

Moderate Exercise: The risks of moderate exercise include:

- Physical discomfort from the test and equipment
- Fatigue
- Muscle aches, cramps, joint pain
- Muscle strain and/or joint injury
- Delayed muscle soreness

Personal Health Information: There is a chance that we could accidentally disclose information that identifies you. We will minimize this risk by removing your identity from samples and keeping your personal information in locked files and password protected databases.

As with any research study, there may be additional risks that are unknown or unexpected.

7. WHAT HAPPENS IF I AM INJURED?

Oregon State University, OHSU and NCATS do not offer to pay for research-related injuries. If you think that you have been injured as a result of being in this study, please contact the study team for possible treatment. We may advise you to contact your primary care provider.

Any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OSU, OHSU or its caregivers and researchers for a claim relating to care or research, and the time you have to bring a claim.

8. WHAT ARE THE BENEFITS OF THIS STUDY?

This research study is being performed for research purposes only. We do not know if you will benefit from being in this study. However, you may learn more about your health.

9. WILL I BE PAID FOR BEING IN THIS STUDY?

You will be paid $255 for completing the entire study. If you stop or are removed from the study, your payment will be according to the following schedule:

Screening:	No payment
Maximal Exercise Test:	$15
1st Metabolic Study Visit:	$100
2nd Metabolic Study Visit:	$140

For your participation, you will also receive a complimentary two-week trial period for the "Power Hour" fitness program offered by Samaritan Athletic Medicine. This free trial period is only available to participants that complete both the initial screening and maximal exercise test, and are deemed medically eligible to participate in the metabolic research study. Participation in this complimentary fitness program is entirely voluntary and cannot begin until after you have ended the metabolic research study.

If you choose to stop or are removed from the study, your tissue samples and information collected will be kept by the study team and continue to be used. Some reasons why you may be removed from the study are:

- If you develop a condition that excludes you (such as becoming pregnant)
- If you do not follow the study procedures
- If the study is stopped

10. WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

The study team will cover costs related to the study. You will not be compensated for transportation or other costs.

11. WHO WILL SEE THE INFORMATION I GIVE?

The study team will have access to your information, which will include your health information for use in the study. The information you provide during this research study will be kept confidential to the extent permitted by law. Research records will be stored securely and only researchers will have access to the records. We may also share your information with other researchers at OHSU who are collaborating on this research study. Federal regulatory agencies (such as the Food and Drug Administration or National Institutes of Health) the Oregon State University and Oregon Health and Science University Institutional Review Boards (committees that review and approve research studies) may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

If the results of this project are published your identity will not be made public. We may share your samples or data with researchers at other universities, but we will not include your name or contact information. There is the potential that your information could be further released and no longer protected by federal privacy laws.

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.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the NIH which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

12. WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Participation in this study is voluntary. If you decide to participate, you are free to withdraw from the study and withdraw your permission for the study and use of your health information at any time without penalty, including the right to receive health care services or insurance coverage for services. If you choose to withdraw from this project before it ends, the researchers may keep information already collected about you and this information may be included in study reports.

13. WHO DO I CONTACT IF I HAVE QUESTIONS?

If you have any questions about this research project or wish to withdraw, please contact:

Sean Newsom, Ph.D. (541) 737-1613 (sean.newsom@oregonstate.edu)

Matt Robinson, Ph.D. (541) 737-1126 (matthew.robinson@oregonstate.edu).

If you have questions about your rights or welfare as a participant, please contact the Oregon State University Institutional Review Board (IRB) Office, at (541) 737-8008 or by email at IRB@oregonstate.edu

14. WHAT DOES MY SIGNATURE ON THIS CONSENT FORM MEAN?

Your signature indicates that this study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Do not sign after the expiration date: 08/01/2019

Participant's Name (printed): _____

_____ _____
(Signature of Participant) (Date)

_____ _____
(Signature of Person Obtaining Consent and Authorization) (Date)