Permission to Take Part in a Human Research Study

Title of research study: Effects of MetAP2 inhibition on bioenergetics and aging-associated characteristics in adipose (fatty) tissue (BIO-AGE)

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Sub-Investigator: Bret H. Goodpaster, Ph.D.
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Daytime Phone Number: 407-303-7100

24-hour Phone Number: 407-303-7100

Sponsor: AdventHealth Orlando

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Why am I being invited to take part in a research study?

We invite you to take part in a research study because you are 18-30 years old or older than 65 years old and meet other study specific criteria:

- Body Mass Index (BMI) ≤ 40 kg/m2
- Normal blood glucose (Non-Diabetic)
- Weight stable (±5 kg) for prior 3 months
- Not currently dieting, Non-pregnant, and Non-smokers
- Sedentary (<20 min of activity, 3x/week)
- Willing to commit to the schedule of assessment visits
- Able to speak and understand written and spoken English
- Understands the procedures and agrees to participate by giving written informed consent

What should I know about a research study

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can ask all the questions you want before you decide.
- If you are an employee of AdventHealth Orlando, you should know that your participation or lack of participation in this study will not affect your employment or relationship with AdventHealth Orlando.

Why is this research being done?

This study is being done to collect fatty tissue from young and older individuals and gather data on the effect of methionine aminopeptidase protein (MetAP2) inhibition on that fatty tissue in the laboratory.

How long will the research last?

We expect that you will be in this research study for up to approximately 4 weeks, dependent on scheduling.

How many people will be studied?

We expect about 10 in Group 1 (18-30 years old) and 10 in Group 2 (≥ 65 years old) will take part in the entire study.

What happens if I agree to be in this research?

If you agree to take part in the study, you will first sign the Informed Consent Form (ICF) before any study related procedures are performed. After signing this ICF, you will undergo an initial screening process to determine if you are eligible to participate in this study**.** Due to COVID-19 the following

research procedures may be conducted or collected remotely: written informed consent process, medical history, concomitant medications, and eligibility criteria.

If this consent is being reviewed and obtained remotely and you decide to participate, we will ask you to sign this consent form and bring it with you to the screening visit.

The study consists of three visits (one screening visit and two outpatient visits). The study duration may be completed approximately 4 weeks, depending on your availability and scheduling. A detailed description of all major study related procedures is given below the description of the study visits.

The fat samples we collect will be used to advance science and public health. Some of the fat samples will be used for cell line development and gene sequencing. This means that some of the cell samples will be used to look at certain parts of your DNA that will help the researchers to understand how your genes respond to lifestyle modifications. These DNA samples and data will also be stored so we can continue to use them in the future. Cell lines are living tissue samples that are grown in a laboratory. A cell line can provide cells in the future without requiring more samples from you.

Screening Visit (outpatient, ~2 hours): Participants will arrive for this outpatient visit after a 10-hour overnight fast. After obtaining informed consent, data collection for assessing eligibility will commence. The screening visit will include:

- Assessment of participant eligibility (may occur remotely)
- Demography collection
- Adverse event (AE)/concomitant medication review
- Physical exam, including health history
- Anthropometrics that include hip, waist, and thigh measurements
- Urine for pregnancy test and toxicology screen
- Screening blood work (including CBC with differential and platelets, comprehensive metabolic panel, lipid profile, blood glucose, ALT, AST, Alkaline Phosphatase, insulin level, HbA1C, TSH)
- A complete medical history (including, but not limited to, alcohol use, concomitant medications, health conditions, allergies and exercise habits; may occur remotely)
- Vital signs (respiratory rate, temperature, heart rate, blood pressure)
- EKG
- Height and weight
- Body mass index (BMI)

Visit 1 (Day 1; outpatient, ~1-2 hours): Participants will arrive at AdventHealth after a 10-hour overnight fast for a fatty tissue biopsy following a standardized procedure. This visit will include:

- Review of medical history
- Vital signs (blood pressure, heart rate, respiratory rate, and temperature)
- Fasting blood draw for archiving blood. Blood draw will be approximately 3 tablespoons (40ml)

- Urine collection for pregnancy for woman of childbearing potential only
- Fatty tissue biopsy You will be placed in a supine position with arms placed at your side while your abdominal skin is marked with a skin marker and cleansed with chlorhexidine. Afterwards, the abdominal fatty tissue biopsy will be performed.

Follow-up (~30 minutes): You will follow up with at TRI within 24-72 hours to ensure no complications or adverse events have occurred.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

- Provide truthful information about your medical history, current medical conditions, and drugs that you are taking.
- Do not take any new prescription or over-the-counter medications that are prohibited in the study without prior approval from the study doctor.
- Do not begin a diet or weight loss program.
- Fast overnight for at least 10 hours prior to scheduled visit as indicated, i.e., no food or beverage except water and no more than one glass of water within 2 hours before the indicated visit.
- Do not donate blood or plasma during the study.
- Tell the study doctor about any problems you have during the study.

What other choices do I have beside taking part in the research?

This research is not designed to diagnose, treat or prevent any disease. Your alternative is to not take part in the research.

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

This section will cover the potential risks we are aware of at this time. You will be informed of any significant new findings that develop during the investigation that may affect your willingness to continue in the study in a timely manner.

Vital Signs/Blood Pressure Testing: You may experience temporary discomfort during blood pressure recordings due to the pressure of the cuff on your arm.

EKG (Electrocardiogram): There is a small possibility there may be some redness or itching if you happen to be allergic to the electrodes' adhesive**.**

Fatty Biopsy: The abdominal fatty biopsy with a needle may cause discomfort, bruising, scar and soreness for several days. There is also the possibility of a vasovagal reaction (reaction of the nervous system due to anxiety) that may cause fainting. Bleeding and infection are rare, but to further reduce these risks, pressure is held, and ice bag are applied to the abdomen post-biopsy to decrease the risk of

bruising. Sterile materials are used to minimize the risk of infection. Additional unusual risks include allergic reactions to the plastic bandage, and skin redness, irritation, chafing from the steri-strips, and and/or loss of sensation of skin around the biopsy site could occur. This loss of skin sensation may be temporary, but in some rare cases, may be permanent. An infrequent risk is that there is an allergic reaction to the Lidocaine is used to numb the abdomen and is given just before the biopsy. Lidocaine has risks which are described next.

Local Anesthetic (Lidocaine): A rare, but possible side-effect of lidocaine is an extreme allergic reaction that could result in symptoms such as severe shortness of breath, swelling of the throat, redness, swelling and tenderness of the skin, and skin rash. To prevent this type of reaction, you will be asked at your screening visit about any problems you have had with lidocaine. If you have had any problems in the past with lidocaine, for your safety, you will not be allowed to be in the study.

Blood Draws: Risks include discomfort, pain, soreness, bleeding, and bruising at the site of the needle insertion (common); phlebitis: an inflammation and then hardening of the vein with tenderness that can be accompanied by several weeks of discomfort in the area where the blood was taken. Risks also include lightheadedness, fainting, and infection (rare).

You should not be or become pregnant while taking part in this research study.

There is a risk of loss of confidentiality of your information. You should know that there are measures in place to prevent this from happening. A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information**.** Please ask the study investigator or study staff if you would like to know more about how your information will be protected while you are in this study

Will being in this study help me in any way?

There is no benefit for study participation. The study is designed to answer questions concerning metabolism and is not a treatment for you specifically. In the future, others may benefit from the information learned from this study.

Are there any costs in this study?

The TRI will provide the study supplies, tests, and procedures at no charge during this study.

You or your insurance company may be billed for any other tests, procedures, or medications that may be necessary for the treatment of your medical conditions, or follow-up regarding incidental findings. These costs are not covered by this research study.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study. If your insurance company does not pay, you may be billed for those charges.

You might have unexpected expenses from being in this study. Ask your study team to discuss the costs that will or will not be covered by the sponsor. This discussion should include who will pay the costs of treating possible side effects.

Will there be compensation for injury?

In the event of research-related injury or illness, medical care will be made available. Generally, this care will be billed to you, your insurance, or other third party. AdventHealth has no program to pay for medical care for research-related injury or illness.

What happens to the information collected for the research?

To the extent allowed by law, we limit your personal information to people who have to review it. We cannot promise complete secrecy. The IRB and other representatives of this organization may inspect and copy your information. It may also be given to governmental agencies in other countries. The information may also be used to meet the reporting requirements of governmental agencies. The information may be reviewed by the AdventHealth IRB. Other AdventHealth representatives may review this research in their oversight and auditing roles.

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

Federal law provides additional protections of your medical records and health information. See the HIPAA section below.

Information that identifies you might be removed from the data or specimens collected for this study. After that information is removed, your data and specimens might be used for future research studies or given to other researchers without your consent.

Can I be removed from the research without my OK?

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason, including:

- if it is in your best interest;
- you do not consent to continue in the study after being told of changes in the research that may affect you;
- you have not followed study instructions;
- the sponsor has stopped the study;
- AdventHealth or other administrative area of AdventHealth has decided to stop the study; or
- administrative reasons require your withdrawal

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What else do I need to know?

It is important that you tell your study doctor if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him or her.

You should contact your study doctor at his/her office number, which is a 24-hour number, call 911, or go directly to an Emergency Room. If you have additional questions or concerns, call the Principal Investigator listed on page one of this document.

You will be told about any new information that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.
This research is being funded by AdventHealth Orlando.

Your specimens (even if identifiers are removed) may be used for commercial profit. You will not share in this commercial profit.

HIPAA Authorization to Release Information for Research

If you have not received a copy of the AdventHealth Orlando Privacy Notice, please request one. If you have questions about your privacy rights, you may contact AdventHealth Orlando's Privacy Officer at PH: (407) 200-2961.

Privacy laws, including the Health Insurance Portability & Accountability Act (HIPAA) and other federal and state laws, rules, and regulations, protect your individually identifiable health information (also called Protected Health Information or PHI). If you agree to be in this study, privacy laws require you to sign this Authorization that describes your rights and explains how your Protected Health Information (PHI) will be used and disclosed for this research study.

By signing this informed consent/HIPAA Authorization, you will be authorizing the principal investigator, his/her research staff, and the sponsor (see top of page one) to use (which includes reviewing your medical records as necessary to conduct the study) and disclose your PHI for the purposes described below. By signing this form, you will also be authorizing your doctors, AdventHealth Orlando personnel, and individuals who provide health care services at AdventHealth Orlando to disclose your PHI for the purposes described below. This includes information from your past, present, and future medical records.

This Authorization does not have an expiration date. This means the researchers and others associated with this study may use and disclose your protected health information for as long as necessary to complete the study.

If you volunteer to take part in this research study, others may learn your identity. Study information may identify you in the following ways.

- Name
- Address
- Telephone number
- Social security number for payment purposes

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This study includes a number of researchers, businesses and government agencies. They may use your health information and share it with others. We want you to know who may use this information and how they may use it.

Who may use and give out information about you?
The Investigator (study doctor) and research staff will have information about your health that tells us your identity. They may give this information to others during and after the study.

Who may see this information?
The study sponsor may see your health information and know your identity. "Sponsor" includes people or companies working for or with the sponsor or owned by the sponsor.

In addition to the study sponsor and its agents, the following people, agencies and businesses may get information from us that identify who you are.

- Doctors and healthcare professionals taking part in the study
- U.S. Department of Health and Human Services (DHHS), which includes:
  - U.S. Food and Drug Administration (FDA)
  - U.S. Office of Human Research Protections (OHRP)
- Government agencies that must receive reports, including reports about certain diseases
- Government agencies in other countries
- AdventHealth Orlando representatives
- Institutional Review Board (IRB)
- Accreditation organizations

What information may be used and shared?
If you decide to be in this study, medical information that identifies you and relates to your participation will be created, used, and/or shared. This may include the following types of medical information.

- Information obtained from procedures used to find out if you are eligible to take part in this study. This may include physical examinations, blood and urine tests, x-rays and other procedures or tests, and any other information that you may release to us, including information about your health history.
- Information from your medical chart.
- Information obtained in the course of the study including information about your response to any study treatments you receive, information related to study visits and phone calls, physical examinations, blood and urine tests, x-rays and other tests or procedures that may be performed, and other medical information relating to your participation in this study.

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Why will this information be used and/or shared?
Information about you and your health, that might identify you, may be given to others to carry out the research study. The sponsor and/or the investigator will analyze and evaluate the results of the study. In addition, if this is a sponsored study (see page one) people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?
If you sign this consent form, you will be giving permission to use and give out the health information listed above for the purposes described above. If you decide not to give permission, you will not be able to be in this research. However, this will not change your relationship with your doctor or with AdventHealth Orlando and you will still be able to receive all benefits to which you are entitled.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this authorization (permission) will never expire (end) unless you revoke (cancel) it in writing.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study. If you want to withdraw your permission and not have your information shared beyond what has already been shared, please send the written notice to:

Lauren M. Sparks, Ph.D.
301 E. Princeton Street, Orlando, FL 32804
(407) 303-7100

When you withdraw your permission, no new health information that might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
If you give permission for the hospital or the investigator to share your identifiable health information to other people or businesses, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Your personal information may be disclosed if required by law. Your records for this study may be sent by facsimile transmission (FAX machine) or over the Internet. It is possible that your records could be sent to the wrong person.

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How long is my information kept?
Research with private health information must be maintained for seven years after the research study has been closed at the AdventHealth Orlando site. The Sponsor may require a longer period of time.

What happens if I agree to be in research, but later change my mind?
Participation in this study is voluntary. You will be free to withdraw consent and discontinue participation from the study at any time without penalty or loss of benefits. If you decide to leave the research, contact the investigator so that the investigator can obtain your written notice of your withdrawal of permission, as described above.

If you stop being in the research, already collected data may not be removed from the study database.

Will I be paid for taking part in this research?

For taking part in this research, you may be paid up to a total of $250 for your time and effort. Your compensation will occur as follows:

- You will be provided a Mastercard® as a means to receive payments for this study. The terms and conditions for this card will be provided to you for review.
- Your payment will be requested within 3 business days from completion of your last study visit.
- If all study visits are not completed, you will receive the following prorated amount for the visits you have completed

Visit	Amount
Screening	$0
Visit 1	$225
Follow-up	$25

For participants who are not AdventHealth Orlando Employees: If you receive more than $600 in payments in a calendar year from AdventHealth Orlando, this income will be reported to the IRS. You may be required to pay tax on this income.

For participants who are AdventHealth Orlando or AdventHealth Medical Group Employees: All payments will be reported as added income to your base salary and will be taxed on a future paycheck.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at the phone number listed above on the first page.

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This research is being overseen by an Institutional Review Board ("IRB"). The IRB is a group of people who review and approved research studies to be conducted at AdventHealth Orlando. You may talk to them at (407) 200-2677 or AH.IRB.General@adventhealth.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

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Signature Block for Adult Subject Able to Consent

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

Printed name of subject	
Signature of subject	Date
Signature of person obtaining consent Printed Name	Date

[Use the following block if a witness will observe the consent process. E.g., short form of consent documentation or illiterate subjects.]

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process Printed Name	Date

If signature of a witness not obtained, confirm the following:

❑ Subject is able to read in this language and write