Targeting the Endothelial Glycocalyx to Enhance Vascular Function and Exercise- Induced Vascular Adaptations in Type 2 Diabetes

NCT# 05205005

Protocol: 2062542

Funding Agency: Veterans Administration

Principal Investigator/Study Chair: Camila Manrique-Acevedo, MD, Jaume Padilla, PhD

Informed Consent version 12.1AU

October 23, 2023

Participant Name: _____ Date:_____

Title of Study: Targeting the Endothelial Glycocalyx to Enhance Vascular Function and Exercise- Induced Vascular Adaptations in Type 2 Diabetes – Phase II

Principal Investigator: Dr. Camila Manrique-Acevedo, MD; Jaume Padilla, PhD

VA Facility: Harry S. Truman VA

KEY SUMMARY INFORMATION ABOUT THIS STUDY

You are being invited to take part in a research study that is being funded by Department of Veterans Affairs. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. Taking part in this study is completely voluntary.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn if taking a dietary supplement will improve your blood vessel health and the adaptations of your blood vessels to exercise. Your participation in this research will last about 3 months.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

Participating in this study may have no direct benefit to you. It is possible that you will learn health information about yourself by participating.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

There are risks to taking part in any research. If you choose to participate in this study, you will need to complete fasting blood work and/or intravenous line placement, hold medications, and avoid tobacco use on days of study visits, and complete several non-routine study tests. Study tests may cause some mild discomfort and include the use of ultrasound and DEXA, which causes radiation exposure. If you choose to participate you have to take either a supplement or placebo pill. This supplement, commercially known as Endocalyx is being used as an investigational drug in this study. It has been filed under the Research Investigational New Drug (IND) application #164629 with the Food and Drug Administration (FDA).

Participation in this study is completely voluntary. You may choose not to participate in this study. If you choose not to participate, there will be no impact on the clinical care that you receive at the Harry S Truman VA Hospital. For a complete description of alternate treatment/procedures, refer to the Detailed Information section of this consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Camila Manrique-Acevedo, MD at the Harry S. Truman Medical Center in Columbia, Missouri. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is: Camila.Manrique-Acevedo@va.gov *or* (573) 882-2554.

DETAILED INFORMATION ABOUT THE STUDY

WHAT IS THE PURPOSE OF THIS STUDY?

By conducting this research project, we hope to learn whether dietary supplementation with glycocalyx precursors (DSGPs) in the form of the supplement, improve glycocalyx integrity and vascular adaptation to exercise. In other words, we would like to learn whether taking this supplement will improve your blood vessel function and exercise tolerance. We hope to find new strategies to treat vascular disease in people with type 2 diabetes.

HOW LONG WILL I BE IN THE STUDY?

This research study is expected to take approximately 6 years. Your individual participation in the project will take about 3 months. We will be enrolling a total of 96 participants in the study interventions. The 24 participants in Aim 1 will participate for about 3 months. The 72 participants in Aim 2 will participate for about 3 months.

WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

If you take part in this study, you will have the following tests and procedures:

Screening
The screening visit will last up to 1 hour. After signing the consent form, medical information will be obtained by the study team, including date of birth, gender, ethnic/racial category, height, body weight (history of body weight gain or loss), waist circumference, vitals (including: heart rate, respirations, temperature, and blood pressure), ECG, and a medical history questionnaire. A fasting blood draw will be taken to test for biochemistries.

Equipment Fitting Visits
Equipment fitting visits at the Clinical Translational Research Unit East/West (CTSU) will last up to 1 hour. In the week prior to both the pre and post assessments, you will have a fitting appointment. You will be fitted with an ambulatory blood pressure monitoring system and instructed on its use. You will be asked to take the monitoring system home with you and wear

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

them over a 24-hour period prior to your pre and post assessments. At this visit, we will also show you how to use the Glycocheck equipment and have you practice its use.

Assessments (Pre and Post)
Assessment visits at the Clinical Translational Research Unit East/West (CTSU) will last up to 8 hours. You will be asked to fast and hold any diabetes medications that you are prescribed on the morning of your assessment visits. You will also be asked to avoid tobacco use on the morning of your assessment visits. If you qualify for the study intervention and choose to participate, you will also undergo measurements including Glycocheck, pulse wave velocity, brachial and femoral artery flow-mediated dilation (FMD), and insulin infusions. You will be randomized to a supplement or placebo treatment. You can find a description of these procedures in this form. The information and/or samples we collect from you for this study will not be used or shared with other investigators for future research studies. This applies even if we remove all information that could identify you from the data and samples. You will also have a fasted blood draw taken to test for biochemistries at the post-assessment visit.

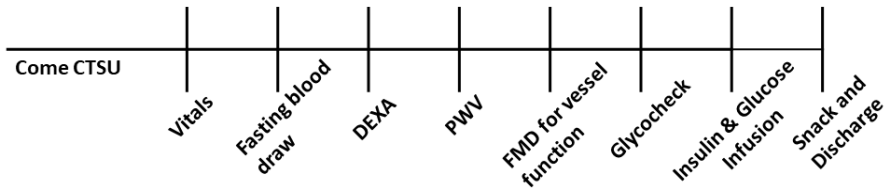

Figure 1. Order of Procedures at the Pre and Post Assessment visits in the University of Missouri Clinical Translational Research Unit East/West (CTSU) . Assessment visits last about 8 hours.

Safety Monitoring
You will have a blood draw to test for biochemistries 7-14 days after beginning the supplement/placebo. This safety visit will occur at the VA Hospital. In addition, participants will be contacted by the study team on a weekly basis to check in. You may be asked to repeat blood draws for safety labs/safety visits if the study safety officer deems it necessary and appropriate for your safety monitoring. You may also be asked to repeat safety blood draws if your specimens are compromised for any reason or there is questionable accuracy of the results.

Procedures and Risks
All the procedures that are performed during this clinical trial are for research purposes only. **The procedures are <u>not</u> part of your routine care at the Truman VA Hospital and Clinics.**

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

Any procedure has possible risks and discomforts. The procedures (listed below) in this study may cause all, some, or none of the risks or side effects listed. Rare, unknown, or unexpected risks also may occur.

To help minimize risk to participants, all medical procedures are performed under the supervision of the Primary Investigator, Dr. Camila Manrique-Acevedo, MD by qualified research staff in a clinical setting.

We will tell you about any new important information we learn that may affect your decision to continue to participate in this study.

Blood drawing and its risks

- *Description:* During this study you will have blood drawn through a needle.
- *Risks*: Drawing blood from your arm can cause minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely. As a result of your participation in this study you will have given blood. If you wish to perform other research after you finish this project, you should let the investigator know that you have donated up to 180mL (about ¾ cups). Your blood volume will be checked during screening to make sure that your volume is in safe limits.
- *Location of Procedure:* Blood draw will be performed by a licensed nurse or phlebotomist in the VA Endocrinology Clinic or the University of Missouri Clinical Translational Research Unit East/West (CTSU).
- *Frequency*: Blood draw will occur at screening, preassessment, safety check, and post assessment visits. You may also be asked to repeat safety blood draws at the discretion of the study safety officer.

Insertion of venous catheters

- *Description:* IVs will be placed to collect blood during study assessments.
- *Risks:* The potential risks of venous catheterization include infection, swelling and discomfort at the catheter insertion sites. Some bleeding may occur during the insertion of the catheters as well after the catheters have been removed. There is also the possibility of fainting, dizziness, and possible pain and bruising as a result of catheter insertion. These risks will be greatly minimized by using sterile procedures and having an experienced registered nurse placing the venous catheters.
- *Location of Procedure:* Insertion of catheters will be performed by a licensed nurse or phlebotomist in the University of Missouri Clinical Translational Research Unit East/West (CTSU) .
- *Frequency:* Insertion of IVs will occur at preassessment and post assessment.

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

Insulin & Glucose infusion

- *Description:* Two IVs will be placed. Glucose (sugar) and insulin will be infused over the course of 1 hour while the nurse and research team continually check blood sugar levels and take ultrasound images of the blood vessels in your legs.
- *Risks:* The potential risks during the infusion include mild nausea or light-headedness, and mild to moderately high or low blood glucose levels. However, blood glucose will be continually monitored throughout the test. Also, drinks and snacks will be available at the completion of testing should you have low blood sugar or feel nauseous.
- *Location of Procedure:* Insulin infusions will be performed at the University of Missouri Clinical Translational Research Unit East/West (CTSU). This procedure is routinely performed by the research team at the Clinical Translational Research Unit East/West (CTSU). This procedure includes the use of insulin in an off-label manner, not approved by the FDA.
- *Frequency:* Insulin infusions will occur at preassessment and post assessment.

Perflutren (Definity)

- *Description:* Contrast will be infused through an IV to visualize the blood cells in the muscles during the insulin infusion.
- *Risks:* A potential side effect from the Perflutren ultrasound contrast agents is temporary back pain, joint pain, headache, shortness of breath and/or flushing. These symptoms occur in about one in 200 subjects and are mild in intensity in 90% of those subjects who experience this reaction. If this happens then let us know and infusion of the agent will be stopped. The back and joint pain will go away in a few minutes. A serious allergic reaction to ultrasound contrast agents is unlikely (1 in 10,000), but possible. Symptoms of an allergic reaction include: Rash, itching, swelling, severe dizziness, chest pain and trouble breathing. We are using this contrast agent to measure blood flow in your leg muscles using a dose approved by the FDA. This procedure includes the use of Definity in an off-label manner, not approved by the FDA
- *Location of Procedure:* Infusion of contrast will occur at the University of Missouri Clinical Translational Research Unit East/West (CTSU).
- *Frequency:* Infusion of contrast will occur at preassessment and post assessment visits.

Heart rate measurements via ECG

- *Description:* Heart rate will be measured.
- *Risks:* Some people may have a skin irritation from the patches that connect the wires on your chest to the computer. Skin and hair are pulled slightly when the patches are removed after the test. Research personnel will attach and remove the patches as carefully as possible.
- *Location of Procedure:* Heart rate will be monitored at the VA Endocrinology Clinic or the University of Missouri Clinical Translational Research Unit East/West (CTSU).

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

- *Frequency:* Heart rate monitoring will occur at screening, preassessment, and post assessment visits.

Glycocheck

- *Description:* A small, light-emitting probe will be placed under your tongue. The probe allows researchers to assess the integrity of your blood vessels.
- *Risks:* There are no risks associated with this test.
- *Location of Procedure:* The Glycocheck procedure will be performed at the University of Missouri Clinical Translational Research Unit East/West (CTSU) by a trained research technician.
- *Frequency:* The Glycocheck procedure will be performed at the preassessment, and the post assessment visits.

Pulse Wave Velocity (PWV)

- *Description:* A special non-invasive device will be used to assess blood pressure and flow. A blood pressure cuff will be wrapped around the upper arm and upper leg of the participant. The cuffs will periodically inflate to squeeze tightly for less than 60 seconds. A pressure sensor, the size of a pencil will be placed over the skin of the neck region to obtain the pressure wave form in the neck vessel (i.e., carotid artery). This procedure takes about 15 minutes.
- *Risks:* The blood pressure cuff will squeeze the arm and leg tightly; however, any discomfort will be alleviated as soon as the pressure in the cuff is released.
- *Location of Procedure:* PWV will be assessed at the University of Missouri Clinical Translational Research Unit East/West (CTSU).
- *Frequency:* PWV will be assessed at both the preassessment and post assessment visits. We will complete this test two- three times per study visit.

Flow-mediated dilation via doppler ultrasound (FMD)

- *Description:* A blood pressure cuff will be inflated on your forearm and/or leg for up to five minutes. During this time, your arm/leg may get numb due to decreased blood flow. An ultrasound image/video of your upper arm/leg will be taken before, during, and after the inflation of the blood pressure cuff. This is a measurement of vascular function. When assessing FMD, the blood pressure cuff will squeeze your arm/leg tightly; however, any discomfort will be alleviated as soon as the pressure in the cuff is released.
- *Risks:* There are no risks associated with this procedure.
- *Location of Procedure:* FMD will be assessed at the University of Missouri Clinical Translational Research Unit East/West (CTSU).
- *Frequency:* FMD will be assessed at both the preassessment and post assessment visits. We will complete this test twice per study visit.

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

Measurement of body composition by DEXA

- *Description:* DEXA is a procedure that measures body composition- how much fat and muscle your body has. It is a type of x-ray machine with a moving arm. This procedure involves lying on a table for 15 minutes while the DEXA machine passes over your body. Although you will need to remain very still and quiet, you will feel nothing and should have no discomfort.
- *Risks:* If you have participated in any other research study involving ionizing radiation exposure in the past 12 months, discuss this with the Investigator to determine if you are eligible to participate in this study. You will be exposed to a small radiation dose which is about 2% of the average radiation dose from all sources (natural background radiation, consumer appliances, radon gas, medical tests, etc.) that a person receives in the United States receives each year. However, radiation effects are cumulative. You should always inform future doctors of your participation in this study. Only postmenopausal participants will be included in the study, therefore no pregnancy test will be pursued prior to DEXA.
- *Location of Procedure:* DEXA will be assessed at the University of Missouri, Clinical Translational Research Unit East/West (CTSU).
- *Frequency:* DEXA will be assessed at both the preassessment and post-assessment visits.

Dietary Recall

- *Description:* You will be interviewed (asked questions about) the foods and beverages that you have recently consumed or asked to keep a record of the foods that you consume for 3 days.
- *Risks:* There are no risks with this procedure.
- *Location of Procedure:* You will be interviewed/instructed by the study registered dietitian or trained research technician in a private setting. This procedure will occur at the University of Missouri Clinical Translational Research Unit East/West (CTSU).
- *Frequency:* Dietary Recall/Assessment will be performed at the preassessment and post assessment visits.

Ambulatory Blood Pressure Monitoring

- *Description:* You will be fitted with an ambulatory blood pressure cuff to wear for a continuous 24-hour period prior to both your pre and post assessment visits. The blood pressure cuff will automatically inflate and deflate periodically during wear. You will also be required carry the small blood pressure machine in a carry case or attached to a belt during this period.
- *Risks:* There are no risks to this procedure. It may cause discomfort due to cuff inflation or interfere with sleeping

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

- *Location of Procedure:* You will be fitted with the ambulatory blood pressure cuff at the Clinical Translational Research Unit East/West (CTSU) by a member of the research team. You will wear the cuff during two separate 24h-hour periods as you do your daily activities.
- *Frequency:* Ambulatory blood pressure monitoring system will be worn for two separate 24-hour periods: one prior to your pre-assessment visit and one prior to your post-assessment visit.

Supplement: Endocalyx

- *Description:* Dietary Supplementation of Glycocalyx Precursors (DSGP) commercially available as Endocalyx™ (Microvascular Health Solutions LLC, Alpine, UT) which includes: glucosamine sulfate, fucoidan, superoxide dismutase, and high molecular weight hyaluronan is the supplement being compared to placebo. You will be required to take 6 capsules of the supplement. This supplement is being used as an investigational drug in this study. It has been filed under the Research Investigational New Drug (IND) application #164629 with the Food and Drug Administration (FDA).
- Risks: There is known risks associated with supplementation with DSGP. Nevertheless, subjects with known allergies to any of the compounds in the supplement (glucosamine extract, fucoidan extract, olive extract, artichoke extract, red and white grapes extract, melon concentrate, hyaluronic acid) will not be included in the study. If subjects exhibit changes in their health status across any system related or unrelated to the study intervention, Dr. Whaley-Connell (safety officer) will be consulted for advice.
- *Location of Procedure:* You will be responsible for taking the study supplement or placebo daily. Capsules are to be swallowed whole and consumed with food. Do not crush or empty capsules. Take 3 capsules every 12 hours with food.
- *Frequency:* You will take the study supplement or placebo daily for two months (+/-4 days). The study team will monitor your dosing compliance weekly.

Randomization and Blinding

- *Description:* You will either take a placebo or a supplement as part of this study. There is an equal but random chance of you being assigned to either the placebo or supplement treatment. This is referred to as randomization. Neither you or the study team will know whether you are taking the placebo or supplement. This is called blinding.
- *Risks: None*
- *Location of Procedure:* You will be responsible for taking the study supplement or placebo daily.
- *Frequency:* You will take the study supplement or placebo daily for two months. The study team will monitor your dosing compliance weekly.

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

Transport via wheelchair

- *Description:* The study team may ask to transport you between clinical research spaces via wheelchair to prevent physical exertion during study visits.
- *Risks:* Potential for fall or physical injury. The study team member responsible for your transportation, will be trained on common wheelchair transportation safety measures to reduce your risk of fall or injury during wheelchair transfer and transportation.
- *Location of Procedure:* Wheelchair transport will occur between the CTSU East and West locations at the University of Missouri
- *Frequency:* Transport will occur at baseline and final visits.

WHAT IS EXPECTED OF ME IF I TAKE PART IN THIS STUDY?

As a study participant, you will be required to do the following:

- Take the study supplement as instructed.
- Keep the study supplement in a safe place for your use only and away from children.
- Keep your study appointments. If you miss an appointment, please contact the investigator or research staff to reschedule as soon as you know you will miss the appointment.
- Complete your diaries as instructed.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.
- While participating in this research study, do not take part in any other research project without approval from the investigators. This is to protect you from possible injury from things such as extra blood drawing, extra X-rays, or potential drug interactions. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

If the investigators discover any medical information that is important for your medical treatment, you will be informed by the primary investigator. Other findings such as body composition results (available at the time of testing) will be shared with you during your participation. None of the findings of this study are meant to diagnose or treat you.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

There are no direct benefits to you as a research participant. It is possible that participating in research may help you to gain health knowledge about yourself.

We hope that the information we get from this study might help others with type 2 diabetes in the future.

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

Taking part in this study will involve collecting private information about you. This information will be protected in the following ways:

- Only approved study staff will have access to research records
- All hard/paper copies of research records will be kept in a locked filing cabinet in a restricted access area.
- All electronic research records will be kept on a VA approved, encrypted hard drive

There are times when we might have to show your records to other people. For example, someone from the Office of Human Research Protections, the Government Accountability Office, the Office of the Inspector General, the VA Office of Research Oversight, the VA Institutional Review Board (IRB), our local Research and Development Committee, and other study monitors may look at or copy portions of records that identify you. The FDA may inspect the records since the study is FDA regulated.

None of your personal information or biospecimens collected as part of the research, even if identifiers are removed, will be used or distributed for future research studies.

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

WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?

There is no cost to you for taking part in this study.
You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

As compensation for your time, you will be paid via check for the completion of study activities. You will be paid $25 after completion of the screening visit, $75 after the baseline visit, and $255 after the final visit. You will also receive travel compensation of $0.41/mile traveled (round trip) from your residence to the Harry S. Truman VA Hospital and Clinics for each of your study visits. If you are asked to repeat safety labs, you will be compensated for applicable travel at a rate of $0.41/mile traveled (round trip) from your residence to the Harry S. Truman VA Hospital and Clinics. The study team will have you complete a W9 form at your screening visit. This process includes the collection of your social security number for the payment processing.

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

If you are injured as a result of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury is due to non-compliance by a study participant with study procedures or if the research is conducted for VA under contract with an individual or non-VA institution.

You may be compensated for injury or harm through a Department of Health and Human Services program called the Countermeasures Injury Compensation Program (CICP). For more information about this program, please contact the Health Resources and Services Administration's CICP by phone at 855-266-2427 or online at https://www.hrsa.gov/cicp/about/index.html.

VA will provide necessary medical treatment should you be injured by being in this study. You will be treated for the injury at no cost to you. This care may be provided by the local VAMC or arrangements may be made for contracted care at another facility. In case of research related injury resulting from this study, you should contact your study team. If you have questions about medical treatment for any study related injuries, you can call the operator at this VA Medical Center and ask for medical administration.

You do not give up any legal rights or release the VA from any liability by signing the form.

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call:

Veterans Administration Office of Research at 573-814-6550, or
You may also call the VA at 573-814-6000 and ask for the Emergency Department.

DO I HAVE TO TAKE PART IN THE STUDY?

Participating in this study is voluntary. If you decide not to participate there will be no penalty or loss of benefit to which you are otherwise entitled.

You may decide to revoke your consent to participate and discontinue your participation at any time without any penalty or loss of benefits.

If you decide to discontinue your participation, you will need to inform the study's primary investigator, Dr. Camila Manrique-Acevedo or one of the study coordinators in writing. This can be done by emailing Dr. Manrique-Acevedo at Camila.Manrique-Acevedo@va.gov or her staff at MUEndoManriqueLab@health.missouri.edu. Before you are terminated from the study, you may

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

be required to complete a final safety questionnaire related to the use of the dietary supplement, Endocalyx.

The research team does not anticipate any adverse event related to the discontinuation of the study intervention.

Any information that is collected by the research team prior to your withdrawal may be used by the investigators for this study. Any specimens that you have provided prior to withdrawal may also be used for this study and cannot be withdrawn.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION

The primary investigator may choose to terminate you from the research study in any of the following cases:

- Failure to attend/complete research visits within the specified time frames
- Behavior that is considered disrespectful or offensive towards research investigators or staff
- Failure to complete study questionnaires or activities within the specified time range
- If the study safety officer deems participation as interfering with routine medical care

If you are terminated from the study, you will be informed by the primary investigator. The study team may request that you complete safety screenings prior to termination. You will receive compensation for all study related activities that you have already completed.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

If you have more questions about this study at any time, you can call Dr. Camila Manrique, MD at (573) 882-2273.
You may contact the University of Missouri Institutional Review Board (IRB) if you:

- Have any questions about your rights as a study participant;
- Want to report any problems or complaints; or
- Feel under any pressure to take part or stay in this study.

The IRB is a group of people who review research studies to make sure the rights of participants are protected. Their phone number is 573- 882-3181. Their email is muresearchirb@missouri.edu.

If you want to talk privately about your rights or any issues related to your participation in this study, you can contact University of Missouri Research Participant Advocacy by calling 888-280-5002 (a free call),or emailing MUResearchRPA@missouri.edu.

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

If you have questions about your rights as a study participant, or you want to make sure this is a valid VA study, you may contact the University of Missouri Institutional Review Board (IRB). This is the Board that is responsible for overseeing the safety of human participants in this study. You may call the University of Missouri Institutional Review Board if you have questions, complaints, or concerns about the study or if you would like to obtain information or offer input.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

Sometimes during a research study, new information becomes available about the intervention that is being studied that might change a person's decision to stay in the study. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your research doctor will arrange for your medical care to continue. If you decide to continue in the study, you might be asked to sign an updated informed consent form. Your research doctor could also decide it to be in your best interests to withdraw you from the study. If so, he or she will explain the reasons and arrange for your usual medical care to continue.

If the research team discovers information during this study that is clinically relevant the team will consult the study's safety officer regarding the disclosure of this information to you, the participant. If the information is deemed relevant to your medical care, the primary investigator will inform you of the findings. The primary investigator may recommend that you follow up with your regular medical care provider regarding the research findings.

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311

Participant Name: _____ Date:_____

Title of Study: Targeting the Endothelial Glycocalyx to Enhance Vascular Function and Exercise- Induced Vascular Adaptations in Type 2 Diabetes – Phase II

Principal Investigator: Dr. Camila Manrique-Acevedo, MD; Jaume Padilla, PhD

VA Facility: Harry S. Truman VA

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr. Camila Manrique-Acevedo, MD has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study. You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it.

I agree to participate in this research study as has been explained in this form.		
_____ Participant's Name	_____ Participant's Signature	_____ Date

_____ Study Representative's Name	_____ Study Representative's Signature	_____ Date

Version 12.1AU *Reconsent? Yes No*

IRB Approval Date: Nov 08, 2023; Written Consent Form ID #668982; Annual Update ID #399311