PI: Salvatore Scali

Study Title: Short-Term Dietary Protein Restriction Modulation of Skeletal Muscle Bioenergetics and Innate Immunity

IRB number: IRB20190098

NCT#: NCT03995979

UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM

to Participate in Research, and

AUTHORIZATION

to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position:_____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study (this "Research Study")?

Short-Term Dietary Protein Restriction Modulation of Skeletal Muscle Bioenergetics and Innate Immunity

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

Principal Investigator:	Salvatore Scali, MD	(352) 548-6470
	24-hour contact:	(352) 413-3098 (pager)
Other research staff:	Joanne Angle,	(352) 548-6217

4. Who is paying for this Research Study?

The sponsors of this study are the Department of Veteran Affairs and the University of Florida.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved?

The purpose of this research study is to determine if healthy volunteers who follow a short-term protein restriction diet have a change in their cells inflammatory response. There is strong scientific data that supports that shortterm protein restrictive diets reduce surgical stress responses. We plan to use the data collected in this study to compare with patients undergoing open abdominal aortic aneurysm (AAA) repair in a future study. Open AAA repair patients have some of the highest rates of perioperative complications compared to other elective non-cardiac surgical patients. We are hoping to use this information to help us understand how to modify the inflammatory response in people with diseased arteries, as well as how the tissue surrounding these blood vessels contributes to the disease process.

Participation for study subjects will be approximately 3 weeks. Research participants will be followed for 14 days once they start the study diet.

b) What is involved with your participation, and what are the procedures to be followed in the research?

Follow a 4 day protein restricted diet using Scandishake® and almond milk which will be provided to you. You may also drink water. No food or other beverages are to be consumed during the 4 day diet.

A blood sample will be obtained before, during and after completion of the 4 day protein restricted diet for a total of 5 samples. A urine sample and cheek swab (saliva) will be collected at the same time points. A stool sample will be collected at 3 time points.

A muscle microbiopsy will be obtained from the front side of your thigh before, during and after the protein restricted diet for a total of 3 samples.

c) What are the likely risks or discomforts to you?

Microbiopsy: There is a small risk of muscle damage, infection, prolonged bleeding but these are very rare. You may experience muscle soreness and bruising at the biopsy site. No sutures are required to heal the puncture, but you will be left with a small scar at the entry site.

Blood draw: The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure.

Protein Restrictive Diet: You may experience a change in bowel habits, constipation, loose stool and cramping. You may experience a change in your energy level during the 4 days of the protein restricted diet.

d) What are the likely benefits to you or to others from the research?

Participation in this research will not provide any additional benefits to you. Our hope is that discoveries from this study will eventually lead to a better understanding of how nutritional interventions may improve the probability of successful outcomes following open AAA surgery.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

This study is not offering an alternative procedure or course of treatment for you. Participation in this study is completely voluntary. You have the choice of not taking part in this study. Your decision whether to participate will have no effect on the quality of your medical care. Please ask questions if there is anything you do not understand.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

Normal clinical care is medical or other treatment or services that you would receive even if you did not participate in this research study.

7. What will be done only because you are in this Research Study?

Research Study procedures includes:

- Signing this Research Informed Consent Form
- Health interview including height and weight measurements, questionnaires
- Collection of 3 tissue samples from your thigh; before and after the protein restrictive diet at Baseline, Day 4 and Day 7 visits
- Collection of 5 blood, urine and saliva samples each at Baseline, Days 2, 4, 7 and 14 visits
- Collection of 3 stool samples on Day 0, Day 3 or 4, Day 7 or 7
- Consumption of ScandiShake® diet plan for 4 days, Days 1-4
- Use of MealLogger app to record meals Days 5-14 after completion of study diet

After signing this consent form, the surgeon investigator and study coordinator will review your medical history to confirm if you are eligible to take part in the study.

Muscle Biopsy: You will have a muscle biopsy obtained from the vastus lateralis muscle of your thigh using a microbiopsy needle. Vascular and muscle tissue cells will be removed with this biopsy and will be prepared for in-depth pathologic and genomic analysis. No other cells or tissues will be taken from you. The muscle biopsy procedure consists of cleansing a small area (3x3 inches) on your thigh with antiseptic solution and administering a topical anesthetic. A small incision approximately 1/4 to 1/8 inch in size will then be made and a sterile needle about the diameter of a pencil lead (1/16 inch) will then be inserted into your vastus lateralis muscle (front side of thigh). A piece of muscle about the size of 2 grains of rice (~2040 mg) will be obtained. The time to insert, cut, and remove the muscle sample will be 3 to 5 seconds. The small skin incision will be closed with a steri-strip and a temporary wrap will be applied to your leg as needed. You will receive instructions on the care of the biopsy site when you have completed the visit.

Blood samples: Approximately 20 mL (1½ tablespoons) of blood will be drawn from your arm in the usual manner before, during and after completion of the 4 day protein restrictive diet.

Urine samples: The samples will be collected via clean catch cup before, during and after completion of the 4 day protein restrictive diet. For women of childbearing potential, a urine pregnancy test will be performed prior to participation as part of the screening process and at the day 7 visit.

Saliva sample: An oral swab will be used inside the subject's cheek to collect saliva before, during and after completion of the protein restricted diet.

Stool sample: The sample will be collected within a 24 hour window before the first tissue sample is obtained and then within 24 hours of Day 4 and Day 7 visits.

Protein Restrictive Diet: Patients will receive the study diet (ScandiShake® [any of 5 flavors]) mixed with almond milk, calculated individually for a total daily volume to achieve 30% caloric restriction and 70% protein restriction, based on ideal body weight for 4 days. Water intake is *ad libitum* (not restricted). The study diet can be consumed throughout the day and night.

Scandishake Mix Vanilla sachets are made from Maltodextrin, vegetable oils (soya bean oil, palm oil), sucrose, skimmed milk, caseinate (from milk), emulsifiers (mono- and di- glycerides of fatty acids), flavor (vanilla), di potassium hydrogen phosphate, sodium chloride, tri magnesium di citrate.

Scandishake Mix Caramel sachets are made from Maltodextrin, vegetable oils (soya bean oil, palm oil), sucrose, skimmed milk, caseinate (from milk), coloring (plain caramel), flavor (caramel), emulsifiers (mono- and di- glycerides of fatty

acids), di potassium hydrogen phosphate, sodium chloride, tri magnesium di citrate.
Scandishake Mix Strawberry sachets are made from Maltodextrin, vegetable oils (soya bean oil, palm oil), sucrose, skimmed milk, caseinate (from milk), flavor (strawberry), emulsifiers (mono- and di- glycerides of fatty acids), di potassium hydrogen phosphate, sodium chloride, tri magnesium di citrate, coloring (carmine).

Scandishake Mix Banana sachets are made from Ingredients - Banana Maltodextrin, vegetable oils (soya bean oil, palm oil), sucrose, skimmed milk, caseinate (from milk), emulsifiers (mono- and di- glycerides of fatty acids), flavor (banana), coloring (beta-carotene), di potassium hydrogen phosphate, sodium chloride, tri magnesium di citrate.

Scandishake Mix Chocolate sachets are made from Maltodextrin, vegetable oils (soya bean oil, palm oil), sucrose, cocoa powder, skimmed milk, caseinate (from milk), flavor (chocolate), emulsifiers (mono- and di- glycerides of fatty acids), di potassium hydrogen phosphate, sodium chloride.

MealLogger App: This is a free app available on smartphones in which you will take a picture of the meals you ingest to approximate your normal food intake after completing the study diet. The purpose of taking a picture is so the app can analyze the content of the meal. This will begin on day 5 and will complete on day 14 of the study. During clinic visits (day 7 and day 14), you will open the app so that study coordinators can record information of your fat/protein/carbohydrate intake of the foods that were consumed. This information will be recorded with the other study data in a de-identified manor.

A timeline of your participation in the study is detailed below:

Screening and enrollment

- The study doctor will determine if you qualify to participate in this study
- Informed Consent
- Detailed medical history, height and weight
- Questionnaire
- Lab kit distribution

Baseline Visit

- Blood collection
- Urine collection
- Stool collection (lab kit given at screening)
- Saliva collection
- Muscle Biopsy Diet kit distribution
- Lab kit distribution
- Diary and visit schedule distribution

Day 1 Start Diet Kit
Day 2 Visit

- Blood collection
- Urine collection
- Saliva collection
- Review diary
- Diet kit distribution

Day 4 Visit

- Blood collection
- Urine collection
- Stool collection (lab kit given to subject)
- Saliva collection
- Muscle Biopsy
- Review diary (start meal log after completion of 4 day meal kit)

Day 7 Visit

- Blood collection
- Urine collection
- Stool collection (lab kit given to subject)
- Saliva collection
- Muscle Biopsy
- Review diary and meal log

Day 14 Visit

- Blood collection
- Urine collection
- Saliva collection
- Collect and review diary and meal log

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 3 of this form.

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect information from you about your medical history, age in years, demographic information, medications, vitamins, herbal supplements, height, weight, and questionnaires including physical activity level.

Other professionals at the University of Florida or Shands Hospital who provide studyrelated care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study.

9. With whom will this health information be shared?

This health information may be shared with:

- the study sponsor (listed in Question 4 of this form);
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- Government agencies which are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.
- North Florida/South Georgia Veterans Health System
- The IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

This research study is expected last approximately 4 months. Your participation in the project will be for approximately 3 weeks.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11.How many people are expected to take part in this Research Study?

We expect to enroll 30 participants in this research study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

Muscle Biopsy Procedure: As with any invasive procedure, complications can occur. The risks associated with muscle biopsies are very small. Some possible complications may include:

- Bruising and discomfort at the biopsy site
- Prolonged bleeding from the biopsy site
- Infection of the biopsy site
- Numbness at the biopsy site

Protein Restrictive Diet: You may experience:

- Constipation or loose stool
- Abdominal cramping
- Increase or decrease in energy
- Weight loss
- Allergic reaction; subjects with nut sensitivities will not be enrolled.

Reproductive risks: Because the low protein diet in this study might affect an unborn baby, you should not become pregnant while on this study. Since this diet will not be given to any patients who are pregnant, all women with childbearing potential must take a pregnancy test prior to undergoing any participation in this study. We encourage all women and adolescents enrolled in this study to use one of the effective birth control methods during treatment and for six months after treatment is stopped. These methods include total abstinence (no sexual intercourse), oral contraceptives ("the pill"), an intrauterine device (IUD), an etonogestrel implant (Implanon), or medroxyprogesterone acetate injections (Depo-Provera shots). If one of these cannot be used, using contraceptive foam and a condom are recommended. You must notify the doctor if you become pregnant during the study.

Blood sample: The risks of drawing blood from a vein can include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and uncommonly, faintness from the procedure.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer.

13a. What are the potential benefits to you for taking part in this Research Study?

There is no anticipated direct benefit to you for being in this study; however, peer reviewed evidence suggests that after completion of a short-term protein and calorie restriction period, resumption of normal dietary intake can result in improved senses of well-being and increased energy for variable amounts of time.

13b. How could others possibly benefit from this Research Study?

Our hope is that discoveries from this study will eventually lead to a better understanding of how short-term dietary changes with protein and calorie restriction can improve a patient's postoperative recovery.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

13d. Will you be allowed to see the research information collected about you for this Research Study?

You may not be allowed to see the research information collected about you for this Research Study, including the research information in your medical record, until after the study is completed. When this Research Study is over, you will be allowed to see any research information collected and placed in your medical record.

14.What other choices do you have if you do not want to be in this study?

This study is not offering an alternative procedure or course of treatment for you. Participation in this study is completely voluntary.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a.Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b.Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- The study doctor may terminate your participation in the study if he/she determines that it is not in your best medical interest to remain in the study
  If you are unable to follow the instructions provided by us, the investigators.
- You no longer meet the inclusion criteria for this study.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

No. There will be no extra cost to you for participating in this Research Study.

17.Will you be paid for taking part in this Research Study?

You will receive payment for the visits that are completed for research purposes and not as part of your standard of care.

You will be paid up to $500 for participation in this study. You will only be paid for the study visits below that you are scheduled for and that you attend.

The study payment and time schedule:

Baseline Visit	(1-1.5 hours)	$100.00
Day 2 Visit	(30-40 minutes)	$ 50.00
Day 4 Visit	(1 hour)	$100.00
Day 7 Visit	(1 hour)	$100.00
Day 14 Visit	(1-1.5 hours)	$150.00

If you are paid more than $75 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. Payments to ***nonresident aliens*** must be processed through the University of Florida Payroll and Tax Services department. If the payments total $600 or more in a calendar year, the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity. If you have any problems regarding your payment contact the study coordinator.

18.What if you are injured while in this Research Study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or

research-related injuries. Please contact your insurance company for additional information.
The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact the Principal Investigator listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

Signature of Participant Date