Determinants of Alpha-aminoadipic Acid (2-AAA) and Relationship to Diabetes: Study 2

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VUMC Institutional Review Board
Informed Consent Document for Research

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Version Date:	02 /01/2021
PI:	Jane F. Ferguson, PhD

Name of participant:_____ Age:_____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

1. **What is the purpose of this study?**

We are studying a metabolite called α-aminoadipic acid (2-AAA). 2-AAA occurs naturally in the body. Different amounts of 2-AAA may alter the risk of developing diabetes. We are interested in whether 2-AAA changes with different levels of dietary lysine.

2. **What will happen and how long will you be in the study?**

You were selected as a candidate based on your 2-AAA levels and other data obtained during phase 1 of the study. We will ask you questions over the phone, by email, or via an electronic questionnaire to determine eligibility.

If eligible, you will complete four study visits, and two dietary interventions. It will take you approximately 4 weeks to complete the study. The 4 study visits will be conducted at Vanderbilt University Medical Center and will take ~30 minutes each. There will be two separate dietary interventions lasting one week each, separated by a 2-week period where you will return to your regular diet. You will meet with a dietitian and be provided a menu, shopping list, and a gift card to purchase all meals and snacks.

We will take samples to measure the level of 2-AAA in your blood and urine before and after the diets. We will look at changes in microbiota in your stool, and we will analyze cells from your blood Based on the measurements, we will ask some participants to return for an additional study. We will also take samples of your DNA to look for genetic factors that influence 2-AAAlevels.

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Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you were selected as eligible based on your participation in the first phase of our study.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:

Fingerprick and Venous Blood Draw: You may experience pain, an allergic reaction, bleeding or bruising where the needle is placed. Occasionally, a person feels faint or lightheaded when his/her blood is drawn. Rarely an infection can develop; it can be treated.

Dietary Intervention and Lysine Supplementation: There are no known risks associated with dietary intervention. Lysine is expected to be well-tolerated by all participants. Lysine is used as a dietary supplement, available over the counter, with no known long-term risks. The proposed dose of lysine may cause mild gastrointestinal upset in some subjects. This is expected to be minor and transient.

Stool Sample Collection: There are no known risks associated with stool sample collection. Sample collection may be inconvenient for some individuals.

Private Health Information: This information will be collected during the course of the study. However, only key study personnel will have access to this information, which will be stored in a HIPAA compliant, password protected database. No protected health information will be shared with employers, insurers, or non-research personnel.

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Good effects that might result from this study:

You will not benefit from taking part in this study. The results of this research study may advance our understanding of a biomarker for Diabetes and help to guide the development of novel preventative and therapeutic strategies. This could benefit patients in the future. You will have the option to receive a nutrition report on completion of your dietary intake forms. This report provides information regarding how your dietary intake compares to U.S. dietary guidance and nutrient requirements.

Procedures to be followed:

Screening:
This will be conducted over the phone, by email, and/or via an electronic survey. If you choose a phone call, we will tell you about the study, ask you questions regarding your medical history, medications, recent changes in diet, and review the inclusion/exclusion criteria to determine your eligibility. If you are eligible, we will ask for your consent and ask for you to confirm your consent with a witness. If you use the electronic survey, you will be asked to provide the same information regarding your medical history and the inclusion/exclusion criteria to determine your eligibility. If you are deemed eligible, you will then be asked for your consent. If you do not qualify for any reason, the study staff will tell you why. If you are a woman and are able to become pregnant, you will have a urine pregnancy test to make sure that you are not pregnant before you receive treatment in this study.

If you provide your consent, we will ask that you:

- Discontinue use of lysine supplements from 2 weeks prior to your first study visit, until the end of the study.
- Discontinue use of dietary supplements from at least 1 day prior to your study visit, until the end of the study.
- Discontinue over-the counter medications and refrain from consuming alcohol.
- If you have changed your diet since you completed the screening study, we will ask you to record your normal intake of all foods and beverages. You will be given a link to an onl ine form, and detailed instructions on how to complete this task.
- Record your dietary intake of all foods and beverages consumed on the day prior to your study visits. You will be given a link to an online form to fill out, and detailed instructions on how to complete this task.
- Complete a survey about your general health.

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Study Visit:
Upon arrival, the consent form will be reviewed to confirm that you still wish to participate. You will be asked to arrive fasting (≥ 8 hours). This means that you cannot eat or drink anything (with the exception of water) for at least 8 hours before your visit. We will reviewyour medical history, medications, and inclusion/exclusion criteria, which will be documented by study personnel to assess for any changes that may potentially exclude you from participating. We will measure your blood pressure, height, weight, waist and hip circumference prior to study interventions. You will be asked to provide a urine sample, and we will prick your finger to provide a drop of blood for glucose measurement. A needle will be inserted in your arm to take a sample of blood (50cc, or about 3 tbsp). You will be provided with a stool collection kit before each visit and will asked to bring a stool sample to each visit. You will be given a health questionnaire to complete at each study visit.

In addition to the in-person appointment, there will be 4 online dietary recall questionnaires to fill out. The surveys are to be completed outside of your in-person appointment. The surveys take about 20-30 minutes each to complete. If you made changes to your diet since your previous participation, we will also ask you to fill out 1 additional dietary questionnaire, which will take 30-60 minutes to complete.

Diet:
You will meet with a dietitian and be provided with a menu, shopping list, and a gift card to purchase foods, during the two diet periods. Each diet lasts for one week. During one of the diets, you will be given lysine supplements. There will be 5 tablets to take each day, at your meal times (5 grams per day total, for 7 days).

Storage of Blood, Urine, Stool and DNA Samples for Future Research
Your samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, and treatments of Diabetes, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, and/or others. If this happens, there are no plans to provide money to you.

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Consent for Genetic Research

We plan to study genes (DNA) and how they affect health, body processes, and disease. Genes act as the blueprint for the body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain disease and how they will respond to different types of medical treatment.

You are being asked to give blood and urine samples for genetic research. Giving samples for research is your free choice, but you will not be eligible to participate in this particular study if you do not want your samples used or stored for genetic research.

Follow-up Studies

We plan to ask some participants to come back for follow-up studies. You are not guaranteed to be asked to participate in future studies, and you do not have to consent to future studies. If you consent to this study, you give us permission to re-contact you to invite you to participate in case you are eligible.

Payments for your time spent taking part in this study or expenses:

You will receive$250 when you complete all aspects of the study. This amount may be taxable and will be reported to the Internal Revenue Service (IRS) as required. We will need to collect your Social Security number and address before you are compensated for taking part in this study.

Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator with the National Institutes of Health (NIH) that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided at Vanderbilt to treat the injury.

There are no plans for Vanderbilt or the National Institutes of Health (NIH) to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt or the National Institutes of Health to give you money for the injury.

Who to call for any questions or in case you are injured:

If you should have any questions about this research study, or if you feel you have been hurt by being a part of this study, please feel free to contact Dr. Jane Ferguson at (615) 875-9896 or the Clinical

Research Coordinator Holly M. Smith at (615) 936-1916. If you cannot reach the research staff, please contact the Cardiac Access Center at (615) 343-9188.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
The study investigator may remove you from the study if you experience complications during any of the discussed procedures. You will also be removed if you are not compliant with treatment or procedures (i.e. not adhering to the diet).

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell the study investigator. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:
A description of this clinical trial will be available on 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 Web site at any time.

Confidentiality:
Your study records and data will be stored in a secure database. The database will reside in a password protected secure website supported by Vanderbilt University. Only study personnel will have access to the database.

Information in the database that will identify you will only be available to study personnel.
Your biological samples will be stored with a study ID label. This label will not include any identifying information. Only key study staff will have access to your identifying information.
Genetic data will be deposited in dbGap, an online controlled-access database. We will not include any identifying information.

All key study personnel at Vanderbilt University involved in the design or conduct of this study will receive the required education on the protection of human participants. This study will follow the

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relevant federal guidelines regarding HIPAA regulations on patient-related information. Only key study personnel will have access to identified information.

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Ferguson, or her staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legalmeans.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Study Results:
In the event new information becomes available that may affect the risks and/or benefits associated with this study or your willingness to participate in it, you will be notified so you can make a decision whether or not to continue your participation in thisstudy.

Your study records and data will be stored in a secure database. The database will reside in a password protected secure website. Information in the database will only be available to study personnel. Your

biological samples will be stored with a study ID label in a locked freezer. This label will not include any identifyinginformation. Onlykey study staff will have access to your identifying information. All key study personnel involved in the design or conduct of this study will receive the required education on the protection of human participants.

If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent.

Authorization to Use/Disclose Protected Health Information

What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchersand their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?

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Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them knowby using the contact informationprovidedin thisconsent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Phone Consent

_____ _____
Date Name of patient/volunteer

Consent obtained by:

_____ _____
Date Signature

_____
Printed Name and Title

Time: _____

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Phone Consent witnessed/confirmed by:

Date Signature

Printed Na ne and Title Time

In-Person Consent:

I confirm that I provided phone consent on the date and time as recorded above. I also confirm that I freely and voluntarily choose to take part in this study.

Date Name of patient/volunteer

Consent obtained by:

Date Signature

Printed Na ne and Title Time