Wake Forest School of Medicine

Department/Section of Biochemistry

Role of PUFA-Gene Interactions in Health Disparities

Informed Consent to Participate in Research
Susan Sergeant Ph. D., Principal Investigator

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are a healthy person. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

This study is a randomized clinical trial to provide the first comprehensive investigation of the role of gene differences on the production and use of certain fats as well as levels of inflammation using special controlled diets (low and high linoleic acid) parallel diets.

The dietary oils used in this study are oils used in preparing some of the foods you will be given (food items, snacks, condiments, smoothies). We will provide the fat content of your diet during the study. You will be provided with extensive dietary guidance to help you make wise food choices that will allow you to comply with the important fat intake requirements of this dietary study since you will be selecting and preparing most of your meals. This is not a weight loss study. It will be important to maintain your current weight.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Three hundred (300) people at this research site will be enrolled in this study.

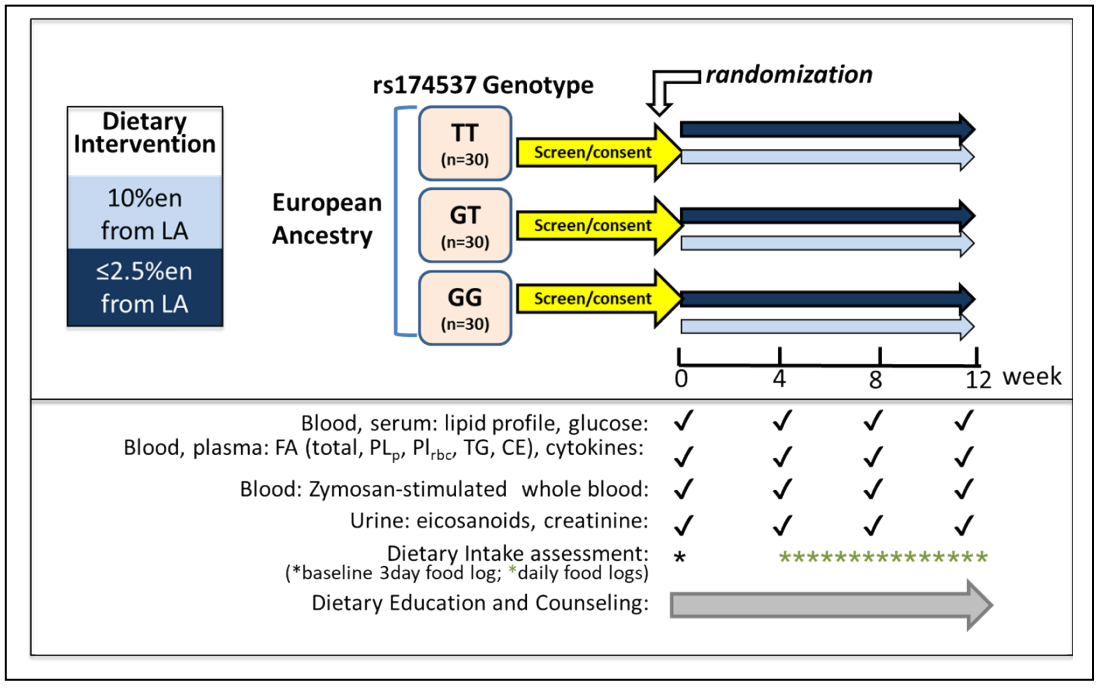
WHAT IS INVOLVED IN THE STUDY?

A diagram of what happens in the study is shown below.

You will have one of three genotypes (GG, GT or TT) in the gene we are examining. Those within each gene grouping will be randomized to begin the study consuming a diet that contains either low or high levels of a common dietary fat, linoleic acid. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in each oil group.

Neither you nor the investigator will know which diet you are consuming at any time during the study. This is done so that a fair evaluation of results can be made. However, this information can be retrieved by the researchers if needed in the case of an unexpected emergency situation.

You will be asked to come in for a consenting/screening visit to sign a consent form and to verify that you still qualify as a healthy person (V1). If you still qualify, you will be asked to come in for a second screening visit (V2) where you will meet with a registered dietitian and undergo measurement of your resting metabolic rate. This is to determine how many calories you will need each day to maintain your present weight. This is not a weight loss study. The dietitian will perform a test to measure the number of calories your body uses at rest (resting metabolic rate, or RMR). We will ask that you come to your visit having fasted for at least 12 hours prior to your appointment time, which means nothing to eat or drink except water prior to that visit. We will also ask that you not exercise or drink alcoholic or caffeinated beverages for the 24 hours prior to your visit. For this test, you will recline comfortably and rest for 20 minutes. Then, while still reclining, a face tent will be placed in front of your nose and mouth for the next 15-20 minutes. Based on the air you breathe in and out, your resting metabolic rate



is calculated. You will breathe normally during this time but will be asked to avoid movement as much as possible. You may speak with the dietitian to make sure you understand the requirements of the study. If you would like to join the study, we will schedule you to begin at a

specific time. Prior to your baseline visit (V3), you will come in for nutritional counseling with the RD. This is to make sure that you know the dietary requirements and recordkeeping requirements that you will need to know during the study.

You will also be asked questions about any food allergies or intolerances that you may have (such as nuts, dairy, fruits, gluten, eggs). Study visits where blood and urine will be collected will be fasting visits in which you cannot eat or drink anything with calories for 8 hours before coming in for your visit (visits 1, 3, 7, 11, and 15). At your baseline visit (V3), you will be given a cooler of study foods. These foods will include smoothies (containing flaxseed oil common to both arms), arm-dependent oil-based condiments (salad dressing, mayonnaise, and margarine) and a variety of prepared foods, each made with the arm-specific oil as well as several packaged snacks and food items specific to your arm of the study. You will also receive a spray-type oil to use for home cooking. You should not use any oils other than those provided by the study.
Participants will be provided with a personalized meal plan and recipes for home preparation of meals that will allow them to adhere to the target fatty acid contents of the two dietary arms. You will donate samples of urine and blood and will have your body measurements, blood pressure and pulse measured. You will return after 4 weeks (visit 7), 8 weeks (visit 11) and 12 weeks (visit 15) for a repeat of the blood and urine collection and body measurements that were done in visit 3. During the study, you will meet weekly with the study dietitian to turn in your unused food and food logs and pick up your food and food logs for the next week (visits 4, 5, 6, 8, 9, 10, 12, 13 and 14). You will also provide a 3-day food record (baseline intake), and daily food checklists. These will be administered by the registered dietitian.

The following table is a summary of what will happen at each visit.

	Visit 1	Visit 2	Nutritional	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visit 15
Assessment	consenting	metabolic screening	counseling session	diet, base	RD vis	RD vis	RD vis	diet, 4 weeks	RD vis	RD vis	RD vis	diet, 8 weeks	RD vis	RD vis	RD vis	diet, 12 weeks
informed consent	X															
Medical History	X															
Inclusion/exclusion Criteria	X															
Metabolic screening & RD assessment		X														
Enrollment				X												
Randomization				X												
Wellness assessment	X			X				X				X				X
Inclusion/exclusion adherence				X				X				X				X
urine collection	X			X				X				X				X
blood collection	X			X				X				X				X
blood chemistries	X			X				X				X				X
blood pressure, pulse	X			X				X				X				X
anthropomorphic measurements	X			X				X				X				X
weight measurement		X		X	X	X	X	X	X	X	X	X	X	X	X	X
diet education			X	X	X	X	X	X	X	X	X	X	X	X	X	
food pick up				X	X	X	X	X	X	X	X	X	X	X	X	
food & log return				X	X	X	X	X	X	X	X	X	X	X	X	X
Participation Survey		X														

If you take part in this study, you will have the following tests and procedures:
Blood collections will be done at five visits. The blood collection done at visit 1 is to determine if your inclusion/exclusion blood values are within the necessary range. We will measure hsCRP, a measure of inflammation and blood glucose and blood lipids. These same blood values

will be measured at each of the other four blood collection visits. These are values frequently done by family physicians to verify a person's health, but we are doing these for research purposes. We will also measure the levels of eicosanoids in your blood. These are chemicals produced when you have inflammation in your body. We are measuring these for research purposes. We will measure the fat content of your serum and your red blood cells. This is for research purposes and will show us how the fats are being processed by your body.

Urine will be collected at visits 1, 3, 7, 11 and 15 to measure inflammatory components (eicosanoids) in your urine. Urinary creatinine will be measured as a reference point for the eicosanoids.

We will measure blood pressure, pulse and body measurements for research purposes and to monitor inclusion/exclusion values.

As mentioned above, you will be divided into three groups based on the genes you carry. You will be randomized to start the study with one of the two diets. This is to make sure that both diets are started in equal numbers of people. During the study, you will receive the foods containing the oils specific to your arm of the study weekly. You will receive a food log to record the foods that you consumed. As mentioned above, neither you nor the research investigators will know to which diet you have been assigned. If you are in the low linoleic acid part of the study, you will receive 2.5 % of your dietary energy as linoleic acid. If you are in the high linoleic acid part of the study, you will receive 10% of your daily energy as linoleic acid.

You will have approximately 20 milliliters (4.1 teaspoons) of blood withdrawn from a vein in your arm on five separate visits. The total amount of blood withdrawn during the study will be approximately 100 milliliters (20.3 teaspoons).

We will give you copies of your test results so you may share them with your personal physician. Even if you do not wish to have any of your medical information shared with your physician, you can still participate in this research study.

When you complete the study (or if you decide to withdraw from the study before completion), we will ask you to complete a short questionnaire in order to help us better design and implement dietary studies in the future.

Storage of Biological Tissue

If you agree to participate in this study, we will draw approximately 100 milliliters of blood (total volume over the course of the study). Most of these samples will be used immediately, but any remaining sample will be kept and may be used in future research to learn more about other diseases. Your sample will be obtained in the WFHS Clinical Research Unit at Wake Forest University Baptist Medical Center. The sample will be stored in the laboratory of Dr. Sergeant, and it will be given only to researchers approved by Dr. Sergeant. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample. In order to participate in this study, you must be willing to provide this sample for future research.

Your blood/tissue sample will be stored with a unique identifier and will not include any identifiable information about you, such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number, and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers, and neither will the code that links your identifiers to the sample.

The research that may be performed with your blood/tissue sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood /tissue will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood/tissue sample will not affect your care.

Your blood/tissue sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research. In the future, research on your specimen may involve whole genome sequencing.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for about 6-9 months. The actual dietary intervention takes 12 weeks, but you may have up to 6 months between your consenting/screening visits and the time you start the study. You may stop participating at any time. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. The most likely side effects related to the oils we are studying include are possible gastrointestinal upset at the beginning of the oil supplementation period if your body is not used to taking oils. You might also experience an allergic reaction (such as rash or hives) to components in the study provided foods. Should you suspect a reaction to one of the provided foods stop consuming it and contact the study RD and the study PI.
You may experience some frustration by the variety of foods you are allowed to consume. We encourage you to discuss this issue with the registered dietitian at your weekly visits.

During the blood draw, you may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally, some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficiency anemia). If you donate blood to the American Red Cross, you should talk with the study doctor about whether or not it is safe to do so while participating in this study. You

should not donate blood more than 2 times per week and no more than approximately one pint (about 500 ml) of blood in an eight week period.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

The risk of harm or discomfort that may happen as a result of taking part in this research study is not expected to be more than in daily life or from routine physical examinations or tests. You should discuss the risk of being in this study with the study staff.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study.

Reproductive Risks and other Issues to Participating in Research

Pregnant and lactating women are excluded from participation in this study. Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your other choice is to not be in the study.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records about your health is considered Protected Health Information. The information we will collect for this research study includes**:** 1. Your identifying information

including your name, address, phone number, email and Social Security number. 2. The results from your laboratory tests and research tests.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research

2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

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

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

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law [list what will be reported, such as child abuse and neglect, or harm to self or others].

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document [restate what will be disclosed, such as including research data in the medical record]."

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Sergeant that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Susan Sergeant, Biochemistry
[redacted]

However, if you take away permission to use your Protected Health Information, you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form, you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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 Web site at any time. Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. All study costs, including any study oils and food items provided by the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid $400.00 (in two installments) if you complete all the scheduled study visits. The first payment ($160) will be paid after completion of Visit 7; the second payment ($240) will be paid after completion of all visits (15). If you withdraw for any reason from the study before completion of all the visits you will be paid for visits completed according to the table below.

visit 1, consent/screen	visit 2	nutritional consultation	visit 3	visit 7	visit 11	visit 15	total compensation for completing entire study
$20.00	$20.00	$20.00	$30.00	$40.00	$90.00	$90.00	$400.00
						subjects will be paid for completion of the study	

The total compensation for the study includes $10.00 for each of the weekly food pickup visits completed (that do not coincide with a blood draw visit) with the registered dietitian.

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by The National Center for Complementary and Integrative Health and the Office of Dietary Supplements of the National Institutes of Health. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted]

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Susan Sergeant, Ph. D. at [redacted] or after hours at [redacted].

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

This study will be enrolling students from the Wake Forest University and/or Wake Forest University Medical Center. In addition to your rights as a research participant noted in the previous section, as a student, you are under no obligation to participate in this study. You may refuse to participate or withdraw from the study at any time and for any reason without affecting your grades, performance evaluations, or assignments. You will not be pressured into participating in this research study by any statements or implied statements that your grades,

performance evaluations or assignments will be affected by your willingness to enroll in the study. Your medical records/information will not be used by the faculty, administration or study staff to make decisions regarding the status of your medical benefits. If you have questions regarding your enrollment in the study and your status as a medical student, please contact the Office of Student Services for additional information.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator,

Dr Susan Sergeant, Ph. D. at [redacted] or after hours at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted]

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):
Subject Signature: Date: Time: am pm
Person obtaining signature (printed):
Person Obtaining Consent: Date: Time: am pm
Study coordinator verifies complete signatures and dates