COVER PAGE

Study: Effect of Yogurt on Mucosal Immunity in the Gastrointestinal Tract
NCT05931471

Document: Informed Consent Form
Date of document: August 4, 2023

Title of research study:

Effect of Yogurt on Mucosal Immunity in the Gastrointestinal Tract

Investigator:

Danielle G. Lemay, Ph.D.

California Experimental Subjects Bill of Rights

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
- Any common or important discomforts and risks.
- Any benefits you might expect.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document.

Key Information about This Research Study

You are invited to take part in a research study. The purpose of this research is to test whether immune functions in the gut change when yogurt is eaten regularly. There is evidence from previous studies that consuming yogurt or other foods containing live microbes can affect gut health and immune function.

You are invited to be in this study because: you are an adult between the ages of 50 and 75, you have not been taking probiotics or eating yogurt or other fermented foods regularly, and you meet all the study eligibility requirements.

Your participation in this research will include 6 visits to the Western Human Nutrition Research Center and will last about 7 weeks (50 days). We expect about 30 people from Davis and the surrounding area to join and to take part in this research.

Being in this study will involve two weeks of not consuming yogurt or other fermented foods, three weeks of consuming yogurt provided by the research study while avoiding other fermented foods, and then two more weeks of not consuming yogurt or other fermented foods. The study will also involve collecting samples of your stool and bringing them to the research center five times during the seven-week study. We will also ask you to complete several questionnaires about your diet, medications you take, bowel movements and gastrointestinal symptoms.

All research studies have some risk. Risks of this study are minimal. These risks are described in detail later in this document. There is not the possibility that you may benefit from participation in this study.

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You may not want to be in this research if you find the following study activities uncomfortable or difficult:

- Collecting samples of your stool and bringing them to the research center five times during the seven-week study
- Visiting the research center for six scheduled visits during the seven-week study
- Completing records of your bowel movements, gastrointestinal symptoms you may have, foods you eat and medications you take
- Consuming lightly sweetened vanilla yogurt two times per day for three weeks
- Avoiding probiotic supplements, foods or drinks containing probiotics, and fermented foods other than the yogurt by the study for seven weeks (Some examples of fermented foods are: sour cream, buttermilk, kimchi, and traditional pickles or sauerkraut)

Your participation in this study is voluntary. You do not have to be in this study if you do not want to. The alternative is not to participate. You will not lose any services, benefits, or rights you would normally have if you choose not to take part.

The rest of this form gives a more complete description of this study. Please read this form carefully. You can ask any questions you need to help you choose whether or not to join this study.

Information to help you understand research is online at https://research.ucdavis.edu/policiescompliance/irb-admin/for-research-participants/

What if I have Questions?

The person in charge of this study is Danielle Lemay, Ph.D. If you have questions or concerns about this study, please contact Dr. Lemay, at 530-752-4748 during business hours (Monday – Friday, 8 am – 5 pm).

If you have any questions about your rights as a research subject or have complaints about the research study or study team, you may talk to a team member at the Institutional Review Board (IRB) by phone: (916) 703-9158, by email: hs-irbeducation@ucdavis.edu, or by mail: 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817. The IRB is a group of people who oversee research.

How is this research funded?

This research is being funded by the California Dairy Research Foundation, also called the sponsor. Sponsors may change or be added. The Western Human Nutrition Research Center is being paid to conduct this study, but the research staff have not received any direct income from the sponsor.

Why is this research being done?

The gastrointestinal (GI) tract, or gut, has the difficult task of absorbing nutrients from food while keeping out substances or microbes that could cause illness. Immune system functions that happen in the GI tract are part of this on-going process. If GI tract immunity fails, the result can be infection, inflammation or inflammatory bowel disease. In a previous study at the Western Human Nutrition

Research Center, we found that people who ate yogurt had higher levels of some markers of GI tract immune function. However, many of the people participating in that study did not eat yogurt, or only ate yogurt a few times during the study. We have designed this study to learn whether markers of GI tract immunity increase when people consume yogurt regularly.

Several studies have studied the health effects of yogurt, or yogurt with probiotics. Those studies had promising findings for yogurt increasing GI tract immune function, but they did not measure all of the immunity markers we will measure. The results of this study will help us understand how yogurt affects immune functions in the GI tract. We will also use this information to design future studies that test whether different types of yogurt or fermented foods have different health effects.

What happens if I say yes, I want to be in this research?

If you decide to join this research study, the researchers will ask you to complete a series of activities over seven weeks. The main activities are: consuming study-provided yogurt during the yogurt intervention period, avoiding probiotics and fermented foods, collecting stool samples, completing visits to the research center, and completing logs and questionnaires.

Yogurt consumption

This study will test the effects of yogurt consumption on GI immune function by asking you to not consume yogurt for two weeks, consume yogurt two times per day for three weeks, and then go back to not consuming yogurt for another two weeks. We call the three weeks of yogurt consumption the 'intervention period.'

At the start of each week during the intervention period, we will give you 16 pre-packaged portions of yogurt in plastic food containers. Each container will have 6 ounces of vanilla flavored whole milk yogurt. Each day, we would like you to consume two containers of yogurt. We will give you 16 portions each week so that you have two for each day, plus two back-ups.

You may have the yogurt as a snack or as part of a meal. We will ask you to record that you ate the study yogurt, and at what time, in a log book. We will provide you with insulated bags for getting the yogurt to your home and bringing back the used containers. Please put the yogurt in your refrigerator at home as soon as possible, and keep it refrigerated until you're ready to eat it. We will ask you to bring back the yogurt containers and the insulated bags each week. Please bring back all of the containers, even though some may still be full, at the end of each week. You do not need to wash the containers.

Avoiding probiotics and fermented foods

We will ask you to avoid taking any probiotic supplements while you are participating in the study. Probiotic supplements include capsules or chewables that contain live probiotics; drinks or tonics that contain probiotics; powders or drink mixes that have added probiotics; and apple cider vinegar or other live microbe-containing products taken as a supplement.

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We will also ask you to avoid consuming fermented foods other than the yogurt provided by the study. By 'fermented foods,' we mean foods that were made by microbial processes and still contain high amounts of live microbes. This includes:

- Cultured dairy products, such as sour cream, kefir, buttermilk or yakult
- Fermented, pickled vegetables, such as cucumber pickles, traditionally-made sauerkraut or other lacto-fermented vegetables (these are usually found in the refrigerated section of grocery stores); kimchi, tsukemono, achaar or other fermented vegetables
- Kombucha, water kefir or other fermented drinks
- Natto or other fermented bean products that are consumed uncooked

Collecting stool samples

We will ask you to collect a sample of your stool at the end of the second, third, fourth, fifth and seventh weeks of the study, for a total of five stool sample collections. We will give you stool sample collection kits that contain gloves, a toilet insert for collecting stool, seven stool sample tubes with scoops in the lid, Ziploc bag and a detailed instructions and sample record sheet. We will also give you a cooler and ice packs for storing and transporting the collected sample to the research center as soon as possible after collection.

Two stool sample collection containers have liquids in them to preserve the stool. The preservative liquid in them is called RNAlater which contains 40% ammonium sulfate and water. It is non-toxic; however, all chemicals should be handled with caution. In case of skin or eye contact, rinse thoroughly with water. Remove contact lenses if present. If any has gotten on clothing, remove the affected clothing and wash before wearing again. If swallowed, drink 1-2 glasses of water.

Visiting the research center

We will ask you to visit the research center at the beginning of the study and at the end of the second, third, fourth, fifth and seventh weeks of the study. At each study visit, you will meet with study staff and have an opportunity to talk with us in person about any questions or concerns you may have.

During the first visit, we will talk with you about all of the study procedures and ask whether you are willing to participate. If you are willing, we will complete a short questionnaire and give you instructions and materials you will need to complete the study activities for the first two weeks of the study.

At the end of the second week, we will ask you to visit the research center to deliver your first stool sample and stool log, collect your first batch of yogurt, and get the instructions and materials you will need for the third week of the study. This process will be repeated at the end of the third, fourth and fifth weeks of the study. You will turn in your yogurt log after the fifth week of the study.

During the final study visit, we will ask you to deliver your final stool sample, return your stool and medication logs and any other study materials you may still have.

Completing logs and questionnaires

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We will ask you to complete the following logs and questionnaires:

- Demographics Questionnaire: a short questionnaire asking basic information about you, to be completed at the research center during the first study visit
- Study Payment Form: a form to collect the information we will need to provide you compensation for participating in the study. We will give this to you at the first study visit for you to complete at home and return at the next visit.
- Medication Log: a record of all medications you take while participating in the seven-week study. The log has a section for recording medications you take every day and a separate section for recording medications you take occasionally. We will give this to you at the first study visit for you to complete at home and return at the end of the study.
- Fermented Foods Intake & GI Symptoms Questionnaire: an online survey with two sections. The first section asks about any fermented foods or probiotic products you may have consumed during the past week. The second section asks about any GI symptoms – such as bloating, diarrhea, etc. – that you may have had during the past week. We will send you a text or email asking you to complete this at the end of each week of the study. It can be completed at home on a tablet, smart phone or computer.
- Stool Log: a record of the date, time and stool consistency of the bowel movements you have. We will ask you to keep this log during the second, fifth and seventh weeks of the study.
- ASA24 Dietary Recalls: an online diet assessment tool asking you to describe all the foods and drinks you had during the previous day. We will ask you to complete the ASA24 three times during the second week of the study and three times during the fifth week of the study.

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Break-down of study activities by day

Day	Participant Activities
0	**Center Visit 1: Informed Consent, Screening, Participant Instructions, Demographics Questionnaire, Fermented Foods Questionnaire**
1-6	Medication Log
7	Fermented Foods and GI Symptoms Questionnaire; Medication Log
8-13	ASA24 dietary recalls (3x); Stool Log, Medication Log
14	Stool sample collection & record Fermented Foods and GI Symptoms Questionnaire Medication Log **Center Visit 2: Drop off stool sample; Pick up yogurt**
15-20	Two 6-ounce servings of yogurt per day, Yogurt Intake Log; Medication Log
21	Two 6-ounce servings of yogurt per day, Yogurt Intake Log Stool sample collection & record Fermented Foods and GI Symptoms Questionnaire Medication Log **Center Visit 3: Drop off stool sample; Return yogurt containers and pick up yogurt**
22-27	Two 6-ounce servings of yogurt per day, Yogurt Intake Log; Medication Log
28	Two 6-ounce servings of yogurt per day, Yogurt Intake Log Stool sample collection & record Fermented Foods and GI Symptoms Questionnaire; Medication Log **Center Visit 4: Drop off stool sample; Return yogurt containers and pick up yogurt**
29-34	Two 6-ounce servings of yogurt per day, Yogurt Intake Log ASA24 dietary recalls (3x); Stool Log, Medication Log
35	Two 6-ounce servings of yogurt per day, Yogurt Intake Log Stool sample collection & record Fermented Foods and GI Symptoms Questionnaire; Stool Log, Medication Log **Center Visit 5: Drop off stool sample; Return yogurt containers**
36-41	Medication Log
42	Fermented Foods and GI Symptoms Questionnaire Medication Log
43-48	Stool Log, Medication Log
49	Stool sample collection & record Fermented Foods and GI Symptoms Questionnaire Stool Log, Medication Log **Center Visit 6: Drop off stool sample**

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

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

- Visiting the research center 6 or more times to complete the initial study visit, pick up yogurt, drop off stool samples, and return study materials such as paper forms, containers and coolers.
- Doing your best to consume the study yogurt as directed.
- Keeping the study yogurt refrigerated until you are ready to eat it.
- Understanding the instructions for stool sample collection and other activities, and asking the study coordinator or the investigators any questions you have about the study or study activities.
- Collecting stool samples at the five designated times during the study.
- Notifying the study staff of any changes in your health, medications, probiotic supplement use, schedule or availability for study activities, or plans to leave the study.

Do I have to be in this study? What if I say "yes" now and change my mind later?

No, you do not have to be in this study. Taking part in research is voluntary. You can choose to be in the study or not be in the study. If you decide to be in the study, you can choose to leave the study at any time.

If you decide not to take part in the study, or if you choose to leave the study, your choice will not affect any treatment relationship you have with healthcare providers or any services you receive from them. No matter what you decide, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

Please let the researchers know if you choose to leave the study. If you stop being in the research, data and specimens that have already been collected will not be removed from the study database. We will remove identifiable information (information that could be used to tell who the data came from) from the data we collect about you.

What are my other choices if I do not take part in this study?

You do not have to be in this research study. You may choose to take part in the study or not.

Can I be removed from the research without my OK?

The researchers may take you out of the study, even if you want to continue, if:

- your health changes and staying in the study is no longer in your best interest;
- you do not follow the study rules or you no longer meet the requirements to be in the study; or

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- the study is stopped by the sponsor or researchers.

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

There are risks to participating in this research. The study team will monitor you to see if you are experiencing any harm related to your participation. If you experience any pain or discomfort, you must inform the study team as soon as possible.

There may be physical risks to participating in this research:

- Consuming the two servings of yogurt each day might cause GI distress or discomfort, and it could cause changes in your bowel habits.
- Two stool sample collection containers have liquid in them to preserve the stool. There is a risk that you could accidentally get preservative liquids from the stool sample collection tubes on your skin or eyes, or swallow the liquid. The preservative liquid is a product called RNALater, which contains 40% ammonium sulfate and water. If contact with skin or eyes, flush with water for several minutes. If swallowed, rinse mouth with water for several minutes. If you feel unwell, call POISON CONTROL CENTER (800) 222-1222 or call 911 for a life-threatening problem.

As with all research, there is a chance of a breach of confidentiality (your personal information could be seen by people outside of the research study without your permission). To minimize the risks of breach of confidentiality, we will not include any information that directly identifies you on the specimens and information we collect, and on the data resulting from the research. Instead, we will use a code on the bio-specimens and information. The code will be linked to your identity but the link will be stored in locked file cabinets in a locked office in the WHNRC that has controlled access (by card key) only to approved WHNRC employees working on human studies. We will maintain your de-identified data on encrypted computers and managed and stored in a password protected, web-based data management application, REDCap. Access to the de-identified data will be limited to only members of the research team who need the access to properly conduct the study. The members of the research team will not know who the data came from. De-identified specimens will be stored in a dedicated freezer at the WHNRC.

However, the Qualtrics online survey you took to determine study eligibility is not part of the study data and is not de-identified. The responses to your medical history, medical conditions, medications, fermented foods consumption and your contact information, including email, phone numbers, and home address, will be stored by UC Davis Cloud Services. Responses will not be used as study data and will not be analyzed.

Researchers will not use your specimens for genetic or genomic testing.

There is a risk that your information could become known to someone who is not a part of this study.

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Will being in this study help me in any way?

Being in this study will not help you directly. But your taking part in the study may benefit other people in the future by helping us learn more about the potential health effects of consuming yogurt.

This study is not a substitute for your regular medical care. You should continue to see your regular medical providers.

Will being in this study cost me anything?

There will be no cost to you for any of the study activities or procedures. Neither you nor your insurance carrier will be charged for your taking part in the research. All costs associated with the study will be paid by the sponsor/department.

Will I be paid or receive anything for being in this study?

We will pay you:

- $15 for the initial study visit
- $20 for each stool sample collection delivered to the research center (maximum of 5 samples)
- $40 for the completion of three stool logs and seven weekly questionnaires (partial completion will be prorated by number completed out of 10 possible)
- $30 for the yogurt pick-ups and consumption log (partial completion will be prorated by number completed out of 3 possible)
- $120 for the completion of the ASA24 dietary recalls (partial completion will be prorated by number completed out of 6 possible)

Payment will be provided after you complete or leave the study in the form of an electronic funds transfer to your bank account. If you complete all the study activities, you will receive $305.00 for being in this study. If you choose to leave or we take you off the study for any reason, you will receive payment the activities you completed, as listed above.

You may be asked for your social security number for payment purposes. It will not be used for any other reason without your permission.

If you receive $600 or more during a calendar year from the USDA for taking part in research, you may receive a 1099 for tax reporting purposes. Reimbursements for travel and other expenses are not included in this amount.

Biospecimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

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What happens if I am injured or get sick because of this study?

If you are injured or get sick because of this study, medical care is available to you through UC Davis Health, your local provider, or emergency services.

- If it is an emergency, call 911 right away or go to the emergency room.
- For non-emergency issues, you can call the UC Davis Health Hospital Operator (916-734-2011), tell the Operator you are in a research study and you wish to talk to the Internal Medicine Resident on call. Someone is available to answer the operator line 24 hours a day.

If you are injured as a result of being in this study, the University of California will provide the necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by the University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, you may contact the IRB Administration at (916) 703-9151 or HS-IRBAdmin@ucdavis.edu.

What happens to the information collected for the research?

We will do our best to limit the use or disclosure of your personal information, including information from this research study and from your medical records, to people who need to review this information. We cannot promise complete confidentiality. Some organizations may be required to inspect and copy your information including the IRB and other University of California representatives responsible for the management or oversight of this study.

We have strict rules to protect your personal information and protected health information (PHI). We will limit who has access to your name, address, phone number, and other information that can identify you. We will remove identifiable information from the data we collect about you. After we remove all of the identifiers, we will place a code on the information. The code will be linked to your identity but the link will be kept in a location that is separate from your study data. We will maintain your study data on encrypted computers and access to the information will be limited to only members of the research team who need the access to properly conduct the study.

However, we cannot promise complete confidentiality. If you agree to be in this study, Federal or state laws may permit or require us to show information to university or government officials responsible for monitoring this study. The following is a list of individuals who may access your records:

- Members of the research team
- Offices and committees responsible for the oversight of research
- Personnel who schedule or perform medical tests or procedures, handle accounting and billing, or do other tasks related to this study
- Collaborating researchers outside of UC Davis, including researchers at USDA ARS

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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.

Will I receive any results from this research?

No, you will not receive results from this research.

Will information or leftover specimens be used for other research?

The data and/or specimens we collect with your identifiable information (e.g., your name, medical record number, or date of birth) as a part of this study may be used to answer other research questions or may be shared with other investigators for other research. If we do so, we will remove all identifiable information before use or sharing. Once identifiers have been removed, we will not ask your consent for the use or sharing of your data and/or specimens in other research. In addition, data that have been de-identified may be uploaded to an NIH- or USDA-managed repository for other researchers to access and use.

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May we contact you by e-mail?

We are requesting your email address so we can schedule visits to the research center, send you reminders about study activities, and follow up on any questions or concerns you may have. Email is generally not a secure way to communicate about your health, as there are many ways for unauthorized users to access email. You should not send sensitive, detailed personal information by email. Email should also not be used to send urgent information. If you need to talk to someone right away, please contact Danielle Lemay, at 530-752-4748 during business hours (Monday – Friday, 8 am – 5 pm) or Charles Stephensen, at 530-304-3528 during evenings and weekends. If Drs. Lemay and Stephensen are unreachable, then Human Studies Manager, Ellen Bonnel, Ph.D., may be contacted at 530-752-4184. You do not have to give your email address to be in this study. Please initial one of the lines below.

_____ Yes, you may use email to contact me for this study.

My email address is: _____

_____ No, I do not want to be contacted by email.

Are there other research opportunities?

If you are interested in being contacted for future research, please write your phone number and/or email below. <u>This is completely optional.</u>

_____(Initials) Yes, I am willing to be contacted for future research opportunities. My phone number and/or email is: _____

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Signature Block for Capable Adult

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

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

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