Title of research study:

Fermented Vegetables and Gut Microbiome Pilot Study

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 determine the tolerability of fermented vegetable consumption and its effect on lactic acid bacteria (LAB) abundance in healthy people. There is evidence from previous studies that eating fermented foods containing live microbes can affect the gut microbiome and gut health, but there is little information on the impact of fermented vegetables, specifically.

You are invited to be in this study because you are an adult between the ages of 18 and 65, you have not been taking probiotics or eating fermented foods regularly, and you meet all study eligibility requirements. Your participation in this research will include 4 visits to the Western Human Nutrition Research Center and will last about 3 weeks (19 days). We expect about 24 people from Davis and the surrounding area to join and take part in this research.

Being in this study will involve one week of not consuming any fermented foods, four days of eating fermented vegetables provided by the research study while avoiding other fermented foods, and one more week of not consuming any fermented foods. The study will also involve collecting samples of your stool and bringing them to the research center three times during the three-week study. Your blood pressure will be measured during each visit, and we will collect a sample of your saliva three times during the study. We will also ask you to complete several questionnaires about your diet, medications you take, bowel movements, and gastrointestinal and other health 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.

Here are some reasons you may not want to be in this research:

- Collecting samples of your stool and bringing them to the research center three times during the 3-week study.
- Collecting samples of your saliva and having your blood pressure measured.
- Visiting the research center for three scheduled visits during the three-week study.
- Completing records of your bowel movements, symptoms you may have, and medications you take.
- Consuming reduced-sodium fermented vegetables two times a day for four days.
- Avoiding probiotic supplements, foods or drinks containing probiotics, and fermented foods other than the fermented vegetables provided by the study for three weeks (Some examples of fermented foods are: yogurt, sour cream, 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://irb.ucdavis.edu/for-research-participants/

What if I have Questions?

If you have any questions about this research, or you believe that you've been injured or harmed as a participant of this research, please contact the investigator, Dr. Danielle Lemay, Ph.D., at 530-752-4748 during business hours (Monday-Friday, 8am-5pm).

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. In the case of an emergency, dial 911 from any phone.

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?

APPROVED by the Institutional Review Board at the University of California, Davis	
Protocol	APPROVED
2210950	April 3, 2025

This research is being funded by the U.S. Department of Agriculture (USDA) Agricultural Research Service, also called the sponsor. Sponsors may change or be added.

Researchers and staff on the study team are employees of the USDA and the University of California.

If you have questions, tell the study coordinator and they will put you in touch with someone to talk to.

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 three weeks. The main activities are: consuming study-provided fermented vegetables during the intervention period, avoiding probiotics and fermented foods other than those provided by the study, collecting stool samples, completing visits to the research center, and completing logs and questionnaires.

Fermented vegetable consumption

This study will test the effects of fermented vegetable consumption on lactic acid bacteria abundance, GI symptoms, fecal consistency and frequency by asking you to not consume fermented foods for one week, consume fermented vegetables two times per day for four days, and then go back to not consuming fermented foods for another week. We call the four days of fermented vegetable consumption the 'intervention period.'

At the start of the intervention period, we will give you 10 pre-packaged portions of fermented vegetables in plastic food containers. Each container will have 50g (about ¼ cup) of reduced-sodium fermented vegetables such as cucumbers, bell peppers, sweet potato, sweet corn, tomato, or other vegetables. The vegetables are blended to produce a uniform consistency. The fermented vegetable blends may contain a combination of ingredients from different categories of vegetables, peppers, salts, preservatives, and other supplements, with examples shown in Table 1 below. There may also be naturally occurring yeast in one or more of the products. Please inform the study coordinator if you have any allergy, sensitivity or dietary restriction to any food or food ingredient.

The blends you receive will be produced at a pilot plant which adheres to FDA regulations for safe food production and handling. The fermented vegetables are kept in cold storage to preserve freshness and are packed into 50g portions under stringent food safety conditions. During the first week of the study, we will provide you with a digital thermometer to monitor your home refrigerator temperature and ensure it will be cold enough to safely store the fermented vegetables.

Each day, we would like you to consume two containers of fermented vegetables, and we ask that you eat the fermented vegetables in a certain order. Please check the labels on each container to know the order you should eat the fermented vegetables. We will give you a total of 10 portions so that you have two for each day, plus two back-ups.

We will ask you to complete an intake questionnaire while you eat each fermented vegetable serving, to record your evaluation of each fermented vegetable serving, the time you ate them, and any comments or concerns you may have. You will be able to access the questionnaire by scanning the QR

code labeled on each container. Please let the study coordinator know if you have any difficulties accessing the questionnaire.

We will provide you with an insulated bag for getting the fermented vegetables to your home and bringing back the used containers. Please put the fermented vegetables in your refrigerator at home as soon as possible, and keep them refrigerated until you're ready to eat them. Do not heat the fermented vegetables prior to consumption. We will ask you to bring back the containers at the end of the intervention period. Please bring back all of the containers, even though some may still be full. You do not need to wash the containers. You will be provided with a printout of instructions and reminders for you to refer to throughout the intervention.

Table 1: Examples of Ingredients Used for the Preparation of the Fermented Vegetable Blends.

<table>
<tr><td rowspan="2">Vegetables
Green Cabbage
Cucumber
White or Yellow Corn
Iceberg Lettuce
White or Yellow Onion
Tomatillo
Golden or White Carrots
Jicama
Radish
Red Tomato Pulp
Purple Beet</td><td>Peppers
Cubanelle
Yellow Bell Pepper
Red Bell Pepper
Orange Bell Pepper
Green Bell Pepper</td><td>Salts
Sodium Chloride
Potassium Chloride
Calcium Chloride
Magnesium Chloride</td></tr>
<tr><td>Preservatives
Sodium Benzoate
Potassium Sorbate</td><td>Other Supplements
Arginine
Citric Acid, Hydrochloric Acid, Lactic acid or similar food-grade acidifier</td></tr>
<tr><td colspan="3">Starter Culture: Lactiplantibacillus pentosus or Lactiplantibacillus plantarum and Lactococcus lactis</td></tr>
</table>

<u>Avoiding probiotics and fermented foods</u>

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

We will also ask you to avoid consuming probiotic or fermented foods other than the fermented vegetables provided by the study. By 'probiotic foods,' we mean any food with 'probiotic' on the label, indicating that it contains active probiotic cultures. By 'fermented foods,' we mean foods that were made by microbial processes and still contain high amounts of live microbes. These foods include:

- Cultured dairy products, such as yogurt, sour cream, kefir, buttermilk, and 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, miso, tempeh, or other fermented bean products that are consumed uncooked

If you are currently taking fiber supplements, which include tablets, chewables, powders, or drinks that provide extra fiber, please continue to take it on the same schedule.

Collecting stool samples

We will ask you to collect stool specimens at the end of the baseline, intervention, and follow-up periods, for a total of three stool collections. During each center visit, we will give you a stool collection kit that contains gloves, a toilet insert for collecting stool, six stool sample tubes with scoops in the lid, a Ziploc bag and a detailed instructions and sample record sheet. We will ask you to collect samples of your stool into the six collection tubes and seal the remaining stool in the bag. We will provide you with a cooler and ice packs for storing and transporting the collected stool samples to the research center within 12 hours after collection. Ideally, stool drop-offs should be completed during your scheduled study visits. If the time of your stool collection is more than 12 hours before your scheduled study visit, please contact the study coordinator to arrange an earlier stool drop-off time.

Two stool sample tubes have liquids in them to preserve the stool. One tube contains RNAlater, a non-toxic mixture of 40% ammonium sulfate and water. The other preservative liquid is DNA/RNA Shield, a proprietary mixture which can be harmful if swallowed. 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. If you feel unwell, call Poison Control Center (800) 222-1222 or call 911 for a life-threatening problem.

Visiting the research center

We will ask you to visit the research center once at the beginning of the study followed by three study visits during the three-week study period. 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, check your vital signs, height, and weight, and give you the instructions and materials you will need to complete the study activities for the first week of the study.

At the end of the first week, we will ask you to visit the research center to deliver your first stool collection and stool log, measure your blood pressure, provide a saliva sample, receive your servings of fermented vegetables, and get the instructions and materials you will need for the next four days of the study. We will ask you to visit the center again at the end of the four-day intervention to turn in

your second stool collection, provide a second saliva sample, have your blood pressure measured, and complete a post-intervention questionnaire.

The final study visit will take place one week after the end of the four-day intervention. At the final visit, we will ask you to deliver your final stool collection, return your stool and medication logs and any other study materials you may still have. We will also ask you to provide a saliva sample and we will complete a final measurement of your blood pressure.

Completing logs and questionnaires

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.
- Medication Log: a record of all medications you take while participating in the three-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.
- Stool Log: a record of the date, time and stool consistency of the bowel movements you have throughout the study.
- Stool Collection and Record: a record of the date, time and stool consistency of the stool samples collected at the three designated timepoints during the study.
- Symptoms & Fermented Foods Questionnaire: an online survey with three sections. The first two sections ask about any GI symptoms – such as bloating, diarrhea, etc. – and general health symptoms that you may have had during the past three days. The third section asks about any fermented foods or probiotic products you may have consumed during the past three days. We will send you a text or email asking you to complete this at the end of each phase of the study. It can be completed at home on a tablet, smart phone or computer.
- Fermented Vegetables Intake Questionnaire: an online survey to be completed while eating each fermented vegetable serving. This will ask you to record when you ate the fermented vegetables and rate their acceptability.
- Fermented Vegetables Post-Intervention Questionnaire : an online survey to be completed during the third study visit. This will ask for your feedback about the fermented vegetables you ate during the intervention.

Breakdown of Participant Activities by Study Day

Study Day	Participant Activities
0	**Center Visit 1: Informed Consent, In-Person Screening, Participant Instructions, Demographics Questionnaire**
1-6	Stool Log Medication Log
7	Stool Log Symptoms & Fermented Foods Questionnaire Medication Log Stool sample collection & record **Center Visit 2: Drop off stool sample, collect saliva sample, measure vitals, pick up fermented vegetables.**
8-11	Two 50g servings of fermented vegetables per day Fermented Vegetables Intake Questionnaire Stool Log Medication Log
12	Stool Log Medication Log Symptoms & Fermented Foods Questionnaire Post-Intervention Questionnaire Stool sample collection & record **Center Visit 3: Drop off stool sample, collect saliva sample, measure vitals, return fermented vegetable containers**
13-18	Stool Log Medication Log
19	Stool Log Symptoms & Fermented Foods Questionnaire Medication Log Stool sample collection & record **Center Visit 4: Drop off stool sample, collect saliva sample, measure vitals**

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 4 or more times to complete the initial study visit, pick up the fermented vegetables, drop off stool samples, complete blood pressure measurements and saliva collections, and return study materials such as paper forms, containers and coolers.
- Doing your best to consume the study-provided fermented vegetables as directed.
- Keeping the fermented vegetables refrigerated until you are ready to eat them, and not heating them.
- 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 three designated times during the study and bringing them to the research center as soon as possible.
- 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 at UC Davis Health 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.

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
- 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 have concerns, please inform the study team as soon as possible.

There may be physical or psychological risks to participating in this research:

- You may experience a foodborne illness, especially if you have certain medical conditions. The fermented vegetables used in the study are produced and packaged using food-safe procedures and were tested in an independent laboratory for the presence of types of bacteria that cause illness. However, the risk of food-borne illness can never be entirely eliminated. You can reduce this risk by always keeping the vegetables cold in your refrigerator or cooler.
- You may have an unknown allergy or reaction to a study food.
- You may strongly dislike a study food.
- A study food might cause GI distress or discomfort, and it could cause changes in your bowel habits.
- You may experience embarrassment or personal discomfort from collecting a stool sample or filling out a questionnaire.
- Two stool sample collection vials 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 liquids are called RNALater, which contains 40% ammonium sulfate and water, and DNA/RNA Shield, a proprietary mixture. If contact with skin or eyes occurs, 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 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 other 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 to determine your genetics or genome.

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

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 effect of fermented vegetable consumption on the gut microbiome and immune function.

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, except for your transportation to and from the study center.

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

We will pay you up to $184 for participating in this study. Payment will be provided in the form of a mailed check or direct deposit after you complete or leave the study. If you choose to leave or we take you off the study before you complete the study, you will receive payment for the activities you completed, as listed below.

We will pay you:

- $16 for the initial study visit
- $72 for the collection and delivery of three stool samples ($24 per sample delivery, maximum of 3 samples)
- $12 for the completion of three Symptoms & Fermented Foods Questionnaires ($4 per questionnaire completed)
- $16 for the completion of eight Intake Questionnaires ($2 per questionnaire completed)
- $32 for completion and delivery of two study logs ($16 for the stool log and $16 for the medication log)
- $36 for attending three study visits to conduct vitals measurements, saliva collections and fermented vegetable pick-up ($12 per completed study visit)

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 research center 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.

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

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) 703-9158 or HS-IRBEducation@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. The information we send to the sponsor will not include information that directly identifies you. Instead, a code will be applied to the data and the link between the code and your identity will be kept at the research site.

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. 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
- U.S. Office for Human Research Protections
- Collaborating researchers outside of UC Davis, including researchers at USDA-ARS
- Companies or groups performing services for the research team, such as administrative service providers who process study payments

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?

We will use your biospecimens and information to conduct this study. Leftover biospecimens and data collected for this research may also be used for future research studies. We will not share any personally identifiable information. Our goal is to make more research possible. These studies may be done by researchers at this institution or other institutions, including commercial entities. Data may be placed in one or more external scientific databases for access and use. We will not ask you for additional permission to share de-identified information or biospecimens.

May we contact you by e-mail?

We are requesting your email address so we can schedule visits to the research center, send 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 at 530-376-3216 during evenings and weekends. If Dr. Lemay is 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: _____

Do not write below this line. For IRB stamp and version date only.

APPROVED by the Institutional Review Board at the University of California, Davis	
Protocol	APPROVED
2210950	April 3, 2025

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	

Do not write below this line. For IRB stamp and version date only.

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