The UNIVERSITY OF CHICAGO
The Division of the Biological Sciences • The University of Chicago Medical Center

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH PROTOCOL GLUTEN CHALLENGE GROUP

Protocol Number: IRB22-1138
Name of Subject: _____
Medical History Number: _____

STUDY TITLE: Tissue destruction and healing in celiac disease

Doctor Directing Research:	Sonia Kupfer, MD
Address:	900 E. 57th St. 9th Floor, KCBD 9120 Chicago, IL 60637
Telephone Number:	(773) 702-7868

KEY INFORMATION

We are asking you to choose whether or not to volunteer for a research study that is gathering information about the basic processes of intestinal (bowel) tissue destruction and healing in people with celiac disease. This section is to give you key information to help you decide whether to participate. We have included detailed information after this section. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is above.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

You are being asked to take part in this research study because you have been diagnosed with celiac disease. Celiac disease is an immune reaction to eating gluten, a protein found in wheat, barley, and rye. When people with celiac disease eat gluten, it triggers an immune response in the intestine (bowel). Over time, this reaction damages the intestine's lining and prevents it from absorbing some nutrients.

The purpose of this study is to learn more about the processes that cause intestinal damage and healing in people with celiac disease. We hope this study will provide resources for scientists and doctors to improve celiac disease research and clinical care.

This study has three groups of participants. Regardless of group assignment, all participants will undergo data collection, blood testing, and intestinal tissue sampling during the study. More details can be found below in the Detailed Consent section. The three study groups are:

- Gluten challenge group: People who have been diagnosed with celiac disease for at least 12 months and are currently on a gluten free diet will be asked to eat a small amount gluten each day as part of this study.
- Gluten de-challenge group: People who are newly diagnosed with celiac disease and are beginning a gluten free diet as part of routine care.
- Control group: People who do not have celiac disease will participate as a comparison group.

You are being asked to join the **gluten challenge group**.

During the study, you will be asked to eat snack bars that have vital wheat gluten (3grams or about 1 teaspoon in each bar). You will be asked to eat the gluten snack bar every day with the same meal for 6 weeks. The level of gluten in these bars is small and should not cause major digestive issues for most people, though you will be monitored throughout the study and can stop the study if needed.

Your participation in this study will last about 7 weeks and will include approximately 5 study visits.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

By participating in this study, you may help future patients who have celiac disease by helping us learn more about processes that cause destruction and healing of the intestinal lining. In addition, you will have close assessment of diet and nutrition during the course of study.

For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You will be asked to ingest gluten during the study. After consuming gluten you may experience worsening of gastrointestinal symptoms, including abdominal pain and diarrhea.

You will be asked to undergo 3 upper endoscopy procedures with biopsy in the time frame of 7 weeks if you participate in this study. If you have successfully completed the DeChallenge group of this study and are rolling over to the gluten challenge group within 1-3 months of study completion, you will be asked to undergo 2 upper endoscopy procedures with biopsy in the time frame of 7 weeks.

Endoscopy means a thin, flexible, lighted tube will be inserted inside the small bowel through your mouth to view your small intestines and take small biopsies. Endoscopies will be done while you may be mildly sedated. While endoscopies are considered a safe procedure, rare complications include tearing of the upper digestive tract and/or bleeding that may require surgery to correct.

During this time you also be required to complete daily diary and weekly questionnaires.

For a complete description of risks, refer to the Detailed Consent Section below.

For a complete description of alternate treatment/procedures, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?
Taking part in this study is voluntary. If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

You may choose not to participate at any time during the study. You will not lose any services, benefits or rights you would normally have if you choose to leave the study. The University of Chicago/University of Chicago Medical Center will not condition (withhold or refuse) treating you on whether you sign this Authorization or revoke your authorization at a later time. If you do not sign this form, you will not receive the research-related intervention(s).

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?
The person in charge of the study is Dr. Sonia Kupfer, of the University of Chicago. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, her contact information is (773) 702-7868.

If you have a research-related injury, you should immediately contact Dr. Kupfer at (773) 702-6800 and ask for pager number 2870.

For questions about your rights as a research subject, please contact the University of Chicago BSD IRB at (773) 702-6505.

DETAILED CONSENT

WHAT IS INVOLVED IN THE STUDY?

Enrollment is competitive. This means that when the target number of subjects enters the study, all further enrollments will be closed. About 30-60 people will take part in the 'gluten challenge group' at the University of Chicago and about 30-60 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 60 healthy people.

If you participate in this study, you will be expected to:

- Eat gluten containing snack bars every day for 6 weeks
- Undergo three (3) endoscopies with biopsies of intestinal tissue. Undergo two (2) endoscopies if you've previously successfully completed the dechallenge group and are screening within 1-3 months of dechallenge study completion.
  An upper endoscopy is a procedure that examines the inside of your esophagus, stomach, and upper portion of the small bowel. During this procedure, a thin, flexible, lighted tube is inserted through your mouth to view your intestines and take small biopsies.
  You will be asked to not to eat for 8 hours before the procedure, but you can have clear liquids up to 2 hours before the procedure. On the day of the test, you will be mildly sedated to help you relax. During the procedure, a thin, flexible tube with a small camera at the tip will be inserted through your mouth and moved through the esophagus and stomach and into the small bowel. The camera allows pictures to be sent to a video screen for the doctor to look at. A tool called forceps is passed down the tube, so the doctor can take tissue samples. The procedure takes 15-30 minutes, but you will be at the clinic for about 2 hours and you will need to have someone available to take you home afterwards. You should not drive or make important decisions for at least 24 hours following the procedure.
- Give urine, blood, and saliva samples
- Complete questionnaires
- Be available for safety assessment phone calls

The procedures for each study visit are described below.

Visit 1 (Screening visit, part 1):

- You will be asked to review, sign, and date the informed consent. The study team will review the study with you and ample time will be given to ask questions
- The study doctor will verify that you qualify for the study
- Physical exam including your height and weight
- Vital signs such as blood pressure, heart rate, and temperature will be collected
- Blood draw (about 1½ tablespoon) will be taken for lab tests. If you're rolling over from the dechallenge group within 1-3 months after study completion, the final lab tests for the dechallenge group will take place of this blood draw.
- You will be asked to complete the following questionnaires electronically via REDCap during the visit to assess your celiac disease symptoms and quality of life:
  - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – It will take about 8 minutes to complete.
  - Celiac Disease Symptom Diary (CDSD©) – It will take about 10 minutes to complete.

- If found eligible, you will be scheduled for Visit 2.

Visit 2 (Screening visit, part 2):

- The study doctor will review blood test results from visit 1 to verify that you qualify for the study.
- Your demographic information (such as your age, sex, race and ethnicity), complete medical history will be collected.
- Current medication will be reviewed.
- Blood draw (about 1½ tablespoon) will be taken for lab tests.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to take part in this study.
- Saliva samples (by spitting into a small tube) will be collected for lab tests.
- Upper endoscopy will be performed to view your small intestine. Up to 14 small intestinal biopsies will be taken during this procedure. Luminal fluid (consists of digestive fluid, food particles and bacteria) from your bowel will be collected as well. If you're rolling over from the dechallenge group within 1-3 months after study completion, the final upper endoscopy from the dechallenge group will take place of this first endoscopy.
- You will be asked to complete the following questionnaires electronically via REDCap to during the study visit to assess your celiac disease symptoms and quality of life:
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – It will take about 8 minutes to complete.
    - Celiac Disease Symptom Diary (CDSD©) – It will take about 10 minutes to complete.
    - Celiac Disease Dietary Adherence Questionnaire (CDAT) – This questionnaire will ask about adherence to a gluten free diet with the exception of the gluten bar used in this study. It will take about 5 minutes to complete.
- The study team will contact you to follow up on any side effects you may feel.

Visit 3 (Day 0):

- You will receive a gluten-containing snack bar to eat at the study clinic.
- Blood draw (about 1 ½ tablespoons) will be taken before you eat the snack bar and 2 hours after you eat the snack bar.
- Urine will be collected for lab tests.
- You will be asked to complete the following questionnaires to assess your celiac disease symptoms and quality of life. Surveys will be completed electronically using a weblink.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – you will be asked to complete this survey **weekly** until end of study. It will take about 8 minutes to complete.
    - Celiac Disease Symptom Diary (CDSD©) – you will complete the diary **daily** until the end of the study. It will take about 10 minutes to complete each entry.
- You will receive gluten containing snack bars to consume daily, at the same time of day, for the next 6 days. You will eat one bar with the same meal, every day. The gluten snack

bars must be kept in the freezer, then thawed to room temperature before eating. Once thawed the bars should be eaten within 4 days of thawing.
- The study team will contact you to follow up on any side effects you may feel, review your answers to questionnaire, and to remind you to eat the snack bars given by the study team.

Only for subjects enrolled after 05/01/2024:
- Hip and waist measurements
- Dual x-ray absorptiometry (DEXA) scan: An X-Ray called DEXA will be performed to measure your body composition and bone mineral density. You will be asked to lay down on your back and have the scanner move over your body and measure how much muscle, bone, fat you have in your body. There is a small amount of radiation exposure from a DEXA scan. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DXA scan is considered safe for adults.

Visit 4 (day 6):
- Blood draw (about 1 ½ tablespoons) will be taken for lab tests.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to continue this study.
- Saliva samples will be collected for lab tests.
- Upper endoscopy with biopsies (up to 14) and luminal fluids collection will take place.
- You will receive gluten-containing snack bars to eat daily for the next 5 weeks. You will eat one bar with the same meal, every day.
- You will be asked to complete the following questionnaires via REDCap to assess your celiac disease symptoms and quality of life.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – It will take about 8 minutes to complete. You will complete this questionnaire prior to endoscopy, and then weekly until the end of study.
    - Celiac Disease Symptom Diary (CDSD©) – It will take about 10 minutes to complete. You be asked to continue to complete this daily until end of study.
    - Celiac Disease Dietary Adherence Questionnaire (CDAT) – It will take about 5 minutes to complete. You will be asked to complete this one time at this visit.
- The study team will contact you weekly to follow up on any side effects you may feel, review your answers to questionnaire, and to remind you to eat the snack bars given by the study team.

Visit 5 (week 6):
- Blood draw (about 1.5 tablespoons) will be taken for lab tests.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to continue this study.
- Saliva samples will be collected for lab tests.
- Upper endoscopy with biopsies (up to 14) and luminal fluids collection will take place.
- You will be asked to complete the following questionnaires via REDCap to assess your celiac disease symptoms and quality of life.

  - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – you will be asked to complete this survey **weekly** until end of study. It will take about 8 minutes to complete.
  - Celiac Disease Symptom Diary (CDSD©) – you will complete the diary **daily** until the end of the study. It will take about 10 minutes to complete.
  - Celiac Disease Dietary Adherence Questionnaire (CDAT) – It will take about 5 minutes to complete.
- The study team will contact you to follow up on any side effects you may feel and to review your answers questionnaire.

Biological sample Storage

Biological samples include the blood, urine, tissue, and luminal fluid collected during this study. All biological samples collected from you will be labeled with a unique participant code. It will include the collection date and time but will not include your name or medical record number.

These samples are collected for the purposes of this study and may also be stored and used for future research studies. This future research may be done at the University of Chicago and Mayo Clinic or by colleagues from an outside institution, including commercial partners.

Your samples may be studied for genetic material (such as DNA and RNA). Genes are made up of DNA, which is short for deoxyribonucleic acid. They act as instructions to your body, determining things like eye color and hair color, but also whether people may be more likely to develop certain conditions. Genes are passed from parent to child. RNA is made from DNA. RNA is short for ribonucleic acid. RNA is a genetic material that has an important role in making proteins. Proteins are the building blocks of your body, cells, and organs. The results of genetic research or testing may be shared with collaborators for research purposes. These results would not contain your identifying information (such as name and medical record number) and would instead be labelled with a unique subject study code. The results of genetic testing and research will not be shared with you.

If you decide to withdraw from the study, you can choose to have your samples destroyed. The information that has already been collected will still be used for the study. However, no further research will be conducted using your samples and your samples will be destroyed. Please see the 'What Are My Rights' section below for additional information.

Samples may be tested, stored, and shared as follows:

University of Chicago

The study team will store your blood, urine, luminal samples, and biopsy tissue. The University of Chicago will conduct genetic analysis for study purposes and will store your DNA and RNA. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples and can be shared with researchers at other institutions and/or companies as well.
Any samples that are shared will be labelled with a unique subject study code. Samples will be labelled with the date and time the sample was collected will not contain any personal identifiers.

Mayo Clinic

The study team will process blood samples and send PBMC (type of immune cells) and serum samples to Mayo for storage. These samples will be labelled with the subject study code and will include the collection date and time but will not contain any identifiers. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples and can be shared with researchers at other institutions and/or companies as well.

California Institute of Technology
The study team will send saliva samples and tissue RNA/DNA to the California Institute of Technology to perform microbiome genetic analysis (genetic testing of all microbes, such as bacteria, fungi, and viruses that naturally live on our bodies). The samples will be labelled with the subject study code and will include collection date and time but will not contain any identifiers. Leftover tissue and saliva samples will be stored indefinitely for future research purposes and these samples can be shared with researchers at other institutions and/or companies.

Other information
In future, identifiers associated with your data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use.

The results from this study will not be shared with you.

Dr. Kupfer may decide to take you off of the study without your consent if:
- You are unable to meet the requirements of the study or your medical condition changes;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

During your participation in this study, you are at risk for the side effects described in this section. The study doctor will discuss these with you.

Gluten consumption
The side effects of ingesting gluten when you have celiac disease may be very mild, or they may be significant. You will be monitored for side effects throughout the study. If you experience significant side effects, you will be asked to stop eating the gluten snack bars. In an effort to minimize any side effects, the amount of gluten in the bars is very small. Potential symptoms may include:

Somewhat likely side effects:
- Bloating
- Abdominal pain
- Nausea

- Diarrhea
- Constipation

Less likely side effects:

- Vomiting
- Fatigue
- Headache
- Brain fog or exhaustion

Upper endoscopy/biopsy risks

An upper endoscopy and biopsy of the intestine are standard and commonly performed medical procedures to examine the small bowel.
Somewhat likely side effects include:

- Tiredness
- Some pain (cramps)
- Discomfort

Rare side effects include;

- Tearing of the upper digestive tract and/or bleeding. This may require surgery to correct.

Biopsy risks may include,

- The removal of tissue samples may result in a small amount of blood in your stools. This should go away. If it persists after 24 hours, please call your study doctor listed on the front page.
- Tenderness
- Infection
- Significant bleeding that requires getting blood from donors

The risk of the sedation medication, usually given during an endoscopy to help you relax, may cause

- allergic reactions,
- nausea,
- skin rash,
- dizziness with a drop in blood pressure,
- a slowing down of your breathing so much that in very rare cases a breathing machine will be used, and
- **death** from sedation-related heart problems.

You will not be permitted to drive immediately after the procedure and, therefore, will need someone to drive you home.

During the endoscopy procedure, the study doctor may come across incidental findings such as ulcers (sores in the stomach tissue lining), H. pylori (bacteria which may cause stomach infections), reflux changes (could cause changes in the tissue lining of the esophagus (tube through which food passes from the throat to the stomach), or polyps (small protrusions in the

lining of the esophagus, stomach or small intestine). Additional tissue samples may be taken for clinical purposes in such cases. If this occurs, the study doctor will discuss the findings with you and you will be referred for the appropriate clinical care

Blood Draw Risks
The risks of giving blood include pain, a bruise at the point where the blood is taken, redness, bleeding, nerve damage, blood clots, which may cause inflammation, and swelling of the vein and infection, and a rare risk of fainting. Care will be taken to avoid these risks.

DEXA Scan Risks
During the scan, you will be exposed to a very low amount of radiation. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DEXA scan is considered safe for adults.

Questionnaire Risks
Some of the questions may seem personal and may make you feel uncomfortable. If you have any questions or concerns while answering these questions, please talk to your study doctor. You may choose not to answer any question that makes you uncomfortable.

Loss of Confidentiality
Any time information is collected about you there is a potential risk for loss of confidentiality. However, the researchers will make every effort to keep your information confidential. Please refer to the 'What About Confidentiality' section for information on what measures will be taken to protect your confidentiality.

Unforeseen Risks
There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could affect whether you wish to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there will be no direct medical benefit to you. Information gathered in this study may benefit other people who have celiac disease.

WHAT OTHER OPTIONS ARE THERE?
You do not have to take part in this study to receive treatment for your celiac disease. Your other option would be to not participate in this study and maintain a gluten-free diet. If you wish you may also participate in another clinical trial.

WHAT ARE THE COSTS?
Clinical services provided during a clinical trial are either research-related or considered part of usual medical care for patients with your disease or condition. Tests, procedures, and activities that are ordered by your medical care team to monitor your disease or condition (whether you are participating in a clinical trial or not) are described as 'usual medical care'. 'Research-related' is the term used to describe any tests, procedures, or activities that you are being asked to undergo

only because of your participation in this clinical trial.

You or your insurance will be financially responsible for the costs of your usual, ongoing medical care. This often includes regular visits with your doctor, lab tests and imaging used to measure your response to treatment, and other tests and procedures deemed medically necessary by your care team. None of the activities done as part of this study are considered part of your usual on going care. Financial responsibilities for routine care may include deductibles and co-payments and this care will be subject to all the same requirements and restrictions of your insurance.

You will not be responsible for the costs of tests or services that are being performed solely for the purposes of this study and would not be performed if you were not participating in this clinical trial. This will often include additional tests performed to answer a research question but not required for your routine clinical care.

If you have questions about whether specific clinical services are research related or part of your usual medical care, please speak to your physician or research contact person.

WHAT HAPPENS IF I HAVE AN INJURY?
If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, you may receive such emergency medical treatment at the University of Chicago Medical Center, UChicago Medicine Ingalls Memorial Hospital, UChicago Medicine Northwest Indiana, UChicago Medicine AdventHealth Bolingbrook, UChicago Medicine AdventHealth Glen Oaks, UChicago Medicine Advent Health Hinsdale, or UChicago AdventHealth LaGrange at no cost to you. You must notify Dr. Kupfer as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure, and is not the result of your disease or condition. The costs of any non-emergency care for such an injury will be billed to you or your insurance in the ordinary manner. If you think that you have suffered a research related injury, you must let Dr. Kupfer know right away.

In the event of an emergency, you should seek care at the nearest emergency room or call 911 and notify the study doctor's office when is possible.

WILL I BE PAID FOR MY PARTICIPATION?
You will be compensated $400 after each endoscopy, $50 after each of two clinic visits, and $200 for successful completion of all questionnaires for a potential total of $1500.
You will receive payments five times during the study, once after each visit.

Additionally, you may be eligible for reimbursement of travel-related expenses, subject to the following limits:

- **Flights**: Economy flights to and from Chicago, up to $1,000.
- **Transportation**: Rides to and from the university (e.g. Uber, Taxi, etc.), up to $150.
- **Meals**: A daily meal allowance up to $75.

- **Overnight Accommodations**: If required, the university will arrange accommodations at Hyatt Place Chicago. Alternatively, accommodations at other hotels can be reimbursed at $200/night.

Reimbursements apply only to expenses incurred during study-related visits. To qualify for reimbursement, you must submit itemized receipts for travel, accommodations, and meals to the study staff. Please consult the study staff before incurring any expenses to ensure eligibility.

As policies at the University of Chicago require that these payments be given in the form of a check, you will need to complete a tax form. Therefore, we will be collecting personal information about you including your name, address, and social security number. In addition, because the process for requesting a check oftentimes takes several weeks, we will mail your check to you when it is ready. Please note that it may take 3-4 weeks after conclusion of your study participation in order for you to receive your payment.

Additionally, you will receive a parking voucher at the end of each study visit.

WHAT ABOUT CONFIDENTIALITY?

There is a risk of potential loss of confidentiality. To minimize this risk, study records that identify you will be kept confidential. Any research data will be stored in a locked drawer in a locked office and/or entered on a password-protected, encrypted, HIPAA-compliant computer. Only study staff will have access to the data. The results from tests and procedures performed as part of this study may become part of your medical record. Any research information in your medical record will be kept indefinitely.

During this study, Dr. Kupfer and her research team will collect protected health information (PHI) about you for the purposes of this research. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago. The PHI consists of any health information that is collected about you, which could include your medical history and new information collected as a result of this study. Some of this information will come from your medical record. The information to be used on this study includes your name, address, medical record number, phone number, email address, social security number (for payment purposes), date of birth, and dates of procedures, tests diagnosis and hospitalizations (if applicable). We will use these identifiers to schedule study visits, collect data from your medical records, monitor your health, stay in contact with you, complete study objectives and distribute study payments.

As part of the study, Dr. Sonia Kupfer and her research team will share information about you as well as the results of your study-related procedures and tests with collaborators at Mayo Clinic and California Institute of Technology who are assisting with the study, the study funder the National Institutes of Health (NIH) and the representatives of the data safety monitoring board (a group of reviewers who monitor safety data during the course of the study).

Data shared could include initials, age, race, ethnicity, the results of research tests and procedures done as part of the study, the dates of study procedures and study test results. This

information is being sent to review the results of the study, to monitor the safety of participants, and to verify the accuracy of the study data.

The University of Chicago Financial Services office will have access to your name, address and social security number when processing your check payment.

Your records may be reviewed by federal agencies whose responsibility is to protect human subjects in research, including the Office of Human Research Protections (OHRP). In addition, representatives of the University of Chicago, including the Institutional Review Board (a committee that oversees research) and the Office of Clinical Research may also view the records of the research. If your research record is reviewed by any of these groups, they may also need to review your entire medical record. The results from tests and/or procedures performed as part of this study may become part of your medical record.

Once health information is shared outside the University of Chicago, please note that your identifiable health information may be shared with someone else. The same laws that the University of Chicago must obey may not protect your health information.

During your participation in this study, you will have access to your medical record. Dr. Kupfer is not required to release to you research information that is not part of your medical record. This consent/authorization form will be kept by the research team for at least 6 years. The study results will be kept in your research record and be used by the research team until completion of this study.

At the time of study completion, either the research information not already in your medical record will be destroyed or information identifying you will be removed from study results.

Data from this study may be used in medical publications or presentations. Your name and any other identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time.

We are collecting your tissue and/or blood as part of this study. We may use your samples for other research studies, including genetic testing, without contacting you, including sharing your samples with others for research purposes here and outside University of Chicago. It is possible that these samples may be shared with a for profit company for research.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Genetic Information Nondiscrimination Act (GINA)

The Genetic Information Nondiscrimination Act (GINA) is a federal law that may help protect you from health insurance or employment discrimination based on genetic information. GINA is a federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;

- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Other Databases

If you agree to take part in this study, your genetic and health information and as applicable a portion of your specimens will be placed into one or more scientific databases. In particular, the National Institutes of Health maintains a database called "dbGaP." The NIH database is a restricted database, meaning a researcher who wants to study information from dbGaP must work with the group overseeing the database to obtain the information. Security measures are in place to protect these data.

Researchers with an approved study will be able to see and use some of your information, but your name and other information that could directly identify you (such as your name or address) will not be placed into the database. There is a risk that someone could use your unique genetic information to trace data back to you or your family, but this risk is very small. There is no direct benefit to you that is expected from any secondary research that may be conducted.

If you decide to withdraw from the study as outlined in the following section, your data will be withdrawn from these databases. However, if your data have already been submitted to an NIH database and distributed to other researchers, or your data have been de-identified and can no longer be linked back to you, your data will not be able to be withdrawn.

Certificate of Confidentiality

To help us protect your privacy, the National Institutes of Health (NIH) has issued a Certificate of Confidentiality for this research. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. There are specific circumstances when the Certificate of Confidentiality does not prevent researchers from disclosing voluntarily, without your consent, information that would identify you as a participant

in the research. For example: suspected child abuse, elder abuse, or urgent risk of harm to self (suicide) or others (homicide).

WHAT ARE MY RIGHTS AS A PARTICIPANT?

If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. Kupfer in writing at the address on the first page. Dr. Kupfer may still use your information that was collected prior to your written notice.

We will tell you about significant new information that may affect your willingness to stay in this study.

You will be given a signed and dated copy of this document. Your authorization to use and disclose your health information does not have an expiration date.

CONSENT

SUBJECT

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____
Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT

I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of person obtaining consent: _____
Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician _____
_____

Date: _____ Time: _____ AM/PM (Circle)

The UNIVERSITY OF CHICAGO
The Division of the Biological Sciences • The University of Chicago Medical Center

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH PROTOCOL GLUTEN DE-CHALLENGE GROUP

Protocol Number: IRB22-1138
Name of Subject: _____
Medical History Number: _____

STUDY TITLE: Tissue destruction and healing in celiac disease

Doctor Directing Research:	Sonia Kupfer, MD
Address:	900 E. 57th St. 9th Floor, KCBD 9120 Chicago, IL 60637
Telephone Number:	(773) 702-7868

KEY INFORMATION

We are asking you to choose whether or not to volunteer for a research study that is gathering information about the basic processes of intestinal (bowel) tissue destruction and healing in people with celiac disease. This section is to give you key information to help you decide whether to participate. We have included detailed information after this section. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is above.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

You are being asked to take part in this research study because you have been diagnosed with celiac disease. Celiac disease is an immune reaction to eating gluten, a protein found in wheat, barley, and rye. When people with celiac disease eat gluten, it triggers an immune response in the intestine (bowel). Over time, this reaction damages the intestine's lining and prevents it from absorbing some nutrients.

The purpose of this study is to learn more about the processes that cause intestinal damage and healing in people with celiac disease. We hope this study will provide resources for scientists and doctors to improve celiac disease research and clinical care.

This study has three groups of participants. Regardless of group assignment, all participants will undergo data collection, blood testing, and intestinal tissue sampling during the study. More details can be found below in the Detailed Consent section. The three study groups are:

- Gluten challenge group: People who have been diagnosed with celiac disease for at least 12 months and are currently on a gluten free diet will be asked to eat a small amount gluten each day as part of this study.
- Gluten de-challenge group: People who are newly diagnosed with celiac disease and are beginning a gluten free diet as part of routine care.
- Control group: People who do not have celiac disease will participate as a comparison group.

You are being asked to join the **gluten de-challenge group.** During the study, you will be asked to maintain a strict gluten-free diet.

Your participation in this study will last about 13 months and will include approximately 3 study visits. At the end of your participation, you may choose to roll over to the gluten challenge group. If you choose to do so, then you will be presented with the gluten challenge group informed consent form. If you choose not to, then your participation is finished.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?
By participating in this study, you may help future patients who have celiac disease by helping us learn more about mechanisms that cause destruction and healing of the gut lining. In addition, you will have close assessment of diet and nutrition during the course of study.

For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?
You will be asked to undergo 3 upper endoscopy procedures with biopsy in the time frame of 13 months if you participate in this study. Endoscopy means a thin, flexible, lighted tube will be inserted inside the small bowel through your mouth to view your small intestines and take small biopsies. Endoscopies will be done while you may be mildly sedated. While endoscopies are considered a safe procedure, rare complications include tearing of the upper digestive tract and/or bleeding that may require surgery to correct.

Over this year you will also be required to complete daily diaries and weekly questionnaires.

For a complete description of risks, refer to the Detailed Consent Section below.

For a complete description of alternate treatment/procedures, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?
Taking part in this study is voluntary. If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

You may choose not to participate at any time during the study. You will not lose any services, benefits or rights you would normally have if you choose to leave the study. The University of Chicago/University of Chicago Medical Center will not condition (withhold or refuse) treating

you on whether you sign this Authorization or revoke your authorization at a later time. If you do not sign this form, you will not receive the research-related intervention(s).

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?
The person in charge of the study is Dr. Sonia Kupfer, of the University of Chicago. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, her contact information is (773) 702-7868.

If you have a research-related injury, you should immediately contact Dr. Kupfer at (773) 702-6800 and ask for pager number 2870.

For questions about your rights as a research subject, please contact the University of Chicago BSD IRB at (773) 702-6505.

DETAILED CONSENT

WHAT IS INVOLVED IN THE STUDY?

Enrollment is competitive. This means that when the target number of subjects enters the study, all further enrollments will be closed. About 30-60 people will take part in the 'gluten de-challenge group' of this study at the University of Chicago and about 30-60 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 60 healthy people.

If you participate in this study, you will be expected to:

- Strictly follow a gluten-free diet (GFD).
- Undergo three (3) endoscopies with biopsies of intestinal tissue
  An endoscopy is a procedure that examines the inside of your esophagus, stomach, and upper portion of the small bowel. During this procedure, a thin, flexible, lighted tube is inserted through your mouth to view your intestine and take small biopsies.
  You will be asked to not to eat for 8 hours before the procedure but you can have clear liquids up to 2 hours before the procedure. On the day of the test you will be mildly sedated to help you relax. During the procedure, a thin, flexible tube with a small camera at the tip will be inserted through your mouth and moved through the esophagus and stomach and into the small bowels. The camera allows pictures to be sent to a video screen for the doctor to look at. Using a small biopsy forceps which will be passed down the tube, the doctor will remove tissue samples. The test takes 15-30 minutes, but you will be at the clinic for about 2 hours and you will need to have someone available to take you home afterwards. You should not drive or make important decisions for at least 24 hours following the procedure.
- Give urine, blood, and saliva samples
- Complete questionnaires
- Be available for safety assessment phone calls

The procedures for each study visit are described below.

Visit 1 (Screening, Day 0):

- You will be asked to review, sign, and date the informed consent. The study team will review the study with you and ample time will be given to ask questions.
- The study doctor will verify if you qualify for the study.
- Your demographic information (such as your age, sex, race and ethnicity), complete medical history will be collected.
- Physical exam, including your height weight
- Vital signs such as blood pressure, heart rate, and temperature will be collected
- Current medication will be reviewed.
- Blood draw (about 1 ½ tablespoons) will be taken for lab tests.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to take part in this study.
- Saliva samples (by spitting into a small tube) will be collected for lab test.

- Upper endoscopy will be performed to view your small intestine. Up to 14 small intestinal biopsies will be taken during this procedure. Luminal fluid (consists of digestive fluid, food particles and bacteria) from your bowel will be collected as well.
- You will be asked to complete the following questionnaires electronically to assess your celiac disease symptoms and quality of life. Surveys will be completed electronically using a weblink.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – you will be asked to complete this survey prior to the endoscopy. It will take about 8 minutes to complete.
    - Celiac Disease Symptom Diary (CDSD©) – you will complete the diary every day for 2-weeks following Visit1. It will take about 10 minutes to complete.
- You will begin a strict gluten-free diet as part of routine care.
- The study team will contact you with the results of the endoscopy, to follow up on any side effects you may feel, review your answers to questionnaires, and to remind you to follow strict GFD.

Only for subjects enrolled after 05/01/2024:

- Hip and waist measurements
- Dual x-ray absorptiometry (DEXA) scan: An X-Ray called DEXA will be performed to measure your body composition and bone mineral density. You will be asked to lay down on your back and have the scanner move over your body and measure how much muscle, bone, fat you have in your body. There is a small amount of radiation exposure from a DEXA scan. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DXA scan is considered safe for adults.

Visit 2 (3month visit):

- Blood draw (about 2 tablespoons) will be taken for lab tests.
- Saliva samples will be collected for lab test.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to continue this study.
- Upper endoscopy with biopsies will be obtained. Luminal fluids collection will take place.
- You will be asked to complete the following questionnaires to assess your celiac disease symptoms and quality of life.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – It will take about 8 minutes to complete. You be asked to continue to complete this survey prior to the endoscopy.
    - Celiac Disease Symptom Diary (CDSD©) – You will be asked to complete the CDSD for 4 weeks around the time of the endoscopy (approximately 2 weeks prior and 2 weeks post endoscopy visit). It will take about 10 minutes to complete.
    - Impact of Adhering to a Gluten Free Diet Questionnaire (IGFDQ©) – It will take about 5 minutes to complete. You will be asked to complete this one time at this visit, prior to the endoscopy.

- The study team will contact you to follow up on any side effects you may feel review your answers to questionnaires, and to remind you to follow strict GFD.

Visit 3 (12-13month visit):

- Blood draw (about 2 tablespoons) will be taken for lab tests.
- Saliva samples will be collected for lab test.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to continue this study.
- Endoscopy with biopsies will be obtained. Luminal fluids collection will take place.
- You will be asked to complete the following questionnaires to assess your celiac disease symptoms and quality of life.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – It will take about 8 minutes to complete. You be asked to continue to complete this survey prior to the endoscopy.
    - Celiac Disease Symptom Diary (CDSD©) – You will be asked to complete the CDSD for 4 weeks around the time of the endoscopy (approximately 2 weeks prior and 2 weeks post endoscopy visit). It will take about 10 minutes to complete.
    - Impact of Adhering to a Gluten Free Diet Questionnaire (IGFDQ©) – It will take about 5 minutes to complete. You will be asked to complete this survey prior to the endoscopy.
    - Celiac Disease Dietary Adherence Questionnaire (CDAT) – It will take about 5 minutes to complete. You will be asked to complete this survey prior to the endoscopy.
- The study team will contact you to follow up on any side effects you may feel and to review your answers to questionnaires.

Only for subjects enrolled after 05/01/2024:

- Hip and waist measurements
- Undergo DEXA scan

<u>Biological sample Storage</u>

Biological samples include the blood, urine, tissue, and luminal fluid collected during this study. All biological samples collected from you will be labeled with a unique participant code. It will include the collection date and time but will not include your name or medical record number.

These samples are collected for the purposes of this study and may also be stored and used for future research studies. This future research may be done at the University of Chicago and Mayo Clinic or by colleagues from an outside institution, including commercial partners.

Your samples may be studied for genetic material (such as DNA and RNA). Genes are made up of DNA, which is short for deoxyribonucleic acid. They act as instructions to your body, determining things like eye color and hair color, but also whether people may be more likely to develop certain conditions. Genes are passed from parent to child. RNA is made from DNA. RNA is short for ribonucleic acid. RNA is a genetic material that has an important role in making proteins. Proteins are the building blocks of your body, cells, and organs. The results of genetic

research or testing may be shared with collaborators for research purposes. These results would not contain your identifying information (such as name and medical record number) and would instead be labelled with a unique subject study code. The results of genetic testing and research will not be shared with you.

If you decide to withdraw from the study, you can choose to have your samples destroyed. The information that has already been collected will still be used for the study. However, no further research will be conducted using your samples and your samples will be destroyed. Please see the 'What Are My Rights' section below for additional information.

Samples may be tested, stored, and shared as follows:

University of Chicago
The study team will store your blood, urine, luminal samples and biopsy tissue. The University of Chicago will conduct genetic analysis for study purposes and will store your DNA and RNA. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples and can be shared with researchers at other institutions and/or companies as well.
Any samples that are shared will be labelled with a unique subject study code. Samples will be labelled with the date and time the sample was collected and will not contain any personal identifiers.

Mayo Clinic
The study team will process blood samples and send PBMC (type of immune cells) and serum samples to Mayo for storage. These samples will be labelled with the subject study code and will include the collection date and time but will not contain any identifiers. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples and can be shared with researchers at other institutions and/or companies as well.

California Institute of Technology
The study team will send saliva samples and tissue RNA/DNA to the California Institute of Technology to perform microbiome genetic analysis (genetic testing of all microbes, such as bacteria, fungi, and viruses that naturally live on our bodies). The samples will be labelled with the subject study code and will include collection date and time but will not contain any identifiers. Leftover tissue and saliva samples will be stored indefinitely for future research purposes and these samples can be shared with researchers at other institutions/or companies.

Other information
In future, identifiers associated with your data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use. The results from this study will not be shared with you.

Dr. Kupfer may decide to take you off of the study without your consent if:

- You are unable to meet the requirements of the study or your medical condition changes;

- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

During your participation in this study, you are at risk for the side effects described in this section. The study doctor will discuss these with you.

Upper endoscopy/biopsy risks

An upper endoscopy and biopsy of the intestine are standard and commonly performed medical procedures to examine the small bowel.
Somewhat likely side effects include:

- Tiredness
- Some pain (cramps)
- Discomfort

Rare side effects include;

- Tearing of the upper digestive tract and/or bleeding. This may require surgery to correct.

Biopsy risks may include,

- The removal of tissue samples may result in a small amount of blood in your stools. This should go away. If it persists after 24 hours, please call your study doctor listed on the front page.
- Tenderness
- Infection
- Significant bleeding that requires getting blood from donors

The risk of the sedation medication, usually given during an endoscopy to help you relax, may cause

- allergic reactions,
- nausea,
- skin rash,
- dizziness with a drop in blood pressure,
- a slowing down of your breathing so much that in very rare cases a breathing machine will be used, and
- **death** from sedation-related heart problems.

During the endoscopy procedure, the study doctor may come across incidental findings such as ulcers (sores in the stomach tissue lining), H. pylori (bacteria which may cause stomach infections), reflux changes (could cause changes in the tissue lining of the esophagus (tube through which food passes from the throat to the stomach), or polyps (small protrusions in the lining of the esophagus, stomach or small intestine). Additional tissue samples may be taken for clinical purposes in such cases. If this occurs, the study doctor will discuss the findings with you and you will be referred for the appropriate clinical care.

You will not be permitted to drive immediately after the procedure and, therefore, will need someone to drive you home.

Blood Draw Risks
The risks of giving blood include pain, a bruise at the point where the blood is taken, redness, bleeding, nerve damage, blood clots, which may cause inflammation, and swelling of the vein and infection, and a rare risk of fainting. Care will be taken to avoid these risks.

DEXA Scan Risks
During the scan, you will be exposed to a very low amount of radiation. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DEXA scan is considered safe for adults.

Questionnaire Risks
Some of the questions may seem personal and may make you feel uncomfortable. If you have any questions or concerns while answering these questions, please talk to your study doctor. You may choose not to answer any question that makes you uncomfortable.

Loss of Confidentiality
Any time information is collected about you there is a potential risk for loss of confidentiality. However, the researchers will make every effort to keep your information confidential. Please refer to the 'What About Confidentiality' section for information on what measures will be taken to protect your confidentiality.

Unforeseen Risks
There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could affect whether you wish to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there will be no direct medical benefit to you.

Information gathered in this study may benefit other people who have celiac disease.

WHAT OTHER OPTIONS ARE THERE?
You do not have to take part in this study to receive treatment for your celiac disease. Your other option would be to not participate in this study and maintain a gluten-free diet. If you wish you may also participate in another clinical trial.

WHAT ARE THE COSTS?
Clinical services provided during a clinical trial are either research-related or considered part of usual medical care for patients with your disease or condition. Tests, procedures, and activities that are ordered by your medical care team to monitor your disease or condition (whether you are participating in a clinical trial or not) are described as 'usual medical care'. 'Research-related' is the term used to describe any tests, procedures, or activities that you are being asked to undergo

only because of your participation in this clinical trial.

You or your insurance will be financially responsible for the costs of your usual, ongoing medical care. This often includes regular visits with your doctor, lab tests and imaging used to measure your response to treatment, and other tests and procedures deemed medically necessary by your care team. The endoscopy and pregnancy test done during screening are considered to be part of your routine care. Financial responsibilities for routine care may include deductibles and co-payments and this care will be subject to all the same requirements and restrictions of your insurance.

You will not be responsible for the costs of tests or services that are being performed solely for the purposes of this study and would not be performed if you were not participating in this clinical trial. This will often include additional tests performed to answer a research question but not required for your routine clinical care.

If you have questions about whether specific clinical services are research related or part of your usual medical care, please speak to your physician or research contact person.

WHAT HAPPENS IF I HAVE AN INJURY?

If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, you may receive such emergency medical treatment at the University of Chicago Medical Center, UChicago Medicine Ingalls Memorial Hospital, UChicago Medicine Northwest Indiana, UChicago Medicine AdventHealth Bolingbrook, UChicago Medicine AdventHealth Glen Oaks, UChicago Medicine Advent Health Hinsdale, or UChicago AdventHealth LaGrange at no cost to you. You must notify Dr. Kupfer as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure, and is not the result of your disease or condition. The costs of any non-emergency care for such an injury will be billed to you or your insurance in the ordinary manner. If you think that you have suffered a research related injury, you must let Dr. Kupfer know right away.

In the event of an emergency, you should seek care at the nearest emergency room or call 911 and notify the study doctor's office when is possible.

WILL I BE PAID FOR MY PARTICIPATION?

You will be compensated $300 for each endoscopy you complete for a potential total of $900.

You will receive payments three times during this study, once after visit 1, once after visit 2, and once after visit 3.

As policies at the University of Chicago require that these payments be given in the form of a check, you will need to complete a tax form. Therefore, we will be collecting personal information about you including your name, address, and social security number. In addition, because the process for requesting a check oftentimes takes several weeks, we will mail your

check to you when it is ready. Please note that it may take 3-4 weeks after conclusion of your study participation in order for you to receive your payment.

Additionally, you will receive a parking voucher at the end of each study visit.

WHAT ABOUT CONFIDENTIALITY?
There is a risk of potential loss of confidentiality. To minimize this risk, study records that identify you will be kept confidential. Any research data will be stored in a locked drawer in a locked office and/or entered on a password-protected, encrypted, HIPAA-compliant computer. Only study staff will have access to the data. The results from tests and procedures performed as part of this study may become part of your medical record. Any research information in your medical record will be kept indefinitely.

During this study, Dr. Kupfer and her research team will collect protected health information (PHI) about you for the purposes of this research. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago. The PHI consists of any health information that is collected about you, which could include your medical history and new information collected as a result of this study. Some of this information will come from your medical record. The information to be used on this study includes your name, address, medical record number, phone number, email address, social security number (for payment purposes), date of birth, and dates of procedures, tests diagnosis and hospitalizations (if applicable). We will use these identifiers to schedule study visits, collect data from your medical records, monitor your health, stay in contact with you, complete study objectives and distribute study payments.

As part of the study, Dr. Sonia Kupfer and her research team will share information about you as well as the results of your study-related procedures and tests with collaborators at Mayo Clinic and California Institute of Technology who are assisting with the study, the study funder the National Institutes of Health (NIH) and the representatives of the data safety monitoring board (a group of reviewers who monitor safety data during the course of the study)

Data shared could include initials, age, race, ethnicity, the results of research tests and procedures done as part of the study, the dates of study procedures and study test results. This information is being sent to review the results of the study, to monitor the safety of participants, and to verify the accuracy of the study data.

The University of Chicago Financial Services office will have access to your name, address and social security number when processing your check payment.

Your records may be reviewed by federal agencies whose responsibility is to protect human subjects in research, including the Office of Human Research Protections (OHRP). In addition, representatives of the University of Chicago, including the Institutional Review Board (a committee that oversees research) and the Office of Clinical Research may also view the records of the research. If your research record is reviewed by any of these groups, they may also need to review your entire medical record. The results from tests and/or procedures performed as part of this study may become part of your medical record.

Once health information is shared outside the University of Chicago, please note that your identifiable health information may be shared with someone else. The same laws that the University of Chicago must obey may not protect your health information.

During your participation in this study, you will have access to your medical record. Dr. Kupfer is not required to release to you research information that is not part of your medical record. This consent/authorization form will be kept by the research team for at least 6 years. The study results will be kept in your research record and be used by the research team until completion of this study.

At the time of study completion, either the research information not already in your medical record will be destroyed or information identifying you will be removed from study results.

Data from this study may be used in medical publications or presentations. Your name and any other identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time.

We are collecting your tissue and/or blood as part of this study. We may use your samples for other research studies, including genetic testing, without contacting you, including sharing your samples with others for research purposes here and outside University of Chicago. It is possible that these samples may be shared with a for profit company for research.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Genetic Information Nondiscrimination Act (GINA)

The Genetic Information Nondiscrimination Act (GINA) is a federal law that may help protect you from health insurance or employment discrimination based on genetic information. GINA is a federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Other Databases

If you agree to take part in this study, your genetic and health information and as applicable a portion of your specimens will be placed into one or more scientific databases. In particular, the

National Institutes of Health maintains a database called "dbGaP." The NIH database is a restricted database, meaning a researcher who wants to study information from dbGaP must work with the group overseeing the database to obtain the information. Security measures are in place to protect these data.

Researchers with an approved study will be able to see and use some of your information, but your name and other information that could directly identify you (such as your name or address) will not be placed into the database. There is a risk that someone could use your unique genetic information to trace data back to you or your family, but this risk is very small. There is no direct benefit to you that is expected from any secondary research that may be conducted.

If you decide to withdraw from the study as outlined in the following section, your data will be withdrawn from these databases. However, if your data have already been submitted to an NIH database and distributed to other researchers, or your data have been de-identified and can no longer be linked back to you, your data will not be able to be withdrawn.

Certificate of Confidentiality

To help us protect your privacy, the National Institutes of Health (NIH) has issued a Certificate of Confidentiality for this research. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. There are specific circumstances when the Certificate of Confidentiality does not prevent researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research. For example: suspected child abuse, elder abuse, or urgent risk of harm to self (suicide) or others (homicide).

WHAT ARE MY RIGHTS AS A PARTICIPANT?

If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. Kupfer in writing at the address on the first page. Dr. Kupfer may still use your information that was collected prior to your written notice.

We will tell you about significant new information that may affect your willingness to stay in this study.

You will be given a signed and dated copy of this document. Your authorization to use and disclose your health information does not have an expiration date.

CONSENT

SUBJECT

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____
Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT

I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of person obtaining consent: _____
Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician _____
_____

Date: _____ Time: _____ AM/PM (Circle)

MAYO CLINIC

Name and Clinic Number

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

IRB#: 22-007133

Study Title: Tissue Destruction and Healing in Celiac Disease (Gluten Challenge Group)

Doctor Directing Research: Dr. Joseph Murray and Colleagues
Address: 200 1st ST SW
Rochester, MN55902-9823

Telephone Number: 507-284-2511

KEY INFORMATION

We are asking you to choose whether or not to volunteer for a research study that is gathering information about the basic processes of intestinal (bowel) tissue destruction and healing in people with celiac disease. This section is to give you key information to help you decide whether to participate. We have included detailed information after this section. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is above.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

You are being asked to take part in this research study because you have been diagnosed with celiac disease. Celiac disease is an immune reaction to eating gluten, a protein found in wheat, barley and rye. When people with celiac disease eat gluten, it triggers an immune response in the intestine (bowel). Over time, this reaction damages the intestine's lining and prevents it from absorbing some nutrients.

The purpose of this study is to learn more about the processes that cause intestinal damage and healing in people with celiac disease. We hope this study will provide resources for scientists and doctors to improve celiac disease research and clinical care.

This study has three groups of participants. Regardless of group assignment, all participants will undergo data collection, blood testing, and intestinal tissue sampling during the study. More details can be found below in the Detailed Consent section. The three study groups are:

MAYO CLINIC

Name and Clinic Number

- Gluten challenge group: People who have been diagnosed with celiac disease for at least 12 months and are currently on a gluten free diet will be asked to eat a small amount gluten each day as part of this study.
- Gluten de-challenge group: People who are newly diagnosed with celiac disease and are beginning a gluten free diet as part of routine care.
- Control group: People who do not have celiac disease will participate as a comparison group.

You are being asked to join the **gluten challenge group**.

During the study, you will be asked to eat snack bars that have vital wheat gluten (3grams or about 1 teaspoon in each bar). You will be asked to eat the gluten snack bar every day with the same meal for 6 weeks. The level of gluten in these bars is small and should not cause major digestive issues for most people, though you will be monitored throughout the study and can stop the study if needed.

Your participation in this study will last about 7 weeks and will include approximately 5 study visits.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

By participating in this study, you may help future patients who have celiac disease by helping us learn more about processes that cause destruction and healing of the intestinal lining. In addition, you will have close assessment of diet and nutrition during the course of study.

For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You will be asked to ingest gluten during the study. After consuming gluten you may experience worsening of gastrointestinal symptoms, including abdominal pain and diarrhea.

You will be asked to undergo 3 endoscopy (esophagogastroduodenoscopy or EGD) procedures with biopsy in the time frame of 7 weeks if you participate in this study.
If you have successfully completed the DeChallenge group of this study and are rolling over to the gluten challenge group within 1-3 months of your study completion, you will be asked to undergo only 2 upper endoscopy procedures with biopsy in the time frame of 7 weeks.

An EGD is a procedure that examines the lining of the esophagus (tube food passes through from throat to stomach), stomach, and small intestine (duodenum). During this time you also be required to complete daily diary and weekly questionnaires.

Endoscopy means a thin, flexible, lighted tube will be inserted inside the small bowel through your mouth to view your small intestines and take small biopsies. Endoscopies will be done

MAYO CLINIC

Name and Clinic Number

while you may be mildly sedated. While endoscopies are considered a safe procedure, rare complications include tearing of the upper digestive tract and/or bleeding that may require surgery to correct.

For a complete description of risks, refer to the Detailed Consent Section below.

For a complete description of alternate treatment/procedures, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?
Taking part in this study is your decision. If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

Take your time to decide. Feel free to discuss the study with your family, friends, healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

You may choose not to participate at any time during the study. You will not lose any services, benefits or rights you would normally have if you choose to leave the study. The Mayo Clinic will not condition (withhold or refuse) treating you on whether you sign this Authorization or revoke your authorization at a later time. If you do not sign this form, you will not receive the research-related intervention(s).

MAYO CLINIC

Name and Clinic Number

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Joseph Murray at the Mayo Clinic. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, you may contact the individuals listed in the table below. For questions about your rights as a research subject, please contact the University of Chicago BSD IRB at (773) 702-6505.

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator(s):** Dr. Joseph Murray **Phone:** 507-284-2631 **Co-Investigator:** Dr. Adam Bledsoe **Phone:** 507-538-1231 **Emergency After Hours:** 507-284-2511 Ask operator to page Dr. Joseph Murray or Dr. Adam Bledsoe **Study Team Contact:** Chadrick Hinson: 507-266-0237 Irina Horwath: 507-284-0375 Carol Van Dyke: 507-266-7842 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55902
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

MAYO CLINIC

Name and Clinic Number

DETAILED CONSENT

WHAT IS INVOLVED IN THE STUDY?

Enrollment is competitive. This means that when the target number of subjects enters the study, all further enrollments will be closed. About 30-60 people will take part in the 'gluten challenge group' at the University of Chicago and about 30-60 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 60 healthy people.

If you participate in this study, you will be expected to:

- Eat gluten containing snack bars every day for 6 weeks
- Undergo three (3) upper endoscopies with biopsies of intestinal tissue.
  - Undergo two (2) endoscopies if you have previously successfully completed the dechallenge group and are screening for the challenge group within 1-3 months of study completion.

  An upper endoscopy is a procedure that examines the inside of your esophagus, stomach and upper portion of the small bowel. During this procedure, a thin, flexible, lighted tube is inserted through your mouth to view your intestine and take small biopsies.
  You will be asked to not to eat for 8 hours before the procedure but you can have clear liquids up to 2 hours before the procedure. On the day of the test you will be moderately sedated to help you relax. During the procedure, a thin, flexible tube with a small camera at the tip will be inserted through your mouth and moved through the esophagus and stomach and into the small bowel. The camera allows pictures to be sent to a video screen for the doctor to look at. A tool called a forceps is passed down the tube, so the doctor can take tissue samples. The procedure takes 15-30 minutes, but you will be at the clinic for about 2 hours, and you will need to have someone available to take you home afterwards. You should not drive or make important decisions for at least 24 hours following the procedure.
- Give urine, blood, and saliva samples
- Complete questionnaires
- Be available for safety assessment phone calls

The procedures for each study visit are described below.

Visit 1 (Screening visit, part 1):

- You will be asked to review, sign, and date the informed consent. The study team will review the study with you and ample time will be given to ask questions
- The study doctor will verify that you qualify for the study
- Physical exam including your height and weight
- Vital signs such as blood pressure, heart rate, and temperature will be collected
- Blood draw (about 1½ tablespoon) will be taken for lab tests.
- You will be asked to complete the following questionnaires electronically via REDCap during the visit to assess your celiac disease symptoms and quality of life:
  - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – It will take about 8 minutes to complete.

MAYO CLINIC

Name and Clinic Number

- Celiac Disease Symptom Diary (CDSD©) –It will take about 10 minutes to complete.
- Celiac Disease Dietary Adherence Questionnaire (CDAT) – It will take about 5 minutes to complete. This questionnaire will ask about adherence to a gluten free diet with the exception of the gluten bar used in this study.

- If found eligible, you will be scheduled for Visit 2.

Visit 2 (Screening visit, part 2):

- The study doctor will review blood test results from visit 1 to verify that you qualify for the study.
- Your demographic information (such as your age, sex, race and ethnicity), complete medical history will be collected.
- Current medication will be reviewed.
- Blood draw (about 1½ tablespoon) will be taken for lab tests.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to take part in this study.
- Saliva samples (by spitting into a small tube) will be collected for lab tests.
- Upper endoscopy will be performed to view your small intestine. Up to 16 small intestinal biopsies will be taken during this procedure. Luminal fluid (consists of digestive fluid, food particles and bacteria) from your bowel will be collected as well.
  - If you're rolling over from the dechallenge group within 1-3 months of study completion, you will not be asked to undergo an endoscopy during this visit.
- You will be asked to complete the following questionnaires electronically via REDCap to during the study visit to assess your celiac disease symptoms and quality of life:
  - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) –It will take about 8 minutes to complete.
  - Celiac Disease Symptom Diary (CDSD©) –It will take about 10 minutes to complete.
  - Celiac Disease Dietary Adherence Questionnaire (CDAT) – This questionnaire will ask about adherence to a gluten free diet with the exception of the gluten bar used in this study. It will take about 5 minutes to complete.
- The study team will contact you to follow up on any side effects you may feel.

Visit 3 (Day 0):

- You will receive a gluten-containing snack bar to eat at the study clinic.
- Blood draws (about 1 ½ tablespoons) will be taken before you eat the snack bar and 2 hours after you eat the snack bar.
- Urine will be collected for lab tests.
- You will be asked to complete the following questionnaires to assess your celiac disease symptoms and quality of life. Surveys will be completed electronically using a weblink.

MAYO CLINIC

Name and Clinic Number

  - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – you will be asked to complete this survey **weekly** until end of study. It will take about 8 minutes to complete.
  - Celiac Disease Symptom Diary (CDSD©) – you will complete the diary **daily** until the end of the study. It will take about 10 minutes to complete each entry.
- You will receive gluten containing snack bars to consume daily, at the same time of day, for the next 6 days. You will eat one bar with the same meal, every day. The gluten snack bars must be kept in the freezer, then completely thawed to room temperature before eating. Once thawed the bars should be eaten within 4 days of thawing.
- The study team will contact you to follow up on any side effects you may feel, review your answers to questionnaire, and to remind you to eat the snack bars given by the study team.

Only for subjects enrolled after 05/01/2024:

- Hip and waist measurements
- Dual x-ray absorptiometry (DEXA) scan: An X-Ray called DEXA will be performed to measure your body composition and bone mineral density. You will be asked to lay down on your back and have the scanner move over your body and measure how much muscle, bone, fat you have in your body. There is a small amount of radiation exposure from a DEXA scan. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DXA scan is considered safe for adults.

Visit 4 (day 6):

- Blood draw (about 1 ½ tablespoons) will be taken for lab tests.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to continue this study.
- Saliva samples will be collected for lab tests.
- Upper endoscopy with biopsies (up to 16) and luminal fluids collection will take place.
- You will receive gluten-containing snack bars to eat daily for the next 5 weeks. You will eat one bar with the same meal, every day.
- You will be asked to complete the following questionnaires via REDCap to assess your celiac disease symptoms and quality of life.
  - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – It will take about 8 minutes to complete. You will complete this questionnaire prior to endoscopy, and then weekly until the end of study.
  - Celiac Disease Symptom Diary (CDSD©) – It will take about 10 minutes to complete. You be asked to continue to complete this daily until end of study.
  - Celiac Disease Dietary Adherence Questionnaire (CDAT) – It will take about 5 minutes to complete. You will be asked to complete this one time at this visit.

MAYO CLINIC

Name and Clinic Number

- The study team will contact you weekly to follow up on any side effects you may feel, review your answers to questionnaire, and to remind you to eat the snack bars given by the study team.

Visit 5 (week 6):

- Blood draw (about 1.5 tablespoons) will be taken for lab tests.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to continue this study.
- Saliva samples will be collected for lab tests.
- Upper endoscopy with biopsies (up to 14) and luminal fluids collection will take place.
- You will be asked to complete the following questionnaires via REDCap to assess your celiac disease symptoms and quality of life.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – you will be asked to complete this survey **weekly** until end of study. It will take about 8 minutes to complete.
    - Celiac Disease Symptom Diary (CDSD©) – you will complete the diary **daily** until the end of the study. It will take about 10 minutes to complete.
    - Celiac Disease Dietary Adherence Questionnaire (CDAT) – It will take about 5 minutes to complete.
- The study team will contact you to follow up on any side effects you may feel and to review your answers questionnaire.

<u>Biological sample Storage</u>

Biological samples include the blood, urine, tissue, and luminal fluid collected during this study. All biological samples collected from you will be labeled with a unique participant code. It will include collection date and time but will not include your name or medical record number.

These samples are collected for the purposes of this study and may also be stored and used for future research studies. This future research may be done at the University of Chicago and Mayo Clinic or by colleagues from an outside institution, including commercial partners.

Your samples may be studied for genetic material (such as DNA and RNA). Genes are made up of DNA, which is short for deoxyribonucleic acid. They act as instructions to your body, determining things like eye color and hair color, but also whether people may be more likely to develop certain conditions. Genes are passed from parent to child. RNA is made from DNA. RNA is short for ribonucleic acid. RNA is a genetic material that has an important role in making proteins. Proteins are the building blocks of your body, cells, and organs. The results of genetic research or testing may be shared with collaborators for research purposes. These results would not contain your identifying information (such as name and medical record number) and would instead be labelled with a unique subject study code. The results of genetic testing and research will not be shared with you.

MAYO CLINIC

Name and Clinic Number

If you decide to withdraw from the study, you can choose to have your samples destroyed. The information that has already been collected will still be used for the study. However, no further research will be conducted using your samples and your samples will be destroyed. Please see the 'What Are My Rights' section below for additional information.

Samples may be tested, stored, and shared as follows:

University of Chicago
The study team will store your blood, urine, luminal samples, and biopsy tissue. The University of Chicago will conduct genetic analysis for study purposes and will store your DNA and RNA. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples and can be shared with researchers at other institutions and/or companies as well. Any samples that are shared will be labelled with a unique subject study code. Samples will be labelled with the date and time the sample was collected. Sample labels will not contain any other personal identifiers.

Mayo Clinic
The study team will process blood samples and send PBMC (type of immune cells) and serum samples to Mayo for storage. These samples will be labelled with the subject study code and will include the collection date and time but will not contain any other personal identifiers. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples and can be shared with researchers at other institutions and/or companies as well.

California Institute of Technology
The study team will send saliva samples and tissue RNA/DNA to the California Institute of Technology to perform microbiome genetic analysis (genetic testing of all microbes, such as bacteria, fungi, and viruses that naturally live on our bodies). The samples will be labelled with the subject study code and will include collection date and time but will not contain any other personal identifiers. Leftover tissue and saliva samples will be stored indefinitely for future research purposes and these samples can be shared with researchers at other institutions and/or companies.

Other information
In future, identifiers associated with your data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use.

The results from this study will not be shared with you.

MAYO CLINIC

Name and Clinic Number

Dr. Murray may decide to take you off of the study without your consent if:

- You are unable to meet the requirements of the study or your medical condition changes;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

During your participation in this study, you are at risk for the side effects described in this section. The study doctor will discuss these with you.

Gluten consumption

The side effects of ingesting gluten when you have celiac disease may be very mild, or they may be significant. You will be monitored for side effects throughout the study. If you experience significant side effects, you will be asked to stop eating the gluten snack bars. In an effort to minimize any side effects, the amount of gluten in the bars is very small. Potential symptoms may include:

Somewhat likely side effects:

- Bloating
- Abdominal pain
- Nausea
- Diarrhea
- Constipation

Less likely side effects:

- Vomiting
- Fatigue
- Headache
- Brain fog or exhaustion

Upper endoscopy/biopsy risks

Most people experience few effects from an upper endoscopy. There is a small chance of a hole (perforation) in the esophagus, stomach, and duodenum, which can require surgery to correct. Infection and bleeding can also happen, but these are rare. This is a small risk of bleeding where tissue was removed from your small intestine during the biopsy.

Biopsy risks may include,

- The removal of tissue samples may result in a small amount of blood-tinged saliva. This should go away. If it persists after 24 hours, please call your study doctor listed on the

MAYO CLINIC

Name and Clinic Number

front page.
- Tenderness
- Infection
- Significant bleeding that requires getting blood from donors

The risk of the sedation medication, usually given during an endoscopy to help you relax, may cause
- allergic reactions,
- nausea,
- skin rash,
- dizziness with a drop in blood pressure,
- a slowing down of your breathing or heart function so much that in very rare cases a breathing machine will be used

You will not be permitted to drive immediately after the procedure and, therefore, will need someone to drive you home. You should not drive or make any important decisions for at least 24 hours following your procedure.

During the endoscopy procedure, the study doctor may come across incidental findings such as ulcers (sores in the stomach tissue lining), H. pylori (bacteria which may cause stomach infections), reflux changes (could cause changes in the tissue lining of the esophagus (tube through which food passes from the throat to the stomach), or polyps (small protrusions in the lining of the esophagus, stomach or small intestine). Additional tissue samples may be taken for clinical purposes in such cases. If this occurs, the study doctor will discuss the findings with you, and you will be referred for the appropriate clinical care.

Blood Draw Risks

The risks of giving blood include pain, a bruise at the point where the blood is taken, redness, bleeding, nerve damage, blood clots, which may cause inflammation, and swelling of the vein and infection, and a rare risk of fainting. Care will be taken to avoid these risks.

DEXA Scan Risks

During the scan, you will be exposed to a very low amount of radiation. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DEXA scan is considered safe for adults.

Questionnaire Risks

Some of the questions may seem personal and may make you feel uncomfortable. If you have any questions or concerns while answering these questions, please talk to your study doctor. You may choose not to answer any question that makes you uncomfortable.

MAYO CLINIC

Name and Clinic Number

Loss of Confidentiality

Any time information is collected about you there is a potential risk for loss of confidentiality. However, the researchers will make every effort to keep your information confidential. Please refer to the 'What About Confidentiality' section for information on what measures will be taken to protect your confidentiality.

Unforeseen Risks

There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could affect whether you wish to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there will be no direct medical benefit to you. Information gathered in this study may benefit other people who have celiac disease.

WHAT OTHER OPTIONS ARE THERE?

You do not have to take part in this study to receive treatment for your celiac disease. Your other option would be to not participate in this study and maintain a gluten-free diet. If you wish you may also participate in another clinical trial.

WHAT ARE THE COSTS?

Clinical services provided during a clinical trial are either research-related or considered part of usual medical care for patients with your disease or condition. Tests, procedures, and activities that are ordered by your medical care team to monitor your disease or condition (whether you are participating in a clinical trial or not) are described as 'usual medical care'. 'Research-related' is the term used to describe any tests, procedures, or activities that you are being asked to undergo only because of your participation in this clinical trial.

You or your insurance will be financially responsible for the costs of your usual, ongoing medical care. This often includes regular visits with your doctor, lab tests and imaging used to measure your response to treatment, and other tests and procedures deemed medically necessary by your care team. None of the activities done as part of this study are considered part of your usual on going care. Financial responsibilities for routine care may include deductibles and co-payments and this care will be subject to all the same requirements and restrictions of your insurance.

You will not be responsible for the costs of tests or services that are being performed solely for the purposes of this study and would not be performed if you were not participating in this clinical trial. This will often include additional tests performed to answer a research question but not required for your routine clinical care.

If you have questions about whether specific clinical services are research related or part of your usual medical care, please speak to your physician or research contact person.

MAYO CLINIC

Name and Clinic Number

WHAT HAPPENS IF I HAVE AN INJURY?

Where to get help:

If you think you may have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research-related injuries?

Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment cost for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

WILL I BE PAID FOR MY PARTICIPATION?

You will be compensated $400 after each endoscopy, $50 after each of two clinic visits, and $200 for successful completion of all questionnaires for a potential total of $1500.
You will be paid for the entire study after visit 5. In order to provide this compensation, the study team will need your Social Security number (for tax purposes).

Additionally, you may be eligible for reimbursement of travel-related expenses, subject to the following limits:

- **Flights**: Economy flights to and from Rochester, up to $1,000.
- **Transportation**: Rides to and from the medical center (e.g. Uber, Taxi, etc.), up to $150.
- **Meals**: A daily meal allowance up to $75.
- **Overnight Accommodations**: If required, the medical center will arrange accommodations at local hotels. Alternatively, accommodations at other hotels can be reimbursed at $200/night.

Reimbursements apply only to expenses incurred during study-related visits. To qualify for reimbursement, you must submit itemized receipts for travel, accommodations, and meals to the study staff. Please consult the study staff before incurring any expenses to ensure eligibility.

Payment for participant in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address, and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end. In addition, because the process for requesting a check oftentimes takes several weeks, we will mail your check to you when it is ready. Please note that it may take 3-4 weeks after conclusion of your study participation in order for you to receive your payment.

MAYO CLINIC

Name and Clinic Number

Additionally, you will receive a parking voucher at the end of each study visit.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?
Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. There is a risk of potential loss of confidentiality. To minimize this risk, study records that identify you will be kept confidential. Any research data will be stored in a locked drawer and/or entered on a password-protected, encrypted, HIPAA-compliant computer. Only study staff will have access to the data. The results from tests and procedures performed as part of this study may become part of your medical record. Any research information in your medical record will be kept indefinitely.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:
- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:
- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:
- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- Researchers involved in this study at other institutions.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

MAYO CLINIC

Name and Clinic Number

While taking part in this study, you will be assigned a code that is unique to you. Samples may include collection dates but does not include any other information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?
Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Genetic Information Nondiscrimination Act (GINA)
The Genetic Information Nondiscrimination Act (GINA) is a federal law that may help protect you from health insurance or employment discrimination based on genetic information. GINA is a federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Other Databases
If you agree to take part in this study, your genetic and health information and as applicable a portion of your specimens will be placed into one or more scientific databases. In particular, the National Institutes of Health maintains a database called “dbGaP.” The NIH database is a restricted database, meaning a researcher who wants to study information from dbGaP must

MAYO CLINIC

Name and Clinic Number

work with the group overseeing the database to obtain the information. Security measures are in place to protect these data.

Researchers with an approved study will be able to see and use some of your information, but your name and other information that could directly identify you (such as your name or address) will not be placed into the database. There is a risk that someone could use your unique genetic information to trace data back to you or your family, but this risk is very small. There is no direct benefit to you that is expected from any secondary research that may be conducted.

If you decide to withdraw from the study as outlined in the following section, your data will be withdrawn from these databases. However, if your data have already been submitted to an NIH database and distributed to other researchers, or your data have been de-identified and can no longer be linked back to you, your data will not be able to be withdrawn.

Certificate of Confidentiality

To help us protect your privacy, the National Institutes of Health (NIH) has issued a Certificate of Confidentiality for this research. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. There are specific circumstances when the Certificate of Confidentiality does not prevent researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research. For example: suspected child abuse, elder abuse, or urgent risk of harm to self (suicide) or others (homicide).

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying ‘no’ will not harm your relationship with your own doctors or with Mayo Clinic.

MAYO CLINIC

Name and Clinic Number

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

MAYO CLINIC

Name and Clinic Number

CONSENT

SUBJECT

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____
Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT

I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of person obtaining consent: _____
Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician _____
_____

Date: _____ Time: _____ AM/PM (Circle)

The UNIVERSITY OF CHICAGO
The Division of the Biological Sciences • The University of Chicago Medical Center

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH PROTOCOL CONTROL GROUP

Protocol Number: IRB22-1138
Name of Subject: _____
Medical History Number: _____

STUDY TITLE: Tissue destruction and healing in celiac disease

Doctor Directing Research:	Sonia Kupfer, MD
Address:	900 E. 57th St. 9th Floor, KCBD 9120 Chicago, IL 60637
Telephone Number:	(773) 702-7868

KEY INFORMATION

We are asking you to choose whether or not to volunteer for a research study that is gathering information about the basic processes of intestinal (bowel) tissue destruction and healing in people with celiac disease. This section is to give you key information to help you decide whether to participate. We have included detailed information after this section. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is above.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

You are being asked to take part in this research study because you have not been diagnosed with celiac disease. Celiac disease is an immune reaction to eating gluten, a protein found in wheat, barley, and rye. When people with celiac disease eat gluten, it triggers an immune response in the intestine (bowel). Over time, this reaction damages the intestine's lining and prevents it from absorbing some nutrients.

The purpose of this study is to learn more about the processes that cause intestinal damage and healing in people with celiac disease. We hope this study will provide resources for scientists and doctors to improve celiac disease research and clinical care.

This study has three groups of participants. Regardless of group assignment, all participants will undergo data collection, blood testing, and intestinal tissue sampling during the study. More details can be found below in the Detailed Consent section. The three study groups are:

- Gluten challenge group: People who have been diagnosed with celiac disease for at least 12 months and are currently on a gluten free diet will be asked to eat a small amount gluten each day as part of this study.
- Gluten de-challenge group: People who are newly diagnosed with celiac disease and are beginning a gluten free diet as part of routine care.
- Control group: People who do not have celiac disease will participate as a comparison group.

You are being asked to join the **control group**.

You will be asked to undergo an upper endoscopy if you participate in this study. Endoscopy means a thin, flexible, lighted tube will be inserted inside the small bowel through your mouth to view your small intestines and take small biopsies.

Your participation in this study will include approximately 2 visits to the study clinic.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?
By participating in this study, you may help future patients who have celiac disease by helping us learn more about mechanisms that cause destruction and healing of the gut lining.

For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?
You will undergo an endoscopy procedure along with biopsy tissue removal if you participate in this study.
Endoscopy procedures will be done while you may be mildly sedated. While endoscopies are considered a safe procedure, rare complications include tearing of the upper digestive tract and/or bleeding that may require surgery to correct.

For a complete description of risks, refer to the Detailed Consent Section below.

For a complete description of alternate treatment/procedures, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?
Taking part in this study is voluntary. If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

You may choose not to participate at any time during the study. You will not lose any services, benefits or rights you would normally have if you choose to leave the study. The University of Chicago/University of Chicago Medical Center will not condition (withhold or refuse) treating you on whether you sign this Authorization or revoke your authorization at a later time. If you do not sign this form, you will not receive the research-related intervention(s).

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?
The person in charge of the study is Dr. Sonia Kupfer, of the University of Chicago. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, her contact information is (773) 702-7868.

If you have a research-related injury, you should immediately contact Dr. Kupfer at (773) 702-6800 and ask for pager number 2870.

For questions about your rights as a research subject, please contact the University of Chicago BSD IRB at (773) 702-6505.

DETAILED CONSENT

WHAT IS INVOLVED IN THE STUDY?

Enrollment is competitive. This means that when the target number of subjects enters the study, all further enrollments will be closed. About 20-40 people will take part in the control group of this study at the University of Chicago and about 20-40 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 60 healthy people.

If you participate in this study, you will be asked to:

- Undergo one endoscopy with biopsies of intestinal tissue
  An upper endoscopy is a procedure that examines the inside of your esophagus, stomach, and upper portion of the small bowel. During this procedure, a thin, flexible, lighted tube is inserted through your mouth to view your small intestine and take small biopsies.
  You will be asked to not to eat for 8 hours before the procedure but you can have clear liquids up to 2 hours before the procedure. On the day of the test you will be mildly sedated to help you relax. During the procedure, a thin, flexible tube with a small camera at the tip will be inserted through your mouth and moved through the esophagus and stomach and into the small bowels. The camera allows pictures to be sent to a video screen for the doctor to look at. Using a small biopsy forceps which is passed down the tube, the doctor will take tissue samples. The test takes 15-30 minutes, but you will be at the clinic for about 2 hours and you will need to have someone available to take you home afterwards. You should not drive or make important decisions for at least 24 hours following the procedure.
- Give urine, blood, and saliva samples
- Be available for a follow-up phone call on side-effects you may feel

The procedures for each study visit are described below.

Visit 1 (Screening):

- You will be asked to review, sign, and date the informed consent. The study team will review the study with you and ample time will be given to ask questions.
- The study doctor will verify if you qualify for the study.
- Current medication will be reviewed.
- Vital signs such as blood pressure, heart rate, and temperature will be collected
- Blood draw (about 1½ tablespoons) will be taken for lab tests.
- If found eligible, you will be scheduled for Visit 2.

Visit 2:

- The study doctor will review blood test results from visit 1 to verify if you qualify for the study.
- Physical exam including your height and weight
- Your demographic information (such as your age, sex, race and ethnicity), complete medical history will be collected.
- Blood draw (about 1½ tablespoons) will be taken for lab tests.
- Saliva samples will be collected for lab test.

- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to take part in this study.
- Upper endoscopy will be performed to view your small intestine. Up to 14 small intestinal biopsies will be taken during this procedure. Luminal fluid (consists of digestive fluid, food particles and bacteria) from your bowel will be collected as well.
- You will be asked to complete the Celiac Disease Symptom Diary (CDSD©) questionnaire electronically via REDCap to assess your celiac disease symptoms and quality of life. It will take about 10 minutes to complete.
- The study team will contact you the day after your endoscopy to follow up on any side-effects you may feel.
- If you previously screened and were withdrawn due to blood test results, you can forgo the screening visit

Biological sample Storage

Biological samples include the blood, urine, tissue, and luminal fluid collected during this study. All biological samples collected from you will be labeled with a unique participant code. It will include the collection date and time but will not include your name or medical record number.

These samples are collected for the purposes of this study and may also be stored and used for future research studies. This future research may be done at the University of Chicago and Mayo or by colleagues from an outside institution, including commercial partners.

Your samples may be studied for genetic material (such as DNA and RNA). Genes are made up of DNA, which is short for deoxyribonucleic acid. They act as instructions to your body, determining things like eye color and hair color, but also whether people may be more likely to develop certain conditions. Genes are passed from parent to child. RNA is made from DNA. RNA is short for ribonucleic acid. RNA is a genetic material that has an important role in making proteins. Proteins are the building blocks of your body, cells, and organs. The results of genetic research or testing may be shared with collaborators for research purposes. These results would not contain your identifying information (such as name and medical record number) and would instead be labelled with a unique subject study code. The results of genetic testing and research will not be shared with you.

If you decide to withdraw from the study, you can choose to have your samples destroyed. The information that has already been collected will still be used for the study. However, no further research will be conducted using your samples and your samples will be destroyed. Please see the 'What Are My Rights' section below for additional information.

Samples may be tested, stored, and shared as follows:

University of Chicago

The study team will store your blood, urine, and biopsy tissue. The University of Chicago will conduct genetic analysis for study purposes and will store your DNA and RNA. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with

researchers at California Institute of Technology for analysis. Coded samples and can be shared with researchers at other institutions and/or companies as well.
Any samples that are shared will be labelled with a unique subject study code. Samples will be labelled with the date and time the sample was collected and will not contain any personal identifiers.

Mayo Clinic
The study team will process blood samples and send PBMC (type of immune cells) and serum samples to Mayo for storage. These samples will be labelled with the subject study code and will include the collection date and time and will not contain any identifiers. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples and can be shared with researchers at other institutions and/or companies as well.

California Institute of Technology
The study team will send saliva samples and tissue RNA/DNA to the California Institute of Technology to perform microbiome genetic analysis (genetic testing of all microbes, such as bacteria, fungi, and viruses that naturally live on our bodies). The samples will be labelled with the subject study code and will include collection date and time and will not contain any identifiers. Leftover tissue and saliva samples will be stored indefinitely for future research purposes. and these samples can be shared with researchers at other institutions and/or companies.

Other information
In future, identifiers associated with your data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use.

The results from this study will not be shared with you.

Dr. Kupfer may decide to take you off of the study without your consent if:
- You are unable to meet the requirements of the study or your medical condition changes;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

During your participation in this study, you are at risk for the side effects described in this section. The study doctor will discuss these with you.

Upper endoscopy/biopsy risks
An upper endoscopy and biopsy of the intestine are standard and commonly performed medical procedures to examine the small bowel.
Somewhat likely side effects include:

- Tiredness
- Some pain (cramps)
- Discomfort

Rare side effects include;

- Tearing of the upper digestive tract and/or bleeding. This may require surgery to correct.

Biopsy risks may include,

- The removal of tissue samples may result in a small amount of blood in your stools. This should go away. If it persists after 24 hours, please call your study doctor listed on the front page.
- Tenderness
- Infection
- Significant bleeding that requires getting blood from donors

The risk of the sedation medication, usually given during an endoscopy to help you relax, may cause

- allergic reactions,
- nausea,
- skin rash,
- dizziness with a drop in blood pressure,
- a slowing down of your breathing so much that in very rare cases a breathing machine will be used, and
- **death** from sedation-related heart problems.

You will not be permitted to drive immediately after the procedure and, therefore, will need someone to drive you home.

During the endoscopy procedure, the study doctor may come across incidental findings such as ulcers (sores in the stomach tissue lining), H. pylori (bacteria which may cause stomach infections), reflux changes (could cause changes in the tissue lining of the esophagus (tube through which food passes from the throat to the stomach), or polyps (small protrusions in the lining of the esophagus, stomach or small intestine). Additional tissue samples may be taken for clinical purposes in such cases. If this occurs, the study doctor will discuss the findings with you and you will be referred for the appropriate clinical care.

Blood Draw Risks

The risks of giving blood include pain, a bruise at the point where the blood is taken, redness, bleeding, nerve damage, blood clots, which may cause inflammation, and swelling of the vein and infection, and a rare risk of fainting. Care will be taken to avoid these risks.

Questionnaire Risks

Some of the questions may seem personal and may make you feel uncomfortable. If you have any questions or concerns while answering these questions, please talk to your study doctor. You may choose not to answer any question that makes you uncomfortable.

Loss of Confidentiality
Any time information is collected about you there is a potential risk for loss of confidentiality. However, the researchers will make every effort to keep your information confidential. Please refer to the 'What About Confidentiality' section for information on what measures will be taken to protect your confidentiality.

Unforeseen Risks
There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could affect whether you wish to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there will be no direct medical benefit to you. Information gathered in this study may benefit other people who have celiac disease.

WHAT OTHER OPTIONS ARE THERE?
You do not have to take part in this study.

WHAT ARE THE COSTS?
There will be no costs to you or your insurance company resulting from your participation in this research study. However, you or your insurance company will be responsible for costs related to your usual medical care.

WHAT HAPPENS IF I HAVE AN INJURY?
If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, you may receive such emergency medical treatment at the University of Chicago Medical Center, UChicago Medicine Ingalls Memorial Hospital, UChicago Medicine Northwest Indiana, UChicago Medicine AdventHealth Bolingbrook, UChicago Medicine AdventHealth Glen Oaks, UChicago Medicine Advent Health Hinsdale, or UChicago AdventHealth LaGrange at no cost to you. Costs of related non-emergency care for an unanticipated research injury will be covered if that care is provided at the University of Chicago Medical Center. You must notify Dr. Kupfer as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure. If you think that you have suffered a research related injury, you must let Dr. Kupfer know right away.

In the event of an emergency, you should seek care at the nearest emergency room or call 911 and notify the study doctor's office when is possible.

WILL I BE PAID FOR MY PARTICIPATION?
You will be compensated $300 for completing the endoscopy. You will receive the payment after the Visit 2. If you are withdrawn from the study before the endoscopy, you will be paid $50 for the screening visit.

As policies at the University of Chicago require that these payments be given in the form of a check, you will need to complete a tax form. Therefore, we will be collecting personal information about you including your name, address, and social security number. In addition, because the process for requesting a check oftentimes takes several weeks, we will mail your check to you when it is ready. Please note that it may take 3-4 weeks after conclusion of your study participation in order for you to receive your payment.

Additionally, you will receive a parking voucher at the end of each study visit.

WHAT ABOUT CONFIDENTIALITY?

There is a risk of potential loss of confidentiality. To minimize this risk, study records that identify you will be kept confidential. Any research data will be stored in a locked drawer in a locked office and/or entered on a password-protected, encrypted, HIPAA-compliant computer. Only study staff will have access to the data. The results from tests and procedures performed as part of this study may become part of your medical record. Any research information in your medical record will be kept indefinitely.

During this study, Dr. Kupfer and her research team will collect protected health information (PHI) about you for the purposes of this research. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago. The PHI consists of any health information that is collected about you, which could include your medical history and new information collected as a result of this study. Some of this information will come from your medical record. The information to be used on this study includes your name, address, medical record number, phone number, email address, social security number (for payment purposes), initials, date of birth, and dates of procedures, tests diagnosis and hospitalizations (if applicable). We will use these identifiers to schedule study visits, collect data from your medical records, monitor your health, stay in contact with you, complete study objectives and distribute study payments.

As part of the study, Dr. Sonia Kupfer and her research team will share information about you as well as the results of your study-related procedures and tests with collaborators at Mayo Clinic and California Institute of Technology who are assisting with the study, the study funder the National Institutes of Health (NIH) and the representatives of the data safety monitoring board (a group of reviewers who monitor safety data during the course of the study). Data shared could include initials, age, race, ethnicity, the results of research tests and procedures done as part of the study, the dates of study procedures and study test results. This information is being sent to review the results of the study, to monitor the safety of participants, and to verify the accuracy of the study data.

The University of Chicago Financial Services office will have access to your name, address and social security number when processing your check payment.

Your records may be reviewed by federal agencies whose responsibility is to protect human subjects in research, including the Office of Human Research Protections (OHRP). In addition, representatives of the University of Chicago, including the Institutional Review Board (a committee that oversees research) and the Office of Clinical Research may also view the records of the research. If your research record is reviewed by any of these groups, they may also need to

review your entire medical record. The results from tests and/or procedures performed as part of this study may become part of your medical record.

Once health information is shared outside the University of Chicago, please note that your identifiable health information may be shared with someone else. The same laws that the University of Chicago must obey may not protect your health information.

During your participation in this study, you will have access to your medical record. Dr. Kupfer is not required to release to you research information that is not part of your medical record.

This consent/authorization form will be kept by the research team for at least 6 years. The study results will be kept in your research record and be used by the research team until completion of this study.

At the time of study completion, either the research information not already in your medical record will be destroyed or information identifying you will be removed from study results.

Data from this study may be used in medical publications or presentations. Your name and any other identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time.

We are collecting your tissue and/or blood as part of this study. We may use your samples for other research studies, including genetic testing, without contacting you, including sharing your samples with others for research purposes here and outside University of Chicago. It is possible that these samples may be shared with a for profit company for research.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Genetic Information Nondiscrimination Act (GINA)

The Genetic Information Nondiscrimination Act (GINA) is a federal law that may help protect you from health insurance or employment discrimination based on genetic information. GINA is a federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Other Databases
If you agree to take part in this study, your genetic and health information and as applicable a portion of your specimens will be placed into one or more scientific databases. In particular, the National Institutes of Health maintains a database called "dbGaP." The NIH database is a restricted database, meaning a researcher who wants to study information from dbGaP must work with the group overseeing the database to obtain the information. Security measures are in place to protect these data.

Researchers with an approved study will be able to see and use some of your information, but your name and other information that could directly identify you (such as your name or address) will not be placed into the database. There is a risk that someone could use your unique genetic information to trace data back to you or your family, but this risk is very small. There is no direct benefit to you that is expected from any secondary research that may be conducted.

If you decide to withdraw from the study as outlined in the following section, your data will be withdrawn from these databases. However, if your data have already been submitted to an NIH database and distributed to other researchers, or your data have been de-identified and can no longer be linked back to you, your data will not be able to be withdrawn.

Certificate of Confidentiality
To help us protect your privacy, the National Institutes of Health (NIH) has issued a Certificate of Confidentiality for this research. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. There are specific circumstances when the Certificate of Confidentiality does not prevent researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research. For example: suspected child abuse, elder abuse, or urgent risk of harm to self (suicide) or others (homicide).

WHAT ARE MY RIGHTS AS A PARTICIPANT?
If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. Kupfer in writing at the address on the first page. Dr. Kupfer may still use your information that was collected prior to your written notice.

We will tell you about significant new information that may affect your willingness to stay in this study.

You will be given a signed and dated copy of this document. Your authorization to use and disclose your health information does not have an expiration date.

CONSENT

SUBJECT

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____
Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT

I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of person obtaining consent: _____
Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician _____
_____

Date: _____ Time: _____ AM/PM (Circle)

MAYO CLINIC

Name and Clinic Number

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

IRB#: 22-007133

STUDY TITLE: Tissue Destruction and Healing in Celiac Disease (Gluten De-challenge Group)

Doctor Directing Research:	Dr. Joseph Murray and Colleagues
Address:	200 1st ST SW Rochester, MN 55902-9823
Telephone Number:	507-284-2511

KEY INFORMATION

We are asking you to choose whether or not to volunteer for a research study that is gathering information about the basic processes of intestinal (bowel) tissue destruction and healing in people with celiac disease. This section is to give you key information to help you decide whether to participate. We have included detailed information after this section. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is above.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

You are being asked to take part in this research study because you have been diagnosed with celiac disease. Celiac disease is an immune reaction to eating gluten, a protein found in wheat, barley, and rye. When people with celiac disease eat gluten, it triggers an immune response in the intestine (bowel). Over time, this reaction damages the intestine's lining and prevents it from absorbing some nutrients.

The purpose of this study is to learn more about the processes that cause intestinal damage and healing in people with celiac disease. We hope this study will provide resources for scientists and doctors to improve celiac disease research and clinical care.

This study has three groups of participants. Regardless of group assignment, all participants will undergo data collection, blood testing, and intestinal tissue sampling during the study. More details can be found below in the Detailed Consent section. The three study groups are:

MAYO CLINIC

Name and Clinic Number

- Gluten challenge group: People who have been diagnosed with celiac disease for at least 12 months and are currently on a gluten free diet will be asked to eat a small amount gluten each day as part of this study.
- Gluten de-challenge group: People who are newly diagnosed with celiac disease and are beginning a gluten free diet as part of routine care.
- Control group: People who do not have celiac disease will participate as a comparison group.

You are being asked to join the **gluten de-challenge group.** During the study, you will be asked to maintain a strict gluten-free diet.

Your participation in this study will last about 13 months and will include approximately 3 study visits. At the end of your participation, you may choose to roll over to the gluten challenge group. If you choose to do so, then you will be presented with the gluten challenge group informed consent form. If you choose not to, then your participation is finished.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

By participating in this study, you may help future patients who have celiac disease by helping us learn more about mechanisms that cause destruction and healing of the gut lining. In addition, you will have close assessment of diet and nutrition during the course of study.

For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You will be asked to undergo 3 separate endoscopy (esophagogastroduodenoscopy or EGD) procedures with biopsy in the time frame of 13 months if you participate in this study. An EGD is a procedure that examines the lining of the esophagus (tube food passes through from throat to stomach), stomach, and small intestine (duodenum).

Endoscopy means a thin, flexible, lighted tube will be inserted inside the small bowel through your mouth to view your small intestines and take small biopsies. Endoscopies will be done while you may be moderately sedated. While endoscopies are considered a safe procedure, rare complications include tearing of the upper digestive tract and/or bleeding that may require surgery to correct.

During this time you will also be required to complete daily diary and weekly questionnaires.

For a complete description of risks, refer to the Detailed Consent Section below.

For a complete description of alternate treatment/procedures, refer to the Detailed Consent.

MAYO CLINIC

Name and Clinic Number

DO YOU HAVE TO TAKE PART IN THE STUDY?

Taking part in this study is your decision . If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

Take your time to decide. Feel free to discuss the study with your family, friends, healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

You may choose not to participate at any time during the study. You will not lose any services, benefits or rights you would normally have if you choose to leave the study. The Mayo Clinic will not condition (withhold or refuse) treating you on whether you sign this Authorization or revoke your authorization at a later time. If you do not sign this form, you will not receive the research-related intervention(s).

MAYO CLINIC

Name and Clinic Number

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Joseph Murray at the Mayo Clinic. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, you may contact the individuals listed in the table below.
For questions about your rights as a research subject, please contact the University of Chicago BSD IRB at (773) 702-6505.

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator(s):** Dr. Joseph Murray **Phone:** 507-284-2631 **Co-Investigator:** Dr. Adam Bledsoe **Phone:** 507-538-1231 **Emergency After Hours:** 507-284-2511 Ask operator to page Dr. Joseph Murray or Dr. Adam Bledsoe **Study Team Contact:** Chadrick Hinson: 507-266-0237 Irina Horwath: 507-284-0375 Carol Van Dyke: 507-266-7842 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55902
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

MAYO CLINIC

Name and Clinic Number

DETAILED CONSENT

WHAT IS INVOLVED IN THE STUDY?

Enrollment is competitive. This means that when the target number of subjects enters the study, all further enrollments will be closed. About 30-60 people will take part in the 'gluten de-challenge group' of this study at the University of Chicago and about 30-60 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 60 healthy people.

If you participate in this study, you will be expected to:

- Strictly follow a gluten-free diet (GFD).
- Undergo three (3) upper endoscopies with biopsies of intestinal tissue.
  An upper endoscopy is a procedure that examines the inside of your esophagus, stomach, and upper portion of the small bowel. During this procedure, a thin, flexible, lighted tube is inserted through your mouth to view your intestine and take small biopsies.
  You will be asked to not to eat for 8 hours before the procedure, but you can have clear liquids up to 2 hours before the procedure. On the day of the test, you will be moderately sedated to help you relax. During the procedure, a thin flexible tube with a small camera at the tip will be inserted through your mouth and moved through the esophagus and stomach and into the small bowel. The camera allows pictures to be sent to a video screen for the doctor to look at. A tool called a forceps is passed down the tube, the doctor can take tissue samples. The procedure takes 15-30 minutes, but you will be at the clinic for about 2 hours and you will need to have someone available to take you home afterwards. You should not drive or make important decisions for at least 24 hours following the procedure.
- Give urine, blood, and saliva samples.
- Complete questionnaires
- Be available for safety assessment phone calls.

The procedures for each study visit are described below.

Visit 1 (Screening, Day 0):

- You will be asked to review, sign, and date the informed consent. The study team will review the study with you and ample time will be given to ask questions.
- The study doctor will verify if you qualify for the study.
- Your demographic information (such as your age, sex, race and ethnicity), complete medical history will be collected.
- Physical exam, including your height weight
- Vital signs such as blood pressure, heart rate, and temperature will be collected.
- Current medication will be reviewed.
- Blood draw (about 1 ½ tablespoons) will be taken for lab tests.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to take part in this study.

MAYO CLINIC

Name and Clinic Number

- Saliva samples (by spitting into a small tube) will be collected for lab test.
- Upper endoscopy will be performed to view your small intestine. Up to 16 small intestinal biopsies will be taken during this procedure. Luminal fluid (consists of digestive fluid, food particles and bacteria) from your bowel will be collected as well.
- You will be asked to complete the following questionnaires electronically to assess your celiac disease symptoms and quality of life. Surveys will be completed electronically using a weblink.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – you will be asked to complete this survey prior to the endoscopy. . It will take about 8 minutes to complete.
    - Celiac Disease Symptom Diary (CDSD©) – you will complete the diary every day for 2-weeks following Visit 1.. It will take about 10 minutes to complete.
- You will begin a strict gluten-free diet as part of routine care.
- The study team will contact you with the results of the endoscopy and then monthly to follow up on any side effects you may feel, review your answers to questionnaires, and to remind you to follow strict GFD.

Only for subjects enrolled after 05/01/2024:

- Hip and waist measurements
- Dual x-ray absorptiometry (DEXA) scan: An X-Ray called DEXA will be performed to measure your body composition and bone mineral density. You will be asked to lay down on your back and have the scanner move over your body and measure how much muscle, bone, fat you have in your body. There is a small amount of radiation exposure from a DEXA scan. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DXA scan is considered safe for adults.

Visit 2 (3month visit):

- Blood draw (about 2 tablespoons) will be taken for lab tests.
- Saliva samples will be collected for lab test.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to continue this study.
- Upper endoscopy with biopsies will be obtained. Luminal fluids collection will take place.
- You will be asked to complete the following questionnaires to assess your celiac disease symptoms and quality of life.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) – It will take about 8 minutes to complete. You be asked to continue to complete this survey prior to the endoscopy.
    - Celiac Disease Symptom Diary (CDSD©) – You will be asked to complete the CDSD for 4 weeks around the time of the endoscopy (approximately 2 weeks

MAYO CLINIC

Name and Clinic Number

prior and 2 weeks post endoscopy visit). It will take about 10 minutes to complete.
    - Impact of Adhering to a Gluten Free Diet Questionnaire (IGFDQ©) – It will take about 5 minutes to complete. You will be asked to complete this one time at this visit, prior to the endoscopy.
- The study team will contact you to follow up on any side effects you may feel, review your answers to questionnaires, and to remind you to follow strict GFD.

Visit 3 (12-13month visit):

- Blood draw (about 2 tablespoons) will be taken for lab tests.
- Saliva samples will be collected for lab test.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to continue this study.
- Upper endoscopy with biopsies will be obtained. Luminal fluids collection will take place.
- You will be asked to complete the following questionnaires to assess your celiac disease symptoms and quality of life.
    - Impact of Celiac Disease Symptom Questionnaire (ICDSQ©) –You be asked to continue to complete this survey prior to the endoscopy. It will take about 8 minutes to complete.
    - Celiac Disease Symptom Diary (CDSD©) – You will be asked to complete the CDSD for 4 weeks around the time of the endoscopy (approximately 2 weeks prior and 2 weeks post endoscopy visit). It will take about 10 minutes to complete.
    - Impact of Adhering to a Gluten Free Diet Questionnaire (IGFDQ©) –You will be asked to complete this survey prior to the endoscopy. It will take about 5 minutes to complete.
    - Celiac Disease Dietary Adherence Questionnaire (CDAT) –You will be asked to complete this survey prior to the endoscopy. It will take about 5 minutes to complete.
- The study team will contact you to follow up on any side effects you may feel and to review your answers to questionnaires.

Only for subjects enrolled after 05/01/2024:

- Hip and waist measurements
- Undergo DEXA scan

<u>Biological sample Storage</u>

Biological samples include the blood, urine, tissue, and luminal fluid collected during this study. All biological samples collected from you will be labeled with a unique participant code. It will include collection date and time but will not include your name or medical record number.

MAYO CLINIC

Name and Clinic Number

These samples are collected for the purposes of this study and may also be stored and used for future research studies. This future research may be done at the University of Chicago and Mayo Clinic or by colleagues from an outside institution, including commercial partners.

Your samples may be studied for genetic material (such as DNA and RNA). Genes are made up of DNA, which is short for deoxyribonucleic acid. They act as instructions to your body, determining things like eye color and hair color, but also whether people may be more likely to develop certain conditions. Genes are passed from parent to child. RNA is made from DNA. RNA is short for ribonucleic acid. RNA is a genetic material that has an important role in making proteins. Proteins are the building blocks of your body, cells, and organs. The results of genetic research or testing may be shared with collaborators for research purposes. These results would not contain your identifying information (such as name and medical record number) and would instead be labelled with a unique subject study code. The results of genetic testing and research will not be shared with you.

If you decide to withdraw from the study, you can choose to have your samples destroyed. The information that has already been collected will still be used for the study. However, no further research will be conducted using your samples and your samples will be destroyed. Please see the 'What Are My Rights' section below for additional information.

Samples may be tested, stored, and shared as follows:

University of Chicago

The study team will store your blood, urine, luminal samples, and biopsy tissue. The University of Chicago will conduct genetic analysis for study purposes and will store your DNA and RNA. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples can be shared with researchers at other institutions and/or companies as well.

Any samples that are shared will be labelled with a unique subject study code. Samples will be labelled with the date and time the sample was collected. Sample labels will not contain any other personal identifiers.

Mayo Clinic

The study team will process blood samples and send PBMC (type of immune cells) and serum samples to Mayo for storage. These samples will be labelled with the subject study code and will include the collection date and time. Sample labels will not contain any other personal identifiers. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples can be shared with researchers at other institutions and/or companies as well.

California Institute of Technology

The study team will send saliva samples and tissue RNA/DNA to the California Institute of Technology to perform microbiome genetic analysis (genetic testing of all microbes, such as bacteria, fungi, and viruses that naturally live on our bodies). The samples will be labelled with

MAYO CLINIC

Name and Clinic Number

the subject study code and will include collection date and time but will not contain any other personal identifiers. Leftover tissue and saliva samples will be stored indefinitely for future research purposes and these samples can be shared with researchers at other institutions and/or companies.

Other information
In future, identifiers associated with your data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use.

The results from this study will not be shared with you.

Dr. Murray may decide to take you off of the study without your consent if:

- You are unable to meet the requirements of the study or your medical condition changes;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

During your participation in this study, you are at risk for the side effects described in this section. The study doctor will discuss these with you.

Upper endoscopy/biopsy risks

Most people experience few effects from an upper endoscopy. There is a small chance of a hole (perforation) in the esophagus, stomach, and duodenum, which can require surgery to correct. Infection and bleeding can also happen, but these are rare. This is a small risk of bleeding where tissue was removed from your small intestine during the biopsy.

Biopsy risks may include,

- The removal of tissue samples may result in a small amount of blood-tinged saliva. This should go away. If it persists after 24 hours, please call your study doctor listed on the front page.
- Tenderness
- Infection
- Significant bleeding that requires getting blood from donors

The risk of the sedation medication, usually given during an endoscopy to help you relax, may cause

MAYO CLINIC

Name and Clinic Number

- allergic reactions,
- nausea,
- skin rash,
- dizziness with a drop in blood pressure,
- a slowing down of your breathing or heart function so much that in very rare cases a breathing machine will be used

You will not be permitted to drive immediately after the procedure and, therefore, will need someone to drive you home. You should not drive or make any important decisions for at least 24 hours following your procedure.

During the endoscopy procedure, the study doctor may come across incidental findings such as ulcers (sores in the stomach tissue lining), H. pylori (bacteria which may cause stomach infections), reflux changes (could cause changes in the tissue lining of the esophagus (tube through which food passes from the throat to the stomach), or polyps (small protrusions in the lining of the esophagus, stomach or small intestine). Additional tissue samples may be taken for clinical purposes in such cases. If this occurs, the study doctor will discuss the findings with you, and you will be referred for the appropriate clinical care.

Blood Draw Risks

The risks of giving blood include pain, a bruise at the point where the blood is taken, redness, bleeding, nerve damage, blood clots, which may cause inflammation, and swelling of the vein and infection, and a rare risk of fainting. Care will be taken to avoid these risks.

DEXA Scan Risks

During the scan, you will be exposed to a very low amount of radiation. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DEXA scan is considered safe for adults.

Questionnaire Risks

Some of the questions may seem personal and may make you feel uncomfortable. If you have any questions or concerns while answering these questions, please talk to your study doctor. You may choose not to answer any question that makes you uncomfortable.

Loss of Confidentiality

Any time information is collected about you there is a potential risk for loss of confidentiality. However, the researchers will make every effort to keep your information confidential. Please refer to the 'What About Confidentiality' section for information on what measures will be taken to protect your confidentiality.

Unforeseen Risks

MAYO CLINIC

Name and Clinic Number

There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could affect whether you wish to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there will be no direct medical benefit to you, except you will receive monitoring of your disease and response to the gluten-free diet.

WHAT OTHER OPTIONS ARE THERE?
You do not have to take part in this study to receive treatment for your celiac disease. Your other option would be to not participate in this study and maintain a gluten-free diet. If you wish you may also participate in another clinical trial.

WHAT ARE THE COSTS?
Clinical services provided during a clinical trial are either research-related or considered part of usual medical care for patients with your disease or condition. Tests, procedures, and activities that are ordered by your medical care team to monitor your disease or condition (whether you are participating in a clinical trial or not) are described as 'usual medical care'. 'Research-related' is the term used to describe any tests, procedures, or activities that you are being asked to undergo only because of your participation in this clinical trial.

You or your insurance will be financially responsible for the costs of your usual, ongoing medical care. This often includes regular visits with your doctor, lab tests and imaging used to measure your response to treatment, and other tests and procedures deemed medically necessary by your care team. None of the activities done as part of this study are considered part of your usual on going care. Financial responsibilities for routine care may include deductibles and co-payments and this care will be subject to all the same requirements and restrictions of your insurance.

You will not be responsible for the costs of tests or services that are being performed solely for the purposes of this study and would not be performed if you were not participating in this clinical trial. This will often include additional tests performed to answer a research question but not required for your routine clinical care.

If you have questions about whether specific clinical services are research related or part of your usual medical care, please speak to your physician or research contact person.

WHAT HAPPENS IF I HAVE AN INJURY?

Where to get help:
If you think you may have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo

MAYO CLINIC

Name and Clinic Number

Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research-related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment cost for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

WILL I BE PAID FOR MY PARTICIPATION?
You will be compensated $300 after each endoscopy you complete for a potential total of $900. You will be paid for the entire study after visit 3. In order to provide this compensation, the study team will need your Social Security number (for tax purposes).

If you are found not eligible to participate in the study based on the blood test results (conducted during visit 1), you will be paid $50 for the blood draw visit. You will receive the payment after visit 1.

Payment for participant in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address, and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end. In addition, because the process for requesting a check oftentimes takes several weeks, we will mail your check to you when it is ready. Please note that it may take 3-4 weeks after conclusion of your study participation in order for you to receive your payment.

Additionally, you will receive a parking voucher at the end of each study visit.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?
Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. There is a risk of potential loss of confidentiality. To minimize this risk, study records that identify you will be kept confidential. Any research data will be stored in a locked drawer and/or entered on a password-protected, encrypted, HIPAA-compliant computer. Only study staff will have access to the data. The results from tests and procedures performed as part of this study may become part of your medical record. Any research information in your medical record will be kept indefinitely.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this

MAYO CLINIC

Name and Clinic Number

research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- Researchers involved in this study at other institutions.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you. Samples may include collection dates but does not include any other information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

MAYO CLINIC

Name and Clinic Number

Is your health information protected after it has been shared with others?
Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Genetic Information Nondiscrimination Act (GINA)
The Genetic Information Nondiscrimination Act (GINA) is a federal law that may help protect you from health insurance or employment discrimination based on genetic information. GINA is a federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Other Databases
If you agree to take part in this study, your genetic and health information and as applicable a portion of your specimens will be placed into one or more scientific databases. In particular, the National Institutes of Health maintains a database called “dbGaP.” The NIH database is a restricted database, meaning a researcher who wants to study information from dbGaP must work with the group overseeing the database to obtain the information. Security measures are in place to protect these data.

Researchers with an approved study will be able to see and use some of your information, but your name and other information that could directly identify you (such as your name or address) will not be placed into the database. There is a risk that someone could use your unique genetic information to trace data back to you or your family, but this risk is very small. There is no direct benefit to you that is expected from any secondary research that may be conducted.

If you decide to withdraw from the study as outlined in the following section, your data will be withdrawn from these databases. However, if your data have already been submitted to an NIH database and distributed to other researchers, or your data have been de-identified and can no longer be linked back to you, your data will not be able to be withdrawn.

MAYO CLINIC

Name and Clinic Number

Certificate of Confidentiality

To help us protect your privacy, the National Institutes of Health (NIH) has issued a Certificate of Confidentiality for this research. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. There are specific circumstances when the Certificate of Confidentiality does not prevent researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research. For example: suspected child abuse, elder abuse, or urgent risk of harm to self (suicide) or others (homicide).

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

MAYO CLINIC

Name and Clinic Number

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

MAYO CLINIC

Name and Clinic Number

CONSENT

SUBJECT

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____
Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT

I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of person obtaining consent: _____
Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician _____
_____

Date: _____ Time: _____ AM/PM (Circle)

MAYO CLINIC

Name and Clinic Number

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

IRB#: 22-007133

STUDY TITLE: Tissue Destruction and Healing in Celiac Disease (Control Group)

Doctor Directing Research: Dr. Joseph Murray and Colleagues
Address: 200 1st ST SW
Rochester, MN 55902-9823

Telephone Number: 507-284-2511

KEY INFORMATION

We are asking you to choose whether or not to volunteer for a research study that is gathering information about the basic processes of intestinal (bowel) tissue destruction and healing in people with celiac disease. This section is to give you key information to help you decide whether to participate. We have included detailed information after this section. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is above.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

You are being asked to take part in this research study because you have not been diagnosed with celiac disease. Celiac disease is an immune reaction to eating gluten, a protein found in wheat, barley, and rye. When people with celiac disease eat gluten, it triggers an immune response in the intestine (bowel). Over time, this reaction damages the intestine's lining and prevents it from absorbing some nutrients.

The purpose of this study is to learn more about the processes that cause intestinal damage and healing in people with celiac disease. We hope this study will provide resources for scientists and doctors to improve celiac disease research and clinical care.

This study has three groups of participants. Regardless of group assignment, all participants will undergo data collection, blood testing, and intestinal tissue sampling during the study. More details can be found below in the Detailed Consent section. The three study groups are:

MAYO CLINIC

Name and Clinic Number

- Gluten challenge group: People who have been diagnosed with celiac disease for at least 12 months and are currently on a gluten free diet will be asked to eat a small amount gluten each day as part of this study.
- Gluten de-challenge group: People who are newly diagnosed with celiac disease and are beginning a gluten free diet as part of routine care.
- Control group: People who do not have celiac disease will participate as a comparison group.

You are being asked to join the **control group**.

You will be asked to undergo an endoscopy (esophagogastroduodenoscopy or EGD) if you participate in this study. Upper endoscopy means a thin, flexible, lighted tube will be inserted inside the small bowel through your mouth to view your small intestine and take small biopsies.

Your participation in this study will include approximately 2 visits to the study clinic.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?
By participating in this study, you may help future patients who have celiac disease by helping us learn more about mechanisms that cause destruction and healing of the gut lining.

For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?
You will be asked to undergo an endoscopy (esophagogastroduodenoscopy or EGD) procedure with biopsy removal if you participate in this study. An EGD is a procedure that examines the lining of the esophagus (tube food passes through from throat to stomach), stomach, and small intestine (duodenum).

Endoscopy means a thin, flexible, lighted tube will be inserted inside the small bowel through your mouth to view your small intestines and take small biopsies. Endoscopies will be done while you may be mildly sedated. While endoscopies are considered a safe procedure, rare complications include tearing of the upper digestive tract and/or bleeding that may require surgery to correct.

For a complete description of risks, refer to the Detailed Consent Section below.

For a complete description of alternate treatment/procedures, refer to the Detailed Consent.

MAYO CLINIC

Name and Clinic Number

DO YOU HAVE TO TAKE PART IN THE STUDY?

Taking part in this study is your decision. If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

Take your time to decide. Feel free to discuss the study with your family, friends, healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

You may choose not to participate at any time during the study. You will not lose any services, benefits or rights you would normally have if you choose to leave the study. The Mayo Clinic will not condition (withhold or refuse) treating you on whether you sign this Authorization or revoke your authorization at a later time. If you do not sign this form, you will not receive the research-related intervention(s).

MAYO CLINIC

Name and Clinic Number

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Joseph Murray at the Mayo Clinic. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, you may contact the individuals listed in the table below.
For questions about your rights as a research subject, please contact the University of Chicago BSD IRB at (773) 702-6505.

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator(s):** Dr. Joseph Murray **Phone:** 507-284-2631 **Co-Investigator:** Dr. Adam Bledsoe **Phone:** 507-538-1231 **Emergency After Hours:** 507-284-2511 Ask operator to page Dr. Joseph Murray or Dr. Adam Bledsoe **Study Team Contact:** Chadrick Hinson: 507-266-0237 Irina Horwath: 507-284-0375 Carol Van Dyke: 507-266-7842 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55902
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

MAYO CLINIC

Name and Clinic Number

DETAILED CONSENT

WHAT IS INVOLVED IN THE STUDY?

Enrollment is competitive. This means that when the target number of subjects enters the study, all further enrollments will be closed. About 20-40 people will take part in the control group of this study at the University of Chicago and about 20-40 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 60 healthy people.

If you participate in this study, you will be asked to:

- Undergo one upper endoscopy with biopsies of intestinal tissue.
  An upper endoscopy is a procedure that examines the inside of your esophagus, stomach, and upper portion of the small bowel. During this procedure, a thin, flexible, lighted tube is inserted through your mouth to view your intestine and take small biopsies.
  You will be asked to not to eat for 8 hours before the procedure, but you can have clear liquids up to 2 hours before the procedure. On the day of the test, you will be moderately sedated to help you relax. During the procedure, a thin, flexible tube with a small camera at the tip will be inserted through your mouth and moved through the esophagus and stomach and into the small bowel. The camera allows pictures to be sent to a video screen for the doctor to look at. A tool called a forceps is passed down the tube so the doctor can take tissue samples. The procedure takes 15-30 minutes, but you will be at the clinic for about 2 hours and you will need to have someone available to take you home afterwards. You should not drive or make important decisions for at least 24 hours following the procedure.
- Give urine, blood, and saliva samples.
- Be available for a follow-up phone call on side-effects you may feel

The procedures for each study visit are described below.

Visit 1 (Screening):

- You will be asked to review, sign, and date the informed consent. The study team will review the study with you and ample time will be given to ask questions.
- The study doctor will verify if you qualify for the study.
- Physical exam including your height and weight
- Current medication will be reviewed.
- Vital signs such as blood pressure, heart rate, and temperature will be collected
- Blood draw (about 1½ tablespoons) will be taken for lab tests.
- If found eligible, you will be scheduled for Visit 2.

MAYO CLINIC

Name and Clinic Number

Visit 2:

- The study doctor will review blood test results from visit 1 to verify if you qualify for the study.
- Your demographic information (such as your age, sex, race and ethnicity), complete medical history will be collected.
- Blood draw (about 1½ tablespoons) will be taken for lab tests.
- Saliva samples will be collected for lab test.
- Urine will be collected for lab tests. If you are a female of childbearing potential, a urine pregnancy test will be done at the beginning of the visit. If the test is positive, you will not be able to take part in this study.
- Upper endoscopy will be performed to view your small intestine. Up to 14 small intestinal biopsies will be taken during this procedure. Luminal fluid (consists of digestive fluid, food particles and bacteria) from your bowel will be collected as well.
- You will be asked to complete the Celiac Disease Symptom Diary (CDSD©) questionnaire electronically via REDCap to assess your celiac disease symptoms and quality of life. It will take about 10 minutes to complete.
- The study team will contact you the day after your endoscopy to follow up on any side-effects you may feel.
- If you previously screened and were withdrawn due to blood test results, you can forgo the screening visit

Biological sample Storage

Biological samples include the blood, urine, tissue, and luminal fluid collected during this study. All biological samples collected from you will be labeled with a unique participant code. It will include collection date and time but will not include your name or medical record number.

These samples are collected for the purposes of this study and may also be stored and used for future research studies. This future research may be done at the University of Chicago and Mayo Clinic or by colleagues from an outside institution, including commercial partners.

Your samples may be studied for genetic material (such as DNA and RNA). Genes are made up of DNA, which is short for deoxyribonucleic acid. They act as instructions to your body, determining things like eye color and hair color, but also whether people may be more likely to develop certain conditions. Genes are passed from parent to child. RNA is made from DNA. RNA is short for ribonucleic acid. RNA is a genetic material that has an important role in making proteins. Proteins are the building blocks of your body, cells, and organs. The results of genetic research or testing may be shared with collaborators for research purposes. These results would not contain your identifying information (such as name and medical record number) and would instead be labelled with a unique subject study code. The results of genetic testing and research will not be shared with you.

If you decide to withdraw from the study, you can choose to have your samples destroyed. The

MAYO CLINIC

Name and Clinic Number

information that has already been collected will still be used for the study. However, no further research will be conducted using your samples and your samples will be destroyed. Please see the 'What Are My Rights' section below for additional information.

Samples may be tested, stored, and shared as follows:

University of Chicago

The study team will store your blood, urine, luminal samples, and biopsy tissue. The University of Chicago will conduct genetic analysis for study purposes and will store your DNA and RNA. These samples will be stored indefinitely for future research purposes. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples can be shared with researchers at other institutions and/or companies as well. Any samples that are shared will be labelled with a unique subject study code. Samples will be labelled with the date and time the sample was collected. Sample labels will not contain any other personal identifiers.

Mayo Clinic

The study team will process blood samples and send PBMC (type of immune cells) and serum samples to Mayo for storage. These samples will be labelled with the subject study code and will include the collection date and time but will not contain any other personal identifiers. Coded samples will be shared with researchers at California Institute of Technology for analysis. Coded samples can be shared with researchers at other institutions and/or companies as well.

California Institute of Technology

The study team will send saliva samples and tissue RNA/DNA to the California Institute of Technology to perform microbiome genetic analysis (genetic testing of all microbes, such as bacteria, fungi, and viruses that naturally live on our bodies). The samples will be labelled with the subject study code and will include collection date and time. Sample labels will not contain any other personal identifiers. Leftover tissue and saliva samples will be stored indefinitely for future research purposes and these samples can be shared with researchers at other institutions and/or companies.

Other information

In future, identifiers associated with your data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use.

The results from this study will not be shared with you.

Dr. Murray may decide to take you off of the study without your consent if:

- You are unable to meet the requirements of the study or your medical condition changes;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

MAYO CLINIC

Name and Clinic Number

WHAT ARE THE RISKS OF THE STUDY?

During your participation in this study, you are at risk for the side effects described in this section. The study doctor will discuss these with you.

Upper endoscopy/biopsy risks

Most people experience few effects from an upper endoscopy. There is a small chance of a hole (perforation) in the esophagus, stomach, and duodenum, which can require surgery to correct. Infection and bleeding can also happen, but these are rare. This is a small risk of bleeding where tissue was removed from your small intestine during the biopsy.

Biopsy risks may include,

- The removal of tissue samples may result in a small amount of blood-tinged saliva. This should go away. If it persists after 24 hours, please call your study doctor listed on the front page.
- Tenderness
- Infection
- Significant bleeding that requires getting blood from donors

The risk of the sedation medication, usually given during an endoscopy to help you relax, may cause

- allergic reactions,
- nausea,
- skin rash,
- dizziness with a drop in blood pressure,
- a slowing down of your breathing or heart function so much that in very rare cases a breathing machine will be used

You will not be permitted to drive immediately after the procedure and, therefore, will need someone to drive you home. You should not drive or make any important decisions for at least 24 hours following your procedure.

During the endoscopy procedure, the study doctor may come across incidental findings such as ulcers (sores in the stomach tissue lining), H. pylori (bacteria which may cause stomach infections), reflux changes (could cause changes in the tissue lining of the esophagus (tube through which food passes from the throat to the stomach), or polyps (small protrusions in the lining of the esophagus, stomach or small intestine). Additional tissue samples may be taken for clinical purposes in such cases. If this occurs, the study doctor will discuss the findings with you, and you will be referred for the appropriate clinical care.

MAYO CLINIC

Name and Clinic Number

Blood Draw Risks
The risks of giving blood include pain, a bruise at the point where the blood is taken, redness, bleeding, nerve damage, blood clots, which may cause inflammation, and swelling of the vein and infection, and a rare risk of fainting. Care will be taken to avoid these risks.

Questionnaire Risks
Some of the questions may seem personal and may make you feel uncomfortable. If you have any questions or concerns while answering these questions, please talk to your study doctor. You may choose not to answer any question that makes you uncomfortable.

Loss of Confidentiality
Any time information is collected about you there is a potential risk for loss of confidentiality. However, the researchers will make every effort to keep your information confidential. Please refer to the 'What About Confidentiality' section for information on what measures will be taken to protect your confidentiality.

Unforeseen Risks
There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could affect whether you wish to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there will be no direct medical benefit to you, except you will receive monitoring of your disease and response to the gluten-free diet.

WHAT OTHER OPTIONS ARE THERE?
You do not have to take part in this study to receive treatment for your celiac disease. Your other option would be to not participate in this study and maintain a gluten-free diet. If you wish you may also participate in another clinical trial.

WHAT ARE THE COSTS?
Clinical services provided during a clinical trial are either research-related or considered part of usual medical care for patients with your disease or condition. Tests, procedures, and activities that are ordered by your medical care team to monitor your disease or condition (whether you are participating in a clinical trial or not) are described as 'usual medical care'. 'Research-related' is the term used to describe any tests, procedures, or activities that you are being asked to undergo only because of your participation in this clinical trial.

You or your insurance will be financially responsible for the costs of your usual, ongoing medical care. This often includes regular visits with your doctor, lab tests and imaging used to measure your response to treatment, and other tests and procedures deemed medically necessary

MAYO CLINIC

Name and Clinic Number

by your care team. None of the activities done as part of this study are considered part of your usual on going care. Financial responsibilities for routine care may include deductibles and co-payments and this care will be subject to all the same requirements and restrictions of your insurance.

You will not be responsible for the costs of tests or services that are being performed solely for the purposes of this study and would not be performed if you were not participating in this clinical trial. This will often include additional tests performed to answer a research question but not required for your routine clinical care.

If you have questions about whether specific clinical services are research related or part of your usual medical care, please speak to your physician or research contact person.

WHAT HAPPENS IF I HAVE AN INJURY?

Where to get help:
If you think you may have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research-related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment cost for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

WILL I BE PAID FOR MY PARTICIPATION?
You will be compensated $300 for completing the endoscopy. You will receive the payment after the Visit 2.

If you are withdrawn from the study before the endoscopy, you will be paid $50 for the screening visit. You will receive the payment after completing Visit 1. In order to provide this compensation, the study team will need your Social Security number (for tax purposes).

Payment for participant in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address, and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end. In addition, because the process for requesting a check oftentimes takes several weeks, we will mail your check to you when it is ready. Please note that it may take 3-4 weeks after conclusion of your study participation in order for you to receive your payment.

MAYO CLINIC

Name and Clinic Number

Additionally, you will receive a parking voucher at the end of each study visit.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?
Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. There is a risk of potential loss of confidentiality. To minimize this risk, study records that identify you will be kept confidential. Any research data will be stored in a locked drawer and/or entered on a password-protected, encrypted, HIPAA-compliant computer. Only study staff will have access to the data. The results from tests and procedures performed as part of this study may become part of your medical record. Any research information in your medical record will be kept indefinitely.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:
- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:
- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:
- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- Researchers involved in this study at other institutions.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

MAYO CLINIC

Name and Clinic Number

How your information may be shared with others:
While taking part in this study, you will be assigned a code that is unique to you. Samples may include collection dates but does not include any other information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?
Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Genetic Information Nondiscrimination Act (GINA)
The Genetic Information Nondiscrimination Act (GINA) is a federal law that may help protect you from health insurance or employment discrimination based on genetic information. GINA is a federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Other Databases
If you agree to take part in this study, your genetic and health information and as applicable a portion of your specimens will be placed into one or more scientific databases. In particular, the

MAYO CLINIC

Name and Clinic Number

National Institutes of Health maintains a database called "dbGaP." The NIH database is a restricted database, meaning a researcher who wants to study information from dbGaP must work with the group overseeing the database to obtain the information. Security measures are in place to protect these data.

Researchers with an approved study will be able to see and use some of your information, but your name and other information that could directly identify you (such as your name or address) will not be placed into the database. There is a risk that someone could use your unique genetic information to trace data back to you or your family, but this risk is very small. There is no direct benefit to you that is expected from any secondary research that may be conducted.

If you decide to withdraw from the study as outlined in the following section, your data will be withdrawn from these databases. However, if your data have already been submitted to an NIH database and distributed to other researchers, or your data have been de-identified and can no longer be linked back to you, your data will not be able to be withdrawn.

Certificate of Confidentiality

To help us protect your privacy, the National Institutes of Health (NIH) has issued a Certificate of Confidentiality for this research. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. There are specific circumstances when the Certificate of Confidentiality does not prevent researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research. For example: suspected child abuse, elder abuse, or urgent risk of harm to self (suicide) or others (homicide).

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

MAYO CLINIC

Name and Clinic Number

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

MAYO CLINIC

Name and Clinic Number

CONSENT

SUBJECT

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____
Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT

I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of person obtaining consent: _____
Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician _____
_____

Date: _____ Time: _____ AM/PM (Circle)