COVER PAGE

Official Title of the Study: Tissue destruction and healing in celiac disease
NCT Number: not yet assigned
Document Date: 2022.10.01

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
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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 7 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 procedures with biopsy in the time frame of 7 weeks if you participate in this study. 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 bowel through your rectum to view your 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 colon 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?

About 45 people will take part in the 'gluten challenge group' at the University of Chicago and about 45 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 40 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
  An endoscopy is a procedure that examines the inside of your bowel. During this procedure, a thin, flexible, lighted tube is inserted through your rectum to view your intestines and take small biopsies.
  A few days before each endoscopy procedure you will need to watch what you eat and drink and the day before you will be given packets of laxatives to drink to clear your bowels. On the day of the test you will be mildly sedated to help you relax. A flexible tube with a small camera at the tip will be inserted through your rectum and moved through the bowels. It may also have a tool to remove tissue, if needed. The camera allows pictures to be sent to a video screen for the doctor to look at. The test takes 30-45 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.
- 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.
  - 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.
- Endoscopy will be performed to view your intestines. 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 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) – 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 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.
    - Celiac Disease Dietary Adherence Questionnaire (CDAT) – You will be asked to complete this one time at this visit. It will take about 5 minutes to complete.
- 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.

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.
- 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 be asked to continue to complete this weekly until 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.
- 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©) –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) – 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 your initials 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 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 and can be shared with other researchers at the University of Chicago as well as other institutions and/or companies. Any samples that are shared will be labelled with a unique subject study code 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 only and will not contain any identifiers. These samples will be stored indefinitely for future research purposes and can be shared with researchers at other institutions and/or companies.

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 only 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.

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

Endoscopy/biopsy risks

A full endoscopy and biopsy procedure may involve some pain and discomfort.
Rare complications include tearing of the colon and/or bleeding that may require surgery to correct and may be **fatal**.

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 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, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center 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.

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 receive payments three times during the study, once after visit 2, once after visit 4, and once after visit 5.

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.
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)

COVER PAGE
Official Title of the Study: Tissue destruction and healing in celiac disease
NCT Number: not yet assigned
Document Date: 2022.10.18

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

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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.

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 procedures with biopsy in the time frame of 13 months if you participate in this study. Over this year you also be required to complete daily diaries and weekly questionnaires. Endoscopy means a thin, flexible, lighted tube will be inserted inside the bowel through your rectum to view your 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 colon 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?

About 45 people will take part in the 'gluten de-challenge group' of this study at the University of Chicago and about 45 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 40 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 bowel. During this procedure, a thin, flexible, lighted tube is inserted through your rectum to view your intestines and take small biopsies.
  A few days before each endoscopy procedure you will need to watch what you eat and drink and the day before you will be given packets of laxatives to drink to clear your bowels. On the day of the test you will be mildly sedated to help you relax. A flexible tube with a small camera at the tip will be inserted through your rectum and moved through the bowels. It may also have a tool to remove tissue, if needed. The camera allows pictures to be sent to a video screen for the doctor to look at. The test takes 30-45 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.
- 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.
- Endoscopy will be performed to view your intestines. 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 each week until end of study. It will take about 8 minutes to complete.
    - Celiac Disease Symptom Diary (CDSD©) – you will complete the diary every day until the end of the study. It will take about 10 minutes to complete.
    - Celiac Disease Dietary Adherence Questionnaire (CDAT) – You will be asked to complete this one time at this visit. It will take about 5 minutes to complete.
    - Impact of a Gluten-free Diet Questionnaire (IGFDQ) – You will be asked to complete this one time at this visit. It will take about 8 minutes to complete.
- You will begin a strict gluten-free diet as part of routine care.
- The study team will contact you monthly to follow up on any side effects you may feel, review your answers to questionnaires, and to remind you to follow strict GFD.

Visit 2 (3month visit):

- 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 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 **weekly** until 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.
    - 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.
    - 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 monthly 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 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 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.

    - Celiac Disease Symptom Diary (CDSD©) – 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.
    - 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 to questionnaires.

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 your initials 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 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 and can be shared with other researchers at the University of Chicago as well as other institutions/or companies. Any samples that are shared will be labelled with a unique subject study code 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 only and will not contain any identifiers. These samples will be stored indefinitely for future research purposes and can be shared with researchers at other institutions/or companies.

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 only 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/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.

Endoscopy/biopsy risks
A full endoscopy and biopsy of the colon are standard and commonly performed medical procedures to examine the large bowel.
Somewhat likely side effects include:
- Tiredness
- Some pain (cramps)
- Discomfort

Rare side effects include;
- Tearing of the colon and/or bleeding. This may require surgery to correct and may be **fatal**.

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.

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, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center 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.

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)

COVER PAGE
Official Title of the Study: Tissue destruction and healing in celiac disease
NCT Number: not yet assigned
Document Date: 2022.10.01

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 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 endoscopy if you participate in this study. Endoscopy means a thin, flexible, lighted tube will be inserted inside the bowel through your rectum to view your 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 along with biopsy tissue removal if you participate in this study. Endoscopies will be done while you may be mildly sedated. While endoscopies are considered a safe procedure, rare complications include tearing of the colon 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?

About 20 people will take part in the control group of this study at the University of Chicago and about 20 people at Mayo Clinic. The entire study will enroll about 180 people diagnosed with celiac disease and 40 healthy people.

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

- Undergo one endoscopy with biopsies of intestinal tissue
  An endoscopy is a procedure that examines the inside of your bowel. During this procedure, a thin, flexible, lighted tube is inserted through your rectum to view your intestines and take small biopsies.
  A few days before the test you will need to watch what you eat and drink and the day before you will be given packets of laxatives to drink to clear your bowels. On the day of the test you will be mildly sedated to help you relax. A flexible tube with a small camera at the tip will be inserted through your rectum and moved through the bowels. It may also have a tool to remove tissue, if needed. The camera allows pictures to be sent to a video screen for the doctor to look at. The test takes 30-45 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.
- 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.

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.

- Endoscopy will be performed to view your intestines. 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.

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 your initials 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 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 and can be shared with other researchers at the University of Chicago as well as other institutions and/or companies. Any samples that are shared will be labelled with a unique subject study code 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 only and will not contain any identifiers. These samples will be stored indefinitely for future research purposes and can be shared with researchers at other institutions and/or companies.

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 only 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.

Endoscopy/biopsy risks
A full endoscopy and biopsy of the colon are standard and commonly performed medical procedures to examine the large bowel.
Somewhat likely side effects include:
- Tiredness
- Some pain (cramps)
- Discomfort

Rare side effects include;
- Tearing of the colon and/or bleeding. This may require surgery to correct and may be **fatal**.

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, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center 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.

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 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 completing Visit 1.

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)