



Clinical Investigation Consent Form

IRB Rev 2026

The Rockefeller University Clinical Research Center

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Title of the research study: *A Randomized Crossover Open-Label Trial of Naproxen and Metformin Safety and Tolerability in the Setting of Prevention of Oral Cancer in Fanconi Anemia*

Informed consent is the first step in deciding whether you want to join this research study. Informed consent is a process of sharing information and having your questions answered. This information will include: the purpose of the research study, what will happen in the study, and possible risks and benefits. All this information will be explained to you in detail. You should keep asking questions until you understand what the study is about and what is being asked of you. You may then want to enroll, or you may decide not to join the study. The decision to participate is entirely up to you. You can always ask additional questions at any time during the study. You have the right to withdraw from the study, and you can change your mind about participating in the study at any time.

Summary of Key Information:

You are being asked to join a research study. The study will take place at The Rockefeller University Clinical Research Center (CRC) and at the University of Minnesota. Joining a research study is voluntary. You can decide not to participate in this study. This consent form tells you about the research. The persons explaining this form to you will answer your questions. You are free to ask as many questions as you want to. You may take an unsigned copy of this form home to read again before deciding if you want to enroll. After you feel that you understand the research, you will be asked to sign this consent form if you decide to enroll. Participating in a research study is not part of your routine medical care. Alternatives to joining this study include continuing regular care with your primary physician and specialists.

The purpose of this study is: To determine the safety and feasibility of metformin and naproxen for preventing oral cancer in people with Fanconi anemia.



The study procedures will include: If you agree to participate, we will review your medical history. After your eligibility is assessed, you will be given the study drugs, along with instructions on how to take them during your participation. There will be a blood draw every six months during on-site study visits, and you will be asked to visit an off-site lab to complete a blood draw mid-study drug intervention. Total blood drawn will be up to 57 mLs (about 11.5 teaspoons). You will also complete an oral exam, including non-identifying photography, oral brushings and oral surgical biopsy (up to five) at every, or every other, study visit. The oral mucosa surgical biopsy is maximum 5mm, or about the size of a pencil eraser. Instructions for post-biopsy care will be provided. We will ask you to complete weekly questionnaires to assess your safety, and that you are tolerating the study drug well.

How long will you be in the study: If you join the research study, you will take part for about 24 months. The study will involve 6 on-site study visits that will last about 3 hours each, and a minimum of 8 calls/telehealth visits that will last about an hour.

Number of participants involved: We plan to enroll at least 40 participants.

Before you decide whether to participate in the study, it is important for you to know the main risks of the study: The main risks associated with the study include: risk of side effects from medications (metformin, naproxen) which are typically mild (e.g. GI discomfort, more described below). There may be a risk of minor bleeding from the oral biopsy, oral brushing, or blood draw, along with some bruising and swelling. There may also be a risk of loss of privacy, although steps will be taken to keep your information secure.

Study drugs: Participants will be randomized to receive naproxen followed by metformin, or metformin followed by naproxen. There is no placebo used in this trial. Participants will be asked to take each study drug for six months.

The possible benefits of participating in this study are: We are investigating the potential benefits of metformin and naproxen, which may slow or prevent the progression of oral cancers in Fanconi anemia.

Researcher's contact number–Rockefeller University: (212) 327-7850 (Dr. May)

University of Minnesota: 612-625-6976 (Dr. Uppgaard)

Sponsor: Some studies are paid for by a sponsor. A sponsor can be a person or organization. This study is sponsored by the Fanconi Cancer Foundation. The Laboratory of Genome Maintenance at Rockefeller is also funded by the National Institutes of Health and Rockefeller University.

I. What this research study is about, and the reason for doing this research.

Finding ways to slow or prevent cancer in people with Fanconi anemia is very important, because these cancers are aggressive and are hard to treat. In this study, we will test two drugs, metformin and naproxen, to see if they can lower the risk of cancer. We will check how safe these drugs are and what side effects they may cause.

To keep an eye on early signs of cancer, we will also look for changes in the mouth, such as cancerous or pre-cancerous lesions, by taking a small tissue sample (a biopsy). Additionally, we



will use a brush, similar to a toothbrush, to look for early signs of cancer in the mouth (biomarkers), before and after treatment, to check for the effectiveness of these drugs in preventing cancer.

In this trial, we aim to evaluate metformin and naproxen to assess safety and impact on non-invasive oral cancer biomarkers, and to establish a framework for future trials to lower the risk of cancer in Fanconi anemia patients. We will determine the safety and feasibility of metformin and naproxen for preventing oral cancer in individuals with Fanconi anemia, which has the potential to delay development of cancer and severity of cancer. Findings from this study could be applied more broadly to cancer prevention in the general population with high risk of oral cancer, such as heavy smokers or alcohol consumers.

This trial is funded by the Fanconi Cancer Foundation (FCF), previously known as The Fanconi Anemia Research Fund. The FCF is a non-profit organization that aims to harness hope through the funding of scientific research, advocacy, education, and support services for individuals and families affected by FA and associated cancers.

II. What is going to happen in this research study?

Study visit outline:

Visit #1, Informed Consent and Screening

- **Eligibility Assessment and Informed Consent** (via Zoom)
- **Medical History Collection:** Demographic data, social history (alcohol, tobacco), genetic testing results, general medical history (including FA history), prior malignancies/oral lesions, medication use.
- **Schedule your baseline visit (in-person)**

Visit #2, Baseline Visit Pre-Intervention (month 0)

- **Medical History Collection:** Demographic data, social history (alcohol, tobacco), genetic testing results, general medical history (including FA history), prior malignancies/oral lesions, medication use
- **Point-of-care tests:** HIV and pregnancy (urine beta Hcg) (if of childbearing potential) tests.
- **Physical Exam:** Targeted oral cavity exam, documentation of any lesions using oral maps, photography/video (non-identifying)
- **Surgical Biopsy of Oral Mucosa:** One lesion selected based on size/appearance for histology and biomarker analysis
- **Oral Brush Sampling:** Standardized brush samples from 6 oral sites + separate brushes for visible lesions (if present)
- **Blood draw for screening:** We will collect a complete blood count (CBC), complete metabolic panel (CMP), Hepatitis B/C panel, Hemoglobin A1c. This will be a total of 12mls (about 2.5 teaspoons).
- **Additional research blood samples:** For germline DNA to compare with somatic biomarkers (up to 3mLs, about half a teaspoon)



- **Buccal Swab:** Swab of inside of cheek will be collected for NanoSeq ultra-sensitive variant detection. Our genetic sequencing testing including NanoSeq is used to detect changes in oral mucosal tissue not visible to the eye.
- At the end of this visit, eligible participants will be randomized to an open-label crossover design of either naproxen for 6-months followed by metformin for 6-months, or metformin for 6-months followed by naproxen for 6-months, with a 2-week washout period between interventions.

Remote Weekly Surveys & Monthly Telehealth Visits (months 1 and 2):

After we complete the first visit process, we will check in on you through weekly online surveys and monthly calls/telehealth visits to review adherence, side effects, symptoms, review submitted oral self-exam findings (instructions at <https://fanconi.de/icare-english/>), any adverse events and/or medication issues. These weekly and monthly reports will continue throughout your participation in the study.

Visit #3, Start of First Arm Treatment (month 3):

- **Point-of-care tests:** A pregnancy test will be done, if of child-bearing potential.
- **Surgical Biopsy of Oral Mucosa:** One lesion selected based on size/appearance for histology and biomarker analysis
- **Oral Brush Sampling:** Standardized brush samples from 6 oral sites + separate brushes for visible lesions (if present)
- **Blood or Skin Sample:** For germline DNA to compare with somatic biomarkers, in addition to a CBC and CMP.
- **Buccal Swab:** Collected for NanoSeq ultra-sensitive variant detection.
- **Training on FAexam App:** For weekly self-oral exams
- **Study Drug Dispensing:** Initiation of randomized intervention (metformin or naproxen)

Remote Weekly Surveys & Monthly Telehealth Visits (months 4 and 5):

Continuation of the weekly online surveys and monthly calls/telehealth visits.

Off-site safety monitoring labs (month 6):

- **Off-site blood draw:** At local laboratory (labs contracted through Quest Diagnostics). Participants will be asked to have a CBC and CMP drawn to monitor for any adverse effects of the intervention. The study team will provide a voucher for these off-site activities.

Remote Weekly Surveys & Monthly Telehealth Visits (months 7 and 8):

Continuation of the weekly online surveys and monthly calls/telehealth visits.

Visit #4, End of First Arm Treatment, Start of washout period (month 9):



- **Physical Exam and Oral Exam:** Repeat oral cavity inspection with mapping, photo/video documentation
- **Oral Brush Sampling:** From standard sites and any lesions
- **Buccal Swab Sample:** For NanoSeq mutation tracking
- **Surgical Biopsy of Oral Mucosa** (if applicable): Of same target lesion sampled at baseline (if lesion persists)
- **Assessment of Adverse Events:** Clinical evaluation and lab safety tests (bloodwork)
- **Study Drug Dispensing:** Initiation of randomized second arm intervention (metformin or naproxen)
- **Pill Counts:** Review of adherence

Start of second intervention (month 10):

- **Switch to Second Study Drug:** After 4-week washout, initiate next arm (metformin or naproxen disbursed at visit #4)

Remote Weekly Surveys & Monthly Telehealth Visits (months 11 and 12):

Continuation of the weekly online surveys and monthly calls/telehealth visits.

Off-site safety monitoring labs (month 13):

- **Off-site blood draw:** At local laboratory (labs contracted through Quest Diagnostics). Participants will be asked to have a CBC and CMP drawn to monitor for any adverse effects of the intervention.

Remote Weekly Surveys & Monthly Telehealth Visits (months 14 and 15):

Continuation of the weekly online surveys and monthly calls/telehealth visits.

Visit #5, End of Second Arm Treatment (month 16):

- **Physical and Oral Exam:** Full repeat evaluation with mapping and imaging
- **Oral Brush Sampling:** Standard sites + lesions
- **Buccal Swab Collection:** For NanoSeq analysis
- **Assessment of Adverse Events:** Clinical evaluation, bloodwork
- **Pill Counts:** Final adherence data collection
- **Surgical Biopsy of Oral Mucosa** (if applicable): Of same target lesion sampled at baseline (if lesion persists)

Remote Weekly Surveys & Monthly Telehealth Visits (months 17, 18, 19, 20, and 21):

Continuation of the weekly online surveys and monthly calls/telehealth visits.
There will not be off-site monitoring labs during the off-drug period.

Visit #6, End of Study (month 22):



- **Physical and Oral Exam:** Full repeat evaluation with mapping and imaging
- **Oral Brush Sampling:** Standard sites + lesions
- **Buccal Swab Collection:** For final NanoSeq analysis
- **Assessment of Adverse Events:** Clinical evaluation, bloodwork
- **Pill Counts:** Final adherence data collection
- **Surgical Biopsy of Oral Mucosa** (if applicable): Of original lesion or new lesion, if needed for comparison
- **End-of-Study Counseling:** Referrals for ongoing care if concerning findings are observed

The total amount of blood that will be collected in this study is up to 45 mLs (about 9 teaspoons). The maximum number of biopsies is: 5 oral biopsies per participant, and 1 skin biopsy per participant.

Test and Procedures Involved with this Study

If you decide to join this study, you will be put in one of two groups. Both groups will get the active drugs, but in different order. The first group will get metformin for 6 months, followed by naproxen for 6 months, while the second group will get naproxen followed by metformin. Which group you end up in is determined by chance. You have a fifty-fifty (50%) chance of being in one of the two groups. The researchers and you will know which drug you are receiving.

Metformin is approved by the U.S. Food and Drug Administration (FDA) for the treatment of diabetes mellitus, and naproxen is approved for treatment of pain. However, in this study, the drug is being used to prevent head and neck squamous cell carcinoma, which is an unapproved/investigational use (also known as "off-label" use) of this medication. This means that the safety and effectiveness of using this drug for your condition has not been fully established or approved by the FDA.

Laboratory testing conducted on your blood or tissues during the research study will fall into two general categories: 1) New York State-approved tests, and 2) experimental tests that have not been certified by New York State.

A New York State-approved test is a standard laboratory test performed by a New York State-approved laboratory during the research study. We will tell your doctor and/or you about any test results that may affect your health. We will give you a copy of all your laboratory results that were performed by a New York State-approved laboratory.

Experimental tests have not been approved by New York State for diagnosis or treatment. By law, we cannot tell you or your doctor the results of experimental tests; however, if we find anything from experimental tests that might be important for your health, we may suggest that you have additional tests performed by a New York State-approved laboratory.



In this study, you will not receive routine care for any medical conditions related to this protocol. and you will not receive routine care for any other medical conditions you may have.

Return of Individual Results:

This study includes the collection and analysis of experimental genetic and molecular biomarkers related to early detection of head and neck squamous cell carcinoma in Fanconi anemia. These biomarkers are investigational and are being evaluated solely to assess their scientific feasibility and performance characteristics. They are not clinically validated, are not interpreted in a CLIA-certified environment, and currently have no established diagnostic, prognostic, or therapeutic relevance for individual patients.

Given their unproven nature, individual biomarker findings will not be returned to participants. Research-grade results may be inaccurate, incomplete, or not reproducible, and their clinical implications—if any—are unknown. Providing such results could expose participants to harm, including unnecessary alarm, false reassurance, or inappropriate changes in clinical management. At present, there is no evidence that these biomarkers can identify cancer, predict cancer risk, or alter clinical decision-making in Fanconi anemia patients.

All data generated from these assays will therefore be used only for research purposes. They will be analyzed in aggregate to understand whether these biomarkers may have future promise but will not be used for individual diagnosis, screening, or care. If, in the future, any biomarker becomes validated for clinical use, this would occur outside the context of the present study, through additional research, regulatory evaluation, and incorporation into clinical guidelines.

In contrast to the biomarkers, histologic evaluation of any biopsy or tissue sample obtained in this study will be performed in a clinical, CLIA-certified setting. Unlike the experimental biomarkers, these pathology results are clinically meaningful and may identify cancerous or pre-cancerous changes. For this reason, any clinically significant findings will be communicated directly to the participant's primary care provider and/or specialty care team so that appropriate medical follow-up can occur. Participants will not receive a separate research report; instead, all actionable histologic results will be integrated into their routine clinical care through their established clinicians.

The study team will provide a plain language summary of the overall results of the study when the study is complete. This study Return of Results report summary usually includes the purpose of the study, who participated (e.g., age, sex, race, ethnicity, if appropriate), what the study involved, and the main results. The combined results from all the participants, will be shared. As the research tests are not validated tests nor certified by New York State for sharing, individual research results are not shared in the summary reports. This study summary will be provided through one or more platforms such as the Fanconi Cancer Foundation Scientific Symposium with specific details provided when the results are ready to be shared. You should update the research team if your contact information changes to be sure to receive notification when the study summary becomes available.



Your medical information and test results will be written in your chart. The researchers or the sponsor of the study may also keep separate records with information about you and your study tests.

Sometimes we will need to look at your earlier medical records. We will ask you to sign a medical release form that will give us permission to obtain your health information from a hospital, doctor, or clinic where you have been treated previously.

A genetic test is a laboratory test of a sample to diagnose the presence of a gene-linked increased risk that you or your children have or will develop a genetically caused disease or condition. Some types of genetic changes are present in only some cells, like cancer tumor cells, and cannot be passed down. A genetic test also includes a study of your DNA. The genetic test that will be performed in this research study is: sequencing of oral brush samples for genetic biomarkers associated with head and neck squamous cell carcinoma.

You may want professional genetic counseling before you sign this consent form.

A positive test result tells a person that they may have a greater risk of having or developing the disease or condition being tested for. If you join this study and have a positive test result, you may want independent testing, to consult your physician, or to have genetic counseling.

III. What are the risks of taking part in this research study?

There may be some risks and discomforts in taking part in this study. These are the ones we know about now:

Privacy Risks: There is the risk that there could be computer security breaches that could reveal your identity. There may be the risk that data about you may become public and could be used by employers or law enforcement agencies. These privacy risks are described in greater detail below.

Metformin: Metformin is a widely used oral medication for the treatment of patients with pre-diabetes and type 2 diabetes and has a well-established safety profile. However, its use—particularly in non-diabetic populations or individuals with comorbidities—carries certain risks:

- **Gastrointestinal Effects:** The most common side effects include nausea, diarrhea, abdominal discomfort, flatulence, and a metallic taste. These symptoms are typically mild and self-limited but may affect adherence.
- **Vitamin B12 Deficiency:** Long-term metformin use has been associated with decreased absorption of vitamin B12, which may lead to deficiency and, in rare cases, anemia or neuropathy.
- **Lactic Acidosis (Rare but Serious):** Metformin carries a rare risk of lactic acidosis, a potentially fatal metabolic complication characterized by elevated blood lactate levels. The risk is increased in patients with renal impairment, hepatic dysfunction, dehydration,



or other conditions associated with hypoxia.

- Hypoglycemia: Although uncommon in non-diabetic individuals and when used as monotherapy, hypoglycemia may occur, especially if combined with other glucose-lowering agents or prolonged fasting.
- Allergic Reactions: Hypersensitivity reactions, though rare, may include rash, pruritus, or in severe cases, anaphylaxis.

Naproxen: Naproxen is a non-steroidal anti-inflammatory drug (NSAID) commonly used for pain and inflammation. While generally well tolerated, its use is associated with several important risks, especially with long-term administration:

- Gastrointestinal Toxicity: The most significant risk includes gastrointestinal irritation, ulceration, bleeding, and perforation. These events can occur without warning symptoms, particularly in individuals with a prior history of ulcers or GI bleeding.
- Cardiovascular Risk: NSAIDs, including naproxen, may increase the risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, particularly with prolonged use or in individuals with preexisting cardiovascular disease.
- Renal Effects: Naproxen can cause renal injury, including acute kidney injury and worsening of preexisting renal insufficiency. Patients with impaired renal function or those taking concomitant nephrotoxic drugs are at increased risk.
- Hepatic Effects: Elevations in liver enzymes and, rarely, hepatotoxicity, have been reported with NSAID use.
- Hypersensitivity Reactions: NSAID-induced hypersensitivity can manifest as urticaria, asthma exacerbation, angioedema, or anaphylaxis. Naproxen is contraindicated in individuals with NSAID hypersensitivity syndromes.
- Hematologic Effects: NSAIDs may impair platelet aggregation and prolong bleeding time. Caution is warranted in patients with bleeding disorders or those on anticoagulant therapy.
- Other Adverse Effects: May include dizziness, headache, skin rash, tinnitus, and, rarely, aseptic meningitis.

Pregnancy-Related Risks: Metformin and naproxen are not approved for use in pregnancy for cancer prevention, and their safety in this context has not been established. Therefore, exposure to either study drug during pregnancy may pose unknown risks to the developing fetus.

- Metformin: Although metformin is commonly used to treat gestational diabetes and is not teratogenic in animal studies at doses several times higher than those used in humans, its effects on fetal development in non-diabetic patients—particularly when used for cancer prevention—are unknown. There may be theoretical risks to fetal growth and development, especially in the setting of unstudied indications.
- Naproxen: As a non-steroidal anti-inflammatory drug (NSAID), naproxen is contraindicated in the third trimester of pregnancy due to the risk of premature closure of the fetal ductus arteriosus, oligohydramnios, and other adverse fetal outcomes. Use during the first and second trimesters may also be associated with increased risk of miscarriage or other complications.



- Lactation: Both metformin and naproxen may be excreted in breast milk. The potential effects on a nursing infant are unknown, and breastfeeding is therefore not permitted during study participation.
- Contraceptive Requirements: Due to these potential risks, all participants of reproductive potential will be required to use adequate contraception during the study period and for a defined time after discontinuation of the study drug (per protocol and/or regulatory guidance). Acceptable methods include:
 - Hormonal contraceptives
 - Intrauterine device (IUD)
 - Barrier methods (condoms with spermicide)
 - Abstinence
 - Sterilization (participant or partner)
- Pregnancy Testing: Female participants of childbearing potential will undergo screening and periodic pregnancy testing during the study. Any participant found to be pregnant before or during the study will be immediately withdrawn from the study and referred for appropriate medical care. Pregnancy during the study will be reported to the IRB and regulatory authorities as required. Women of childbearing potential will be asked to use a reliable form of contraception or to abstain from sexual activity for the duration of the study, including the safety monitoring window following the drug intervention. Acceptable birth control methods will be clearly reviewed with each participant, and may include hormonal contraception, intrauterine devices, or barrier methods used consistently. Study staff will confirm understanding of these requirements at enrollment and reinforce them at each study visit to ensure participant safety.

Venipuncture: Potential risks associated with venipuncture include discomfort or pain, ecchymosis, bleeding, nerve damage, phlebitis, and infection at the needle insertion site. Additional risks include lightheadedness and a vasovagal response.

Oral Biopsy: An oral lesion biopsy is a minor surgical procedure where a small piece of oral mucosa is removed (approximately the size of a pencil eraser) after it has been numbed with local anesthesia. The biopsy will be done by staff with special training as a licensed otolaryngologist physician or an oral and maxillofacial surgeon. To prevent infection the biopsy will be done with sterile equipment. Prior to biopsy, we will ask for current complete blood count results (from the previous month if counts are stable) to assure platelet counts are sufficient. This will be pertinent in FA participants before bone marrow transplantation (BMT); in participants post-BMT this will be less of a concern. During the injection of the numbing medicine, participant may experience a sensation of burning, like a bee sting, though this will last only seconds. They may feel pressure or tugging while the biopsy is being performed. They may experience soreness at the biopsy site during healing. Rarely, a local wound infection may occur at the site of biopsy.

Brushing: Overall, brush biopsies are well-tolerated and are not associated with severe side effects apart from a mild bleeding potential and some soreness after the brush biopsy. We will question participants regarding a bleeding tendency during tooth brushing.

Other risks:



- You may be upset to learn that you have a greater chance of having a disease or condition. Even if genetic tests show that you do not have a greater risk of disease, you may still be upset if you know that others in your family have that higher risk of disease. When genetic tests become available, you may want to have genetic counseling or a talk with your own doctor.
- Genetic tests may show information that has nothing to do with the research study. For example, when parents and children are both tested, the tests may show if the parents are the biological parents of the child. If we learn this information from these tests, you will not be told.

There may be other risks and discomforts that we do not know about now, but we will tell you if any new information is discovered that might affect your decision to participate or remain in the study.

IV. What are the alternatives to participating in this research study?

At the present time, the researchers do not know of any other procedures or treatments for cancer prevention in Fanconi anemia. The alternative to participating in this study is not to participate.

V. What are the benefits of taking part in this research study?

The benefits you might expect from taking part in this research study are:

- You may find out during the research study that the metformin and/or naproxen is helpful to you. This study includes procedures/therapies that may change the treatment you would otherwise receive, for example by showing a benefit from metformin and/or naproxen, or by showing that those medications do not provide the expected benefit.
- You may learn during participation whether the study helps you directly or not, for example if we learn that your number of oral lesions is reduced.
- There may be no direct benefit to you. Instead, others may benefit in the future from what we learn from this study.

VI. Who will be able to see the information learned about you in this research study?

We will keep your personal information private and will do our best to keep this information confidential. We will listen to what you say about what we may do with this information, and we will follow the law. For example, by New York State law, the RUCRC must inform the New York State Department of Health if we find that you have a reportable communicable disease, such as a viral disease like COVID-19, or a sexually transmittable disease, like chlamydia, hepatitis, gonorrhea, syphilis, and HIV-1. Also, the researchers must report to the authorities if



they believe that child abuse or neglect has happened, or to prevent serious harm to you or others.

At the University of Minnesota site, we will not ask you about child or vulnerable adult abuse, but if you tell us about child or vulnerable adult abuse, we may be required by law to report to authorities. Communicable, infectious, or other diseases will be reported under Minnesota's Reportable Disease Rule. Certain wounds or conditions are required to be reported under state or federal law.

During this study, only the researchers will know that your samples came from you, because your stored samples will be identified only by a special code instead of your name. As a result, others who study your samples will not know that they came from you and will not be able to figure out that they came from you. For example, the data received by sponsors would be identified only by a code. However, auditors and regulators from government agencies that oversee research, and people at the RUCRC and at Rockefeller University, as well as at the University of Minnesota, may see your information in the course of their duties. Staff that view data with personal identifiers have received privacy training and are required to adhere to privacy and confidentiality laws and policies.

Organizations that may inspect and copy of University of Minnesota participant information include the University of Minnesota Institutional Review Board (IRB) which is a committee that provides ethical and regulatory oversight of research, and other representatives of the University of Minnesota, including those that have responsibilities for monitoring or ensuring compliance, such as the Quality Assurance Program of the Human Research Protection Program (HRPP).

Your privacy is very important to us, and we will use many safety measures to protect your privacy. However, despite all the safety measures that we will use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Therefore, it is possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them. We may deposit your genetic data to databases/repositories available to others for research. While neither the public nor the controlled-access databases/repositories developed for this project will contain information that is traditionally used to identify you, such as your name, address, telephone number, or social security number, people may develop ways in the future that would allow someone to link your genetic or medical information in a database/repository back to you. For example, someone could compare information in one database/repository with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you. Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or that person's blood relatives. Moreover, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a blood relative) carry a genetic disease or that your biological parentage differs from what it had previously been understood to be. All confidential information, inclusive of genetic diseases and biological parentage, will be



guarded and would be disclosed only as legally required under the applicable law.

We are committed to respecting your privacy and keeping your personal information confidential. When choosing to take part in this study, you are giving us permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule or what you may know as “HIPAA”) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the separate HIPAA Authorization form that we have provided and discussed. The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

If the researchers publish the results of this study, they will not mention your name or other information that could identify you.

Federal law mandates that both interventional and observational clinical trials be registered at <http://www.ClinicalTrials.gov>. Interventional studies are those in which the research participants are assigned by the investigator to a treatment or other intervention, and their outcomes are measured. Observational studies are those in which individuals are observed and their outcomes are measured by the investigators.

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

Genetic Information Nondiscrimination Act

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal in the United States of America for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. For participants at Rockefeller, additional information is available in the RUCRC Participant Handbook

There may also be privacy risks that we have not foreseen.

VII. What are the payment arrangements?

There is no cost to you for the research center visits, lab testing, study procedures or drugs involved in this study. Travel costs to the study site will be re-imbursed partially or fully.

If you decide to participate in this study, you will be compensated for completing the following activities at the RUCRC or at the University of Minnesota:

Blood draw - \$25

Skin biopsy - \$50

Oral biopsy - \$50



The maximum compensation if participants undergo all possible procedures for the duration of the study is \$450. The off-site labs will be paid via voucher but will not have additional compensation.

For participants at Rockefeller, payment will be made to participants who are eligible for and want to receive payment and who fill out a brief form with tax identification information from The Rockefeller University Finance Office. Your information will remain confidential unless required to be disclosed by federal, state, or local laws. If you do not want to complete the form, you can still participate in the study but will not be eligible for compensation.

If research using your samples helps develop a drug or another product that is sold to the public, the drug company, the Rockefeller University, and the Rockefeller University researcher may share in some of the profits. For example, a cell line produced from your samples could be used to make a product for sale. There are no plans to pay you any money resulting from such discoveries. However, by signing and dating this form, you do not give up any rights you may have.

For participants at the University of Minnesota, payment will be made using a pre-paid debit card called Greenphire ClinCard. It works like a bank debit card. We will give you a debit card and each time you receive a payment for participation in this study, the money will be added to the card after each completed visit.

You may use this card at any store that accepts MasterCard or you can use a bank machine to remove cash. However, there may be fees drawn against the balance of the card for cash withdrawals (ATM use) and inactivity (no use for 6 months). We will give you the ClinCard Frequently Asked Questions information sheet that answers common questions about the debit card. You will also receive letters with additional information on how you can use this card and who to call if you have any questions. Be sure to read these letters, including the cardholder agreement, for details about fees.

The debit card system is administered by an outside company. The company, Greenphire, will be given your name, address, date of birth, and social security number. They will use this information only as part of the payment process. Greenphire will only need your social security number if the payment exceeds \$1999. Greenphire will not receive any information about your health status or the study in which you are participating.

Additionally, you will have the option to receive updates related to appointment reminders and payment reminders and updates via text message and email message (Standard text messaging rates will apply). You will have the opportunity to opt-in to receive these messages, you are not required to provide your cell phone or email address to be enrolled in the study or use a ClinCard. If you choose to receive messages and decide at a later date that you want to stop these messages, you will have the ability to opt-out. If you choose to receive any communications via texts or emails, you will be asked to sign a separate form.

Payment you receive as compensation for participation in research is considered taxable income. If payment to an individual equals or exceeds \$2000 in any one calendar year, the University of



Minnesota is required to report this information to the Internal Revenue Service (IRS). Research payments to study participants that equal or exceed \$2000 during any calendar year will result in a FORM 1099 (Miscellaneous Income) being issued to you and a copy sent to the IRS.

VIII. What happens if you don't want to stay in this study or your participation is ended?

You can choose if you want or do not want to be part of this study. If you do not join, there is no penalty, and no one will hold this against you. You may change your mind and stop taking part in this study at any time, and this will not be held against you. Information about you up to the time you stop participating in the study may remain a part of the study.

During this study, the researchers may learn new information that might make you change your mind about whether you want to stay in the study. You will be given that information promptly.

If you decide to join the study now but later want to stop, you should let the researcher know. The way to let us know is by contacting us at:

For participants at Rockefeller University: (212) 327-7850 (Dr. May)

For participants at University of Minnesota: (612)-625-6976 (Dr. Uppgaard)

If you stop taking part in the study, this is what may happen: You may be encouraged to return for an early termination visit to ensure your safety and welfare. The procedures that may occur during an early termination include return study drug, physical examination, and safety labs. There is no obligation to continue the study, and you may stop participation at any time. Stopping the study does not affect your medical care or your ability to participate in future research studies.

The researchers may stop you from continuing to take part in this study, even if you do not choose to stop being in it. You may be asked to leave the study if: you have a severe adverse event related to a study drug, you have a new cancer diagnosis or other medical problem that causes an unacceptable increase in the risk of study participation.

If you stop or if you cannot finish the study for any reason, we will pay you for the part of the study that you have finished.

IX. Whom do you call if a medical problem results from this research study?

If you believe that this study has led to a medical problem, you should call the researcher listed below right away. The researcher will help you get appropriate, available medical care.

If you are a participant at Rockefeller University, contact:

Name: Francis May, MD

Phone No.: (212) 327-7850

Email: fmay@rockefeller.edu



If you are a participant at the University of Minnesota, contact:

Name: Rachel Uppgaard, DDS

Phone No.: (612) 625-6976

Email: uppg0003@umn.edu

The Rockefeller University does not plan to pay for medical care that you may have as a result of taking part in this study at the RUCRC. However, you do not give up any rights you may have to seek compensation by signing and dating this consent form.

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company. If you think that you have suffered a research related injury, let the study physicians know right away.

X. Whom do you contact if you have questions about the research study?

Please ask as many questions as you want about this research study and this consent form. If you agree to take part in this study and have questions later, contact the following researcher:

If you are a participant at Rockefeller University, contact:

Name: Francis May, MD

Phone No: (212) 327-7850

Email: fmay@rockefeller.edu

If you are a participant at the University of Minnesota, contact:

Name: Rachel Uppgaard, DDS

Phone No.: (612) 625-6976

Email: uppg0003@umn.edu

If you have any concerns about your experience while taking part in this research study, you may contact The Rockefeller University Institutional Review Board (IRB) Office at (212) 327-8410, or the Office of Clinical Research at (212) 327-7396.

For participants at University of Minnesota: To share feedback privately with the University of Minnesota Human Research Protection Program (HRPP) about your research experience at University of Minnesota, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team
- You cannot reach the research team
- You want to talk to someone besides the research team
- You have questions about your rights as a research participant
- You want to get information or provide input about this research



The University of Minnesota HRPP may ask participants at their site to complete a survey that asks about their experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous. If you are not asked to complete a survey, but you would like to share feedback, please contact Dr. Uppgaard or the University of Minnesota HRPP.

XI. Consent to the use, storage and sharing of your samples and other data for separate research studies

The scientific value of your samples and the information obtained from them is greatly increased if we can share them with other scientists at universities and pharmaceutical or technological companies worldwide. Your samples and information will be used for biomedical research including genetic analyses. You will not be provided with details of any specific research studies or their purpose. In general identifiers will be removed from the identifiable private information or identifiable biospecimens. Thereafter the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative. The genetic information obtained from your DNA is called genotype. The information about your disease condition and the physiology of your cells is called phenotype. We may:

- store, use, and share for many years your biospecimens, materials or information derived from them, and information including genotype and phenotype data*, and other data collected in this study with other investigators at Rockefeller and elsewhere, possibly worldwide, and including pharmaceutical and technology companies, sample and/or data banks/repositories for separate studies for many years. Your biospecimens will either be stripped of information identifying them as yours or coded (we will hold the key to the code) so that they cannot be identified as having come from you. Other data related to your biospecimens, but that does not identify you, may accompany the specimens; and
- put anonymous data information from the analyses in a completely public database, available to anyone on the Internet; and
- put your coded genotype and phenotype* medical data information and data information from more detailed analyses of your coded samples in a National Institutes of Health (NIH) controlled-access database/repository. The information in this database/repository will be available only to qualified researchers from academic institutions and commercial organizations, both domestic and foreign who have received approval from an NIH Data Access Committee.

* The genetic information obtained from your DNA is called genotype. The information about your disease condition and the physiology of your cells is called phenotype.

Any time in the future, you may withdraw your consent to use any samples that have not already been used in research or shared. If you withdraw your consent, the remaining unused samples will be destroyed, unless the samples cannot be identified as having come from you. Data generated using your samples will continue to be used.



We realize that some people may not want to have their samples and/or data stored and shared with others and if that is your feeling, then you should not participate in this study.

XXI. May we have permission to contact you about future studies?

For participants enrolled at Rockefeller: May we contact you by phone or email to find out if you are interested in hearing about new research studies? (We will not share your contact information for any other purpose). Contact would be made by the staff of the Rockefeller Clinical Research Support Office for recruitment. If you decide at any time that you no longer want to be contacted, please tell us, and we will no longer attempt to contact you.

Would you like us to contact you about future research studies?

Please add your initials on the line next to your choice:

Yes _____ No _____

If you say "no" to this question, this will not affect your participation in this study.

AGREEMENT TO PARTICIPATE -- SIGNATURES REQUIRED

I have read this consent form, and my questions have been answered.

A copy of this consent form will be given to you. Please keep a copy of the form as it contains important information that you may wish to refer to during the research study and afterwards.

I hereby voluntarily consent to take part in this research study.

Name of the Study Participant (Print) _____

Signature of Study Participant

Date (To Be Filled in by Study Participant)



Adult not legally capable of giving consent

Name of the Study Participant (Print) _____

Name of Legal Representative (Print) _____

Signature of Legal Representative

Date (To Be Filled in by Representative)

- Documentation, such as a health care proxy, showing authorization to act as a legal representative, is attached.



Protocols Involving Children

I hereby voluntarily consent to have my child take part in this research study.

Name of Child (Print) _____

Name of Parent or Legal Guardian (Print) _____

**Signature of the Parent or Legal
Guardian**

**Date (To Be Filled in by Parent or Legal
Guardian)**

Name of Parent or Legal Guardian (Print)

**Signature of Parent or Legal
Guardian**

**Date (To Be Filled in by Parent or Legal
Guardian)**



Protocols Involving Pregnant Parents and Fetuses

I hereby consent, as the pregnant parent, to take part in this research study.

Name of Pregnant Parent (Print) _____

**Signature of Pregnant Parent
Parent)**

Date (To Be Filled in by Pregnant

Signature of the Person Conducting the Informed Consent Discussion

I have explained the research protocol and this consent form to the participant and have answered the participant's questions about this research study and/or the consent process.

Name of Person Discussing Consent (Print)

Signature

Date