Fanconi Anemia
RESEARCH FUND, INC.

Deutsche Fanconi-
Anämie-Hilfe e.V.

APPROVED
AS MODIFIED
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WIRB®

CONSENT to RESEARCH

TITLE: Reducing the burden of squamous cell carcinoma in Fanconi anemia

PROTOCOL NO.: FARF-DE-001-2013
WIRB® Protocol #20130937

SPONSOR: Fanconi Anemia Research Fund

INVESTIGATOR: Amy E. Frohnmayer, MA
Suite 201
1801 Willamette Street
Eugene, Oregon 97401
United States

SITE(S): Camp Sunshine
35 Acadia Road
Casco, Maine 04015
United States

STUDY-RELATED PHONE NUMBER(S): Amy E. Frohnmayer, MA
541-687-4658 (Office Hours)

If you are serving as a guardian or are providing parental permission for a child in this study, the terms "you" and "your" refer to the person for whom you are providing consent or parental permission.

This consent form may contain words that you do not understand. Please ask the study staff to explain any words or information that you do not clearly understand. You may print an unsigned copy of this consent form to think about or discuss with family or friends before making the decision whether or not to participate.

SUMMARY

This research study is designed for persons with Fanconi anemia. You are being invited to participate in a research study to reduce the burden of Squamous Cell Carcinoma (SCC) in Fanconi anemia (FA) through improved detection, characterization and long-term prevention.

The purpose of this consent form is to help you decide if you want to be in the research study. Please read this form carefully. To be in a research study you must give your informed consent. "Informed consent" includes:

- Reading an unsigned copy of this consent form and keeping it for your record
- Asking questions to the investigator or staff about anything that is not clear, and
- Taking the time to think about it and to talk to family or friends before you make your decision.

You should not join this research study until all of your questions are answered.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- You are free to say yes or no, or to drop out after joining. The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.
- Any data you contribute about yourself like your health data, your medical records, your genome, etc., may become part of the research record and will be looked at and/or copied by the sponsors of this study, selected staff or partners and with government or regulatory agencies for auditing purpose in this country or abroad. You also have the option to authorize sharing your de-identified data (without your name) with other groups for research purposes.

After reading and discussing the information in this consent form you should know:

- Why this research study is being done;
- What will happen during the research;
- What device or procedures will be used;
- Any possible benefits to you;
- The possible risks to you;
- The other medical procedures, drugs or devices that could be used instead of being in this research study; and
- How problems will be treated during the study and after the study is over.

PURPOSE OF THE STUDY

The purpose of this study is to reduce the burden of Squamous Cell Carcinoma (SCC) in Fanconi anemia patients through early detection, characterization and long-term prevention. A secondary goal is to create large datasets of FA health data that are easier to re-use for future analysis, to stimulate collaborations and innovation within FA scientific research and to allow any participant to play an active role in the research process.

FA patients have higher risks of developing abnormal lesions in the oral cavity (mouth) and they need to have their mouths and throats examined by a specialist regularly. Not all lesions are abnormal, but when experts find suspicious lesions or visible abnormalities they need to be removed or treated as soon as possible. However, even careful visual screening for lesions can miss some early-stage abnormalities that may develop into serious health problems later. Another way to screen lesions for abnormalities is to softly brush small amounts of cells from the oral cavity and to test the cells for the presence of abnormal DNA or cell components. In a previous study with a small number of participants this method seemed effective for early detection and monitoring of oral lesions. However, we do not know if this method is suitable to trace early stages of cancer in FA individuals as well.

The current study aims to inform FA individuals and their families of the risks of oral and oropharyngeal Squamous Cell Carcinoma; to collect, test and analyze brush samples from participants with follow-up over time; to determine the value of novel assay (new testing) methods in the early detection of SCC in FA; to provide materials and to stimulate research collaborations and innovation, and ultimately to reduce the burden of SCC in people with FA.

The experimental components of this study are:

- A health questionnaire
- Non-invasive oral cavity screening: photographs and maps of oral lesions
- Sample collection with self-administered soft-brush biopsy procedure
- Cellular and molecular analysis of samples
- Report of cytological results of visible lesions to individuals and their treating physicians if applicable
- Optional additional sample collection for research and methods development
- Optional transfer of de-identified data onto a centralized data repository (Synapse) to be used in future research.

While we believe that promoting research is crucial to the rapid advancement of scientific and medical knowledge, we also recognize that it carries a unique set of potential risks and considerations for participants. This document is designed to help

you understand those risks and to make an informed choice about whether to participate in this study.

PROCEDURES

In order to preserve your privacy, you will be given a personal random code to be used instead of your name on all study materials, samples, photographs etc. This unique code cannot be used to directly re-identify you.

- **Step 1: Questionnaire**

We will ask you to fill out a health questionnaire to determine your overall health and your exposure to environmental risk factors. You'll be asked for personal and health-related information. We may ask to review your medical records, so we can learn about previous treatments and how you have been doing in the past. Some of the questions may be sensitive. If a question makes you feel uncomfortable, you may choose not to answer.

- **Step 2: Non-invasive oral cavity screening**

We will visually inspect your mouth for lesions, take photographs of the visible lesions, and map the lesions on an individual oral cavity drawing/map. The photographs will be centered on the oral region below the eyes and will not contain facial features that can easily identify you.

- **Step 3: Sample collection**

We will guide you to use little brushes to carefully swab away small amounts of material from multiple places in your mouth. This is minimally invasive but generally painless. The brush containing the sample will be placed on a tube labeled with your unique participant's code and sent to laboratories for analysis. Your name will not appear on any samples collected.

- **Step 4: Data analysis and reporting**

The samples brushed for the LOH analysis (LOH = loss of heterozygosity) will be tested for specific early pre-cancerous markers. Because this technique is not a validated test, you will not receive the results of this analysis. The samples brushed from areas with visible lesions in your mouth will be analyzed via conventional cytology to look at the shape and morphology of cells. In case they look suspicious, DNA cytometry will be performed to look at the DNA and cell division pattern. We will report the results of the cytological analysis to you (your parents if you are a minor) as well as to your

local treating physician so that future action can be taken if needed. Leftover samples will be stored for future analysis at the laboratories.

RISKS AND DISCOMFORTS

The soft brush is minimally invasive as it collects material from multiple areas in the mouth. It is generally painless but it may give a tickling sensation. You may have some redness of the brushed area, which disappears within a few hours or 1 to 2 days. In a European study, less than 10% of participants with visible lesions reported some slight pain and bleeding of the brushed lesions for a couple of minutes. Longer lasting bleedings, swelling or infections cannot be excluded but have not been observed so far.

If you have had unusual gum or nose bleeding or bruising in the past two weeks or if your platelet count is less than 20,000, we recommend that the sample collection be done at a local dental practice or hospital.

Receiving results from the cytology and DNA cytometry tests may cause emotional stress. The test results will need to be discussed with your local ENT doctor who solely can diagnose malignancy with the help of a classical scalpel biopsy.

To respect your privacy, information that can directly identify you, such as your name or phone number, will be removed from the research data. However, even with removal of this information, it is sometimes possible to re-identify an individual given enough cross-reference information about him or her. This risk, while very low, should still be contemplated prior to enrolling.

There may be side effects that are not known at this time.

NEW INFORMATION

You will be told about anything new that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

BENEFITS

You may not benefit directly from your participation in this study.

We hope the information we learn from this study will help people with Fanconi anemia in the future. In particular, we hope that early diagnosis of suspicious oral lesions will allow individuals to seek earlier treatment and potentially lead to increased survival. The characterization of genetic changes in malignant oral lesions

could result in improved prevention, patient care and/or therapy for these lesions. Sharing information and improved communication between scientists, local physicians and FA participants could stimulate further cooperative research in FA.

COSTS

There are no costs to participate in this study.

PAYMENT FOR PARTICIPATION

You will not be compensated for your participation in the study. Neither you nor your heirs will receive financial or any other benefits from any discoveries made using the information and/or specimens that you provide.

ALTERNATIVE TREATMENT

This is not a treatment study. Your alternative is not to participate in this study.

CONFIDENTIALITY

With your consent, your treating physician may give information from your medical records to the study sponsor. Your medical records will remain confidential and will only be reviewed by the sponsor and the study staff for this study and with your approval. Your medical records may be also shared with the U.S. Food and Drug Administration

(FDA) and the Western Institutional Review Board (WIRB®)

Photographs will be centered on the lesions. For instance, photographs of oral lesions will focus on the oral region, below the eyes, and will not contain facial features that can easily identify you.

A unique code identifier will be used in place of your name on all material collected for analysis and on the research data.

Total confidentiality cannot be guaranteed because of the need to give information to these parties. The results of this research study may be presented at meetings or in publications. Your identity will not be given out during those presentations.

COMPENSATION FOR INJURY

THIS STUDY DOES NOT PROVIDE ANY COMPENSATION, HEALTH OR MEDICAL CARE TO PARTICIPANTS.

There is no particular physical or health-related risk due to participating in this study.

If you are injured or get sick as a result of being in this study, call the study investigator immediately. The study investigator will help coordinate emergency medical treatment. Your medical insurance will be billed for this treatment. The sponsor will not pay charges that your insurance does not cover. No payment is available from the study sponsor.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

To withdraw from this study, contact the investigator Amy Frohnmayer by e-mail study@fanconi.org or call the Fanconi Anemia Research Fund Office at 1-541-687-4658.

The study doctor or study sponsor may stop your participation in this study without your consent at any time and for any reasons.

SOURCE OF FUNDING FOR THE STUDY

The sponsor, **Fanconi Anemia Research Fund and Deutsche Fanconi-Anaemie-Hilfe**, will pay for this research study.

QUESTIONS

Contact Amy Frohnmayer by e-mail study@fanconi.org or call the Fanconi Anemia Research Fund Office at 1-541-687-4658 for any of the following reasons:

- If you have any questions about this study or your part in it, or
- If you have questions, concerns or complaints about the research.

If you have questions about your rights as a research participant or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120

Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who independently review research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

DONATING ADDITIONAL SAMPLES FOR OTHER RESEARCH

We propose to take additional samples for other research in Fanconi anemia

A saliva sample to assess the presence of known molecules (DNA and proteins) that correlate with the progression to malignancy in non-FA individuals.

A second brush biopsy to study the specific bacteria (microbiome) present in your mouth.

Your unique code identifier will be used in place of your name on these samples. You and your doctor will not receive a report about this research. The result of this research will not affect your care.

You do not have to contribute these additional samples to participate in the primary research study. You are free to say yes or no.

Do you agree to contribute additional samples?				
Saliva:	(Circle one):	**YES**	**NO**	Initials
Date:				
Second Brush Biopsy:				
(Microbiome)	(Circle one):	**YES**	**NO**	Initials

After any of your samples have been tested, there may be some samples left over. We would like to ask your permission to donate these leftover samples for future research and/or methods development. This may include genetic research and/or research on other health problems and/or research conducted in non-profit or for profit companies. You and your doctor will not receive a report about this research.

The result of this research will not affect your care. You will not receive payment for donating additional samples for research.

You do not have to donate your samples for research. You are free to say yes or no.

Do you agree to donate your leftover samples to research?				
(Circle one):	**YES**	**NO**	Initials	Date:

USE OF DATA FOR FUTURE RESEARCH

Several databases are available to help researchers understand different diseases. These databases contain information and other data helpful to study diseases. As part of this study we would like to include your research data into these databases. Your data may benefit future research.

All your personal information will be removed. Your name, address, etc, will not be in the database. Your unique code identifier will be used in place of your name when your data is released onto these databases. The data will be made available to selected database users who have agreed to specific terms and conditions including using the data in an ethical manner, to do no harm and not attempt to re-identify or re-contact you.

Although you can withdraw from the study at any time, you cannot withdraw the de-identified data that have already been distributed through research databases.

The main risk of donating your de-identified data to a centralized database is the potential loss of privacy and confidentiality in case of public disclosure due to unintended data breaches, including hacking or other activities outside of the procedures authorized by the study. In such a case, your data may be misused or used for unauthorized purposes by someone sufficiently skilled in data analysis to try to re-identify you.

Is it OK if we send your de-identified research information, including photographs and unnamed health-related information to one or more databases for future research?				
(Circle one):	**YES**	**NO**	Initials	Date:

CONSENT

Consent and Assent Instructions:
The consent form must be signed by participants 15 years and older and by a parent who provides permission for their child under 18. Verbal assent is required for participants aged 7-14 years using the assent section below.

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

By signing this consent form I have not given up any of my legal rights.

	I have read about the uncertainty and risks of this research.
	I consent to provide tissue samples to this study.
	I authorize the use and disclosure of my health information to the parties listed in the separate HIPAA Authorization section.

All boxes must be checked to create consent.

_____

Participant (age 15+)/ Printed Name, Signature, Date

_____

Parent or legal guardian/ Printed Name, Signature, Date

ASSENT For Participants Ages 7 – 14:

Person conducting the assent discussion and a parent who provides permission for their child 7 to 14 must sign the assent section below.

Statement of person conducting assent discussion:

1. I have explained all aspects of the research to the participant to the best of his or her ability to understand.
2. I have answered all the questions of the participant relating to this research.
3. The participant agrees to be in the research.
4. I believe the participant's decision to enroll is voluntary.
5. The study staff agree to respect the participant's physical or emotional dissent at any time during this research when that dissent pertains to anything being done solely for the purpose of this research.

_____

Person Conducting Assent Discussion/ Printed Name, Signature, Date

Statement of Parent or Guardian:

My child appears to understand the research to the best of his or her ability and has agreed to participate.

_____

Parent or legal guardian/ Printed Name, Signature, Date

HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

TITLE	**Reducing the burden of Squamous cell carcinoma in Fanconi anemia**
SPONSOR(S)	**Fanconi Anemia Research Fund** **Deutsche Fanconi-Anaemie-Hilfe**
INVESTIGATOR(S)	**Amy Frohnmayer, MA**

State and federal privacy laws protect your personal health information. The purpose of this form is to give your permission to use, create or share your health information to do the research named above.

What information may be used and given to others?

Any personal information you provide or authorized such as information from your medical or other health records, photographs of oral lesions, oral map, responses to study questionnaires and some analysis results will be included in your research record.

Who may use and give out information about you?

By signing this form you are giving permission to your treating physician or designated organizations to disclose your personal health information to the study sponsor, investigators, study coordinators and study staff to do the research described above. Some people or organizations may need to look at your research records for quality assurance or data analysis.

Who might get this information?

Study information collected about you will be given to the study sponsor, investigators, study coordinators and study staff. Information generated during this research may also be shared with your designated treating physician. "Sponsor" means any persons or companies worldwide that are working for or with the sponsor, or are owned by the sponsor.

Study information may be given to governmental agencies in the US and other countries where the study may be considered for approval. Medical records which identify you and the consent form signed by you may be looked at and/or copied for research or regulatory purposes by:

- The US National Institute of health, National Cancer Institute, Office for Human Research Protection, and other agencies as required,
- Governmental agencies in other countries, and
- Western Institutional Review Board® (WIRB®) or other Institutional Review Board who watch over the safety, effectiveness and conduct of the research.
- Others, if the law requires

Why will the study information be used and/or given to others?

- To conduct the research and study the results
- To see if the research was done right and/or to replicate the study
- To encourage future translational research programs in FA

We will not use your personal information in any reports about this study such as scientific publications or presentations.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

May I review or copy my information?

Yes, at any time by contacting the study sponsor in writing.

May I withdraw or revoke (cancel) my permission?

Yes, but your permission will not stop automatically. You are free to decide at any time that you no longer want your data or other information to be used as part of this study. You will need to notify the study sponsor in writing. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information or research material that has already been gathered may still be used in this research.

Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission.

Expiration

This permission will expire when the purpose of the study have been met.

Signature

I agree to let my/my child's doctor and other health care providers use, create, and share health information that identifies me/my child with the Sponsor.

Name and address of doctor or Health Care Provider(s): _____

_____

_____
Participant (age 14+)/ Printed Name, Signature, Date

_____
Parent or legal guardian/ Printed Name, Signature, Date