UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

(For ILD Patients)

Study Title: Fibroblast specific inhibition of LOXL2 and TGFβ1 signaling in patients with pulmonary fibrosis.

Protocol Number:	17-23008
Version Date:	01/30/2018
Investigational Product:	Epigallocatechin-3-gallate (EGCG)
IND Number:	144120
NCT Number:	NCT03928847

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This is a clinical research study. Your study doctor(s), Harold Chapman MD, Harold Collard MD, and Jasleen Kukreja MD from the UCSF Departments of Medicine and Surgery, will explain the study to you.

Research studies include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because X-Rays of your chest show signs of lung fibrosis (scarring on your lungs) of uncertain cause and you are scheduled for a diagnostic surgery to take out a small piece of lung tissue to define the cause. The investigators want to know if epigallocatechin gallate (EGCG) which can reduce lung scarring on animals can do the same on patients with this disease. EGCG is the main component of green tea and can be obtained online as a food supplement.

Why is this study being done?

Studies from UCSF show that EGCG can block lung scarring (fibrosis) in experimental animals. The purpose of this study is to determine if EGCG will also block fibrosis promoting factors that drive scarring in humans if EGCG is given before scheduled diagnostic surgery of patients with signs of lung scarring on X-rays. Experiments will be done to test this question on otherwise discarded lung tissues. Urine samples will be obtained to measure fragments of the scar before and after EGCG treatment (the more scarring in the lung, the more scar fragments in the urine). If drug treatment reduces scar fragments in the urine, we will know that drug treatment also reduces lung scarring. EGCG is a widely used, and commercially available, dietary supplement enriched in green tea. It is hoped that the information gained from these studies will lead to the development of a new treatment approach and a larger scale true clinical trial of EGCG in lung fibrosis.

This study is being supported by federal funding from the National Institute of Health and a gift from Three Lakes Partners, a foundation devoted to developing new drugs to treat lung fibrosis disease. This disclosure is made so that you can decide if this relationship will affect your willingness to participate in this study.

How many people will take part in this study?

About 20 people will take part in this study.

What will happen if I take part in this research study?

If you agree to participate in this study, the following will happen:

Schedule of Study for ILD Patients

Procedure	Screen	Day 1	Day 14
Informed Consent	x		
Eligibility Assessment	x		
Demographic Data	x		
Medical History	x		
Age	x		
EGCG Administration		Daily	
Blood Collection		x	x
Urine Collection		x	x
Lung Tissue Collection			x

- **EGCG randomization**: If you agree, you will be randomly assigned to EGCG-treated group or untreated control group. You will get no EGCG if you are in control group. If you are in

the EGCG-treated group, four capsules of EGCG (total 600 mg) will be given to you orally, once daily, for 2-3 weeks before surgery (see Schedule of Study). You can take the capsules at ILD clinic or at home, including the early morning day of surgery.

- **Blood drawing (venipuncture):** Once at the time of the first EGCG dose and again at the time of surgery, a blood sample will be drawn at ILD clinic by inserting a needle into a vein in your arm. You will need to fast from all food and drink, except water, starting 10 hours prior to the blood draw. Participants should not drink green tea or eat green tea or cocoa product prior to the blood draw. Each sample will be approximately 3 teaspoons; a total of about 6 teaspoons will be drawn for the whole study.

- **Urine collection:** If you agree, urine specimens will be obtained at ILD clinic once at the time of the first EGCG dose and again at the time of surgery.

- **Donation of lung tissue**: If you agree, otherwise discarded lung tissues from your VATs biopsy will be transported to the Chapman Lab and processed for assays. In addition, no tissues will be removed from your body solely for the purpose of this study, and the surgical procedure for VATs biopsy will not be affected in any way by the collection of tissue samples.

- **Specimen storage**: Your specimens will be labeled with a unique identifying number and stored in a locked freezer located in the Health Science East Building at 513 Parnassus Avenue.

- **Experimental research**: Urine specimens will be processed for measurable substance indicative of disease. Blood samples will be processed and blood level of EGCG will be measured. Lung tissues will be processed for assays of proteins that are linked to lung fibrosis or single cell analysis for gene profiling (measurement of the expression of thousands of genes at once, to create a global picture of cellular function). Your specimens will be kept until it is used up or destroyed at the completion of the study. Your own tissues will not be used for commercial purposes.

- **Medical record review**: If you agree to participate, investigators will review your medical records, to gather information about your disease in an attempt to correlate your disease severity with the results of the tests that are performed on your specimens and blood in the laboratory. But as your participation is complete after the surgery there will be no further review of your medical records.

How long will I be in the study?

You will be asked to take EGCG once daily for 2-3 weeks, the time between your pre-surgical outpatient clinic visit and the day of your surgery.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely. It is important to tell the study doctor if you are thinking about stopping so any risks from the EGCG can be evaluated by your doctor. The study doctor may also stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

Can I participate if I am pregnant?

No. A urine pregnancy test will be performed for consented subjects of childbearing potential prior to the study. All potential subjects of childbearing potential will be also counselled to use appropriate contraception. We will exclude pregnant subjects from participation in the trial.

What side effects or risks can I expect from being in the study?

The following are the risks of your participation in the study. If you have questions regarding these risks, the investigators or other designated research personnel will answer these questions:

Randomization risks: You will be assigned to a treatment program by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

Adverse effects from EGCG: There is potential risk for adverse effects from oral ingestion of EGCG. Previous trials taking 800 mg EGCG per day and lasting 6 months to a year in patients noted no adverse effects. It appears mild liver transaminitis (elevated levels of liver enzymes, can be an indicator of liver disorders) may occur but this is rare and even less likely in the short duration you will take EGCG. However, liver function test (measuring liver enzymes in the blood) will be obtained at Visit 1 and Visit 2 without extra blood draw and liver function will be monitored. You should talk to your study doctor about any side effect you experience while taking part in the study.

Physical risks: The risks of venipuncture (obtaining blood with a needle) include temporary discomfort from the needle stick, bruising, and rarely, infection.

Confidentiality: Donating specimens may involve a loss of privacy, but information about you will be handled as confidentially as possible. Your name will not be used in any published reports from research performed using your specimen. The manager of the tissue bank and select tissue bank staff members will have access to information about you but they will not release any identifying information about you to researchers using your specimen. The UCSF Committee on Human Research may see information about you to check on the tissue bank. The tissue bank staff will protect your personally identifiable health information as described in this consent form.

Risk of inadequate specimens for diagnostic purposes: Providing parts of your surgically-removed tissue for research could, in rare cases, result in too little tissue being available for your doctors to make a clinical diagnosis (or complete other clinically important tests). To minimize this risk, a Pathologist (or a pathology designee) carefully evaluates every tissue specimen at the

time of surgery to decide if it can safely be provided for research. With this process in place, we believe the risk of negatively impacting your clinical care through providing tissue for research is extremely small (below 1%).

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

There is no direct benefit at present for you individually. There is the potential for improved therapy of pulmonary fibrosis progression if EGCG has the predicted biological impact and for a new non-invasive biomarker (a measurable substance indicative of disease) to track drug responses that may benefit future subjects with IPF.

What other choices do I have if I do not take part in this study?

If you choose not to participate in this study, this will not affect any aspect of your care at UCSF. You may still be asked to designate unused portions of your lung biopsy for laboratory assessment but you are under no obligation to do that as well. In any case, if you choose not to participate in this study, you will still be guaranteed exactly the same medical and surgical treatment as is appropriate for your condition.

Please talk to your doctor about your choices before deciding if you will take part in this study.

How will information about me be kept confidential?

All records will be coded and permanently kept in locked files with access limited to the study investigators. All collected specimens will be assigned a corresponding code number by the study investigators and will then be processed without knowledge of your identity. Only the UCSF investigators who are part of this study have access to the records that link this coded ID number to you during the study.

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. Your signed consent form will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the National Institutes of Health
- Representatives of the University of California

The testing developed to assess fibrosis promoting factors in your lungs are experimental and not standard clinical testing, it is not FDA approved. Therefore, the result findings cannot be interpreted as directly affecting the course of your fibrosis. Nonetheless you will be offered the opportunity to have the research results made available to you at your request. **Please note, no part of this investigation is designed to cure your condition**. The research will not change the care you receive.

Will any research-related procedures be billed to me?

The cost of Standard of Care will be billed to your insurance. The sponsor has agreed to pay for EGCG capsules and all procedures associated with this research study.

Will I be paid for taking part in this study?

You will be paid $200 for taking part in this study. You will also receive reimbursements for parking and travel-related expenses. If any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. Harold Chapman, Dr. Harold Collard, or Dr. Jasleen Kukreja, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call Drs. Chapman, Collard, and Kukreja at 415-514-1210.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, treatment will be available. The costs of the treatment may be covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to Dr. Harold Chapman about any questions or concerns you have about this study. You may call Dr. Chapman at 415-514-1210.

For questions about your rights while taking part in this study, call the office of the **Committee on Human Research**, UCSF's Institutional Review Board (a group of people who review the research to protect your rights) at 415-476-1814.

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will also be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent