

# Pine Street Foundation

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## Recruitment package, introductory letter

April 24, 2008

Hello,

We invite you to be a research volunteer, to help in the discovery of a new non-invasive test for **ovarian cancer**. If you are a woman who:

- has been newly diagnosed with **ovarian cancer** and has not yet begun treatment, or
- has **endometriosis**, or
- has **polycystic ovarian syndrome**, then...

we would like to obtain samples of your exhaled breath. We will analyze those breath samples for substances call biomarkers that may be useful in diagnosing these medical problems.

***If you are a healthy woman who would like to be a "healthy control" volunteer, you may also join this project.***

**120 women** are needed to participate in this research trial.

Our primary goal is to analyze samples of exhaled breath for molecules that could identify ovarian cancer. We will collect samples of exhaled breath using a simple noninvasive device. Those exhaled breath samples will be analyzed using both a chemical method called GC/MS and a biological method (professionally trained dogs). (Note: you will not be "sniffed" by the dogs directly. They will be sniffing the breath sample you provide, at a different location.)

***You may have heard of our prior work using dogs to detect lung and breast cancer, broadcast on CNN and the Discovery Channel.***

Our team will be the first to use analysis of exhaled breath to research the diagnosis of ovarian cancer. We expect that this work will lead to progress in the way epithelial ovarian cancer is detected and diagnosed

***It is simple and it is easy to participate. We ask only that you visit our research office, to breathe into our simple, safe, and non-invasive collection***

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***device. We will also ask you to have your doctor send us some of your medical records.***

The study will last two years, and will involve up to 4 visits to San Anselmo, California. Compensation will be provided for travel expenses.

***To learn more about this clinical research study, contact our study representatives by calling 415-407-1357.***

This research is sponsored by the Congressionally Mandated Medical Research Program. This study is being conducted by:

The Pine Street Foundation  
124 Pine Street, San Anselmo, CA 94960,  
In collaboration with the University of Maine, UC Davis,  
and UCSF

Please read this section prior to your visit,  
and if you have no other questions:

- \* sign the consent form (pages 14-15), and
- \* fill out the history questionnaire (pages 17-18), then
- \* mail or fax them back to:

Pine Street Foundation  
124 Pine Street  
San Anselmo, CA 94960  
415-485-1065

- \* and call us at 415-407-1357 to schedule your visit

**Patient Informed Consent Form**

Study approval date      October 24, 2007

Study renewal date      October 24, 2008

**The Ovarian Cancer Detection Research Project**

**Full Study Title:**

**Early Detection Of Epithelial Ovarian Cancer Using Exhaled Breath Markers: GC/FT-ICR Mass Spectrometry And Canine Olfaction**

**What is the Purpose of this Study?**

The purpose of this study is to determine if we can find chemicals in exhaled breath that may help to diagnose ovarian cancer. This kind of research has been done before with breast cancer and lung cancer. Up to 120 women will be participating in this research to help detect ovarian cancer through a simple exhaled breath test.

We are asking you to participate in this research study being conducted by the Pine Street Foundation in collaboration with the University of Maine, the University of California at Davis Medical Center, and the University of California at San Francisco. The sponsoring agency funding this study is the Congressionally Directed Medical Research Programs (CDMRP), which originated from a unique partnership among the public, Congress, and the Department of Defense. Grassroots advocacy organizations provided much of the impetus that led to this program being established in 1992.

The principal investigator for the study is Dr. Touradj Solouki (Associate Professor of Chemistry at the University of Maine). The site principal investigator at the Pine Street foundation is Michael McCulloch.

**What Happens to me and other Study Participants?**

If you agree to participate in this study, we will ask you to breathe through a plastic tube for 30 to 60 minutes. Blowing through this tube is not strenuous. The breath samples are provided at 124 Pine Street, San Anselmo. We will ask you to fill out a short questionnaire about your health history.

The breath samples which you provide will be analyzed in two ways: by chemical analysis at the laboratory of Dr. Solouki, and by a “bio-sensor” (dogs being trained to detect cancer) at the Pine Street Foundation. This research is being done using only exhaled breath samples (you will not have direct contact with the dogs in trained in this study unless you specifically request to meet them).

This study is expected to last two years. We may also contact you afterward if the study continues beyond that point.

### **Who is eligible to participate in this study?**

Women who are seeing their doctor because they have a pelvic mass which may be ovarian cancer, and/or have a high CA-125 blood test result. You should:

- (1) be 21 years of age or older
- (2) have no prior diagnosis of any cancer
- (3) live in California and close enough to our sampling station (San Anselmo) to facilitate convenient re-sampling,
- (4) be able to read and write English sufficient to provide informed consent and comply with study requirements
- (5) be willing to provide written informed consent
- (6) be willing to provide a breath sample which requires approximately 30 to 60 minutes to conduct
- (7) be a non-smoker.

You should be willing to provide a breath sample as near as possible to the time of biopsy or surgery, and prior to initiation of treatment, so as to avoid any delay in treatment by your participating in our research.

If you do not have ovarian cancer, you should:

- (1) be 21 years of age or older
- (2) have no prior diagnosis of ovarian cancer, breast cancer (including ductal carcinoma in situ),

- fallopian tube cancer, or primary papillary serous carcinoma of the peritoneum
- (3) have tested negative for BRCA1 or BRCA2 mutation (if known) OR have no first- or second-degree relative with a BRCA1 or BRCA2 mutation (if known).
  - (4) live in California and close enough to our sampling station (San Anselmo) to facilitate convenient re-sampling,
  - (5) be able to read and write English sufficient to provide informed consent and comply with study requirements
  - (6) be willing to provide written informed consent
  - (7) be willing to provide a breath sample which requires approximately 30 to 60 minutes to conduct
  - (8) be a non-smoker.

**Is there anything special I should do before visiting your research office to provide my breath sample?**

We ask that you schedule your visit for the morning, before breakfast, and that you avoid for 3 days prior to breath sampling:

alcohol intake, and the following medications or vitamin supplements:

Cox-2 inhibitor medications,  
vitamin E,  
omega-3 fatty acids,  
antioxidants,  
bromelain,  
COQ -10,  
curcumin,  
vitamin A.

**What are the Potential Benefits to Others and Me?**

There is no treatment involved in this research. While this study may have no direct benefit to you, this research may benefit others by helping us develop a new way to detect ovarian cancer in its early stages.

**What are the Risks of this Study?**

We do not believe there are any risks to you in participating in this study, aside from your time and inconvenience, and the small possibility of a breach of confidentiality and anxiety/stress related to participation in a research study.

### **Confidentiality of Your Records**

After you have filled out your questionnaire and provided us with your biopsy report, these records and your exhaled breath sample will be coded with an anonymous record number. Your confidential data will be stored in a locked filing cabinet in a locked office at 124 Pine Street. The only person with access to the master list of names will be Michael McCulloch, Research Director at the Pine Street Foundation, and his research assistant. The master list of names and your confidential records will be kept in our files for 5 years after the completion of the study.

### **Statement of Voluntary Participation**

Your participation in this study is voluntary. Participating in this study requires that you provide a breath sample, authorize your doctor to fax us your medical records, and fill out a study questionnaire. Participating in this study will not affect your current or future medical care with your physician(s). You are free to take part in, or withdraw from the study at any time. If you refuse to participate in this study, there will be no penalty or loss of benefits.

Providing a breath sample, filling out the short questionnaire, and allowing us to ask your doctor for copies of your medical records are required if you would like to participate in this study. You may participate in the study even if you do not wish for your exhaled breath sample to be used in a future research project. In a section of this form which you will see below, we will ask you below to indicate whether you give permission for us to save your exhaled breath sample for use in a future study.

If you decide to withdraw from this study, there will be no consequences to your decision. The following steps will be taken for the orderly end of your participation:

1. You will be contacted by the site principal investigator Michael McCulloch, and thanked for your participation.
2. We will discard the paper record of your name and contact information, which was to be used for subject follow-up.

3. We will discard the paper copies of your medical records, and any other documents containing any information that could identify you.
4. We will retain your anonymous breath sample, as well as your anonymous questionnaire results and anonymous diagnostic data. Your breath sample, questionnaire results and diagnostic data will have been identified only by an anonymous ID number.

**Your participation in this research study may be terminated by us if you:**

1. You call or write us telling us that you would like to withdraw from the study.
2. You do not wish to visit our research center for providing your breath sample.
3. You decide not to provide a breath sample or follow the instructions provided above what you should do before giving the sample.
4. You decide not to authorize your doctor to fax us your medical records.
5. You decide not to fill out the study questionnaire.

**Subject Payment**

You will not be reimbursed for participating in this study. However, we may reimburse you for reasonable transportation costs.

Other than medical care that may be provided and any other payment specifically stated in the consent form, there is no other compensation available for your participation in this research.

**Conflict of Interest and Investigator**

**Payment**

No physicians who may refer you to this study are being paid any bonus fees, nor are any of the healthcare providers at Pine Street Foundation, other than reasonable administrative costs. Even though no conflict of interest is expected, you may still elect to withdraw from this study at any time.

**Costs to the Subject**

There are no costs to you for your participation in this study.

### **Experimental Subject's Bill of Rights**

We are giving you a copy of the California Experimental Subject's Bill of Rights and a copy of this consent form for your own records.

### **New Findings and Study Result**

You may be told of any important new findings during the course of this study. You may also request to be informed of the results of the study at its conclusion. All significant new findings developed during the course of research which may relate to your willingness to continue participation will be provided to you.

### **Investigator's Name and Number**

You may contact Michael McCulloch, MPH, the site principal investigator at Pine Street Foundation (415-407-1357, [mm@pinestreetfoundation.org](mailto:mm@pinestreetfoundation.org), 124 Pine Street, San Anselmo, CA 94960-2674) with any questions about:

- the research,
- your rights as a research subject, or
- about a possible research-related injury.

Name and full contact information for the Principal Investigator:

Touradj Solouki, Ph. D.  
Associate Professor of Chemistry  
The Chair (2002-2005) Young Mass Spectrometrists: American  
Society for Mass  
Spectrometry (YMS - ASMS)  
5706 Aubert Hall, 373  
University of Maine  
Orono, ME 04469-5706  
Tel: (207) 581-1172  
Fax: (207) 581-1191  
E-mail: [solouki@maine.edu](mailto:solouki@maine.edu)

### **A Message for you from the Study Sponsor**

Because this research is funded by the U.S. Army, the following is made available to you:

“If you are hurt or get sick because of this research study, you can receive medical care at an Army hospital or clinic free of charge. You will only be

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treated for injuries that are directly caused by the research study. The Army will not pay for your transportation to and from the hospital or clinic. If you have questions about this medical care, talk to the sub-contracting institution's Principal Investigator for this study, (Michael McCulloch: 415-407-1357). If you pay out-of-pocket for medical care elsewhere for injuries caused by this research study, contact the sub-contracting institution's Principal Investigator (Michael McCulloch: 415-407-1357). If the issue cannot be resolved, contact the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of the Staff Judge Advocate (legal office) at (301) 619-7663/2221."

For your reference, we are providing contact information for the four closest VA hospitals to the study area. However, we cannot guarantee that you would be able to be seen at any of these facilities in a timely fashion:

San Francisco VA Medical Center  
4150 Clement Street  
San Francisco, CA 94121-1598  
Phone: (415) 221-4810 or (800) 733-0502  
Fax: (415) 750-2185

VA Palo Alto Health Care System  
3801 Miranda Avenue  
Palo Alto, CA 94304-1290  
Phone: (650) 493-5000 or 800-455-0057  
Fax: (650) 852-3228

VA Palo Alto, Menlo Park Division  
795 Willow Road  
Menlo Park, CA 94025  
Phone: (650) 493-5000

VA Palo Alto, Livermore Division  
4951 Arroyo Road  
Livermore, CA 94550  
Phone: (925) 373-4700

### **California Experimental Subject's Bill of Rights**

**Any person requested to consent to participate as a subject in a research study involving a medical experiment, or is requested to consent on behalf of another, has the right to:**

As an "experimental" or "research" subject you have the following rights:

1. Be told what the study is trying to find out.
2. Be told what will happen to you and whether any of the procedures, drugs, or devices is different from what would be used in standard practice.
3. Be told about the frequent and/or important risks, side effects, or discomforts of the research drugs, devices, or procedures.
4. Be told if you can expect any benefit from participating and, if so, what the benefit might be.
5. Be told the other choices you have and how they compare to being in the study.
6. Be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study.
7. Be told what sort of medical treatment is available if any complications arise.
8. Refuse to participate at all or to change your mind about participation after the study is started. This decision will not affect your right to receive the care you would receive if you were not in the study.
9. Receive a copy of the signed and dated consent form.
10. Be free of pressure when considering whether you wish to agree to be in the study.

If you have any general questions about the study and your rights as a research subject, you should ask the researcher Michael McCulloch at 415-407-1357.

You may also contact the Institutional Review Board responsible for the protection of the rights of research subjects during this study. Their name is Independent Review Consulting (IRC), and they can be reached during business hours at 415-485-0717.

## **Myths and Realities in Informed Consent for a Clinical Trial**

### **A Guide to Understanding Informed Consent**

If you and your physician have found a clinical trial that is of interest to you and for which you are eligible (that is, you meet requirements such as type and stage of cancer, age, treatment history, overall health, and others), you will need information in order to make a decision about whether to participate in the trial. Making a decision about participating in a research study involves understanding the potential risks and benefits as well as your rights and responsibilities. The presentation and discussion of these important issues are part of the process called informed consent. This guide will tell you what to expect during the informed consent process, explain its importance to clinical research participants, and describe how it fits into a larger system that protects the welfare of people who take part in clinical trials.

### **A Definition of Informed Consent**

You may already have experience with signing consent forms for other kinds of medical procedures, such as surgery, or for cancer treatments such as radiation or chemotherapy. However, informed consent for a clinical trial involves much more than just reading and signing a piece of paper. Rather, it involves two essential parts: a document and a process.

The informed consent document provides a summary of the clinical trial (including its purpose, the treatment procedures and schedule, potential risks and benefits, alternatives to participation, etc.) and explains your rights as a participant. It is designed to begin the informed consent process, which consists of conversations between you and the research team. If you then decide to enter the trial, you give your official consent by signing the document. You can keep a copy and use it as an information resource throughout the course of the trial.

The informed consent process provides you with ongoing explanations that will help you make educated decisions about whether to begin or continue participating in a trial. Researchers and health professionals know that a written document alone may not ensure that you fully understand what participation means. Therefore, before you make your decision, the research team will discuss with you the trial's purpose, procedures, risks and potential benefits, and your rights as a participant. If you decide to participate, the team will continue to update you on any new information that may affect your situation. Before, during, and even after the trial, you will have the opportunity to ask questions and raise concerns. Thus, informed consent is an ongoing, interactive process, rather than a one-time information session.

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## **Myth and Reality**

You may find it helpful to know some of the most common misperceptions about informed consent and clinical trials. Even if these do not represent your thinking about informed consent, they can serve as a helpful reminder of what the process is really about before you go through it.

<b>Myth:</b>	Informed consent is designed primarily to protect the legal interests of the research team.
<b>Reality:</b>	The purpose of the process is to protect you and other participants by providing access to information that can help you make an informed choice. It also is designed to make you aware of your rights as a participant.
<b>Myth:</b>	The most important part of this process is signing the informed consent document.
<b>Reality:</b>	Actually, the heart of this process is your ongoing interaction and discussions with the research team and other medical personnel—before, during, and after the trial. The document is designed to get this conversation started.
<b>Myth:</b>	My doctor knows best; he or she can tell me whether or not I should consent to participate.
<b>Reality:</b>	Your doctor is likely to be a valuable source of advice and information, but only you can make this decision. No one—not even medical experts—can predict whether a treatment, screening, prevention, or supportive care method under evaluation in a trial will prove successful. The informed consent process is designed to help you weigh all of the information and make the right choice for you or your child.
<b>Myth:</b>	Once I sign the consent form, I have to enroll and stay enrolled in the trial.
<b>Reality:</b>	That's not true. Even after you sign the form, you are free to change your mind and decide not to participate. You also have the right to leave a clinical trial at any time for any reason, without forfeiting access to other treatment.
<b>Myth:</b>	Medical personnel are busy, so I can't really expect them to keep me informed as the trial progresses or listen to my questions.
<b>Reality:</b>	The research team has a duty to keep you informed, make sure that you understand the information they provide, and answer your questions. If you ever feel that you are not getting what you need, do not hesitate to speak up. You will be given the name and phone number of a key contact person who can answer your questions throughout the course of the trial. Keep in mind that people like you are making this research possible through their willingness to participate.

**Sample Donation**

During this study you will be asked to provide exhaled breath samples. These samples will be used for research to develop a new way of diagnosing ovarian cancer and may also be used for purposes that are currently unknown. There is a chance that the samples that you are donating under this study may be used in other research studies and may have some commercial value. (If a commercial value is anticipated, that value should be clearly described at this point.) Should your donated sample(s) lead to the development of a commercial product, one of more of the investigators will own it and may take action to patent and license the product. The investigators do not intend to provide you with any compensation for your participation in this study nor for any future value that the sample you have given may be found to have. If you give us permission to retain your anonymous breath samples, anonymous questionnaire results and anonymous diagnostic data, you will not receive any notice of future uses of your sample(s). In order to participate in this research study, you will be required to provide exhaled breath samples.

**Confidentiality**

All data and medical information obtained about you, as an individual, will be considered privileged and held in confidence; you will not be identified in any presentation of the results. Complete confidentiality cannot be promised to subjects. It should be noted that representatives of the U.S. Army Medical Research and Materiel Command are eligible to review research records as a part of their responsibility to protect human subjects in research.

Please check this if you give us permission to obtain an exhaled breath sample from you for use in this research project.

Please check this if you give us permission to contact your doctor for medical records.

Please check this if you give us permission to allow us to retain your exhaled breath sample for possible use in future research projects.

Please check this if you would like us to contact you in future with the results of the study at its conclusion. We will maintain a list of people who

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give us permission. Site principal investigator Michael McCulloch will be responsible for providing you with these research results.

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\_\_\_\_\_  
Your printed or typed name

\_\_\_\_\_  
Date

\_\_\_\_\_  
Your signature

\_\_\_\_\_  
Your permanent address

## **The Ovarian Cancer Detection Research Project**

### **Full Study Title**

### **Early Detection Of Epithelial Ovarian Cancer Using Exhaled Breath Markers: GC/FT-ICR Mass Spectrometry And Canine Olfaction**

This questionnaire asks you for information related only to the objectives of this study.

Since this is first time that researchers have initiated a study to analyze samples of exhaled breath for compounds which may help us to detect ovarian cancer, we are using a new questionnaire which has not been used before in research.

This questionnaire will be identified only by your Study ID number, which will help us to protect your confidentiality.

Instructions for completing the questionnaire:

1. Please fill in Part 1 of the questionnaire before the day you come to Pine Street Foundation to provide your breath sample.
2. We will ask you to fill in Part 2 of the questionnaire on the day that you provide your exhaled breath sample.
3. You may feel free to refuse to answer specific questions, there will be no repercussions to your existing medical care.
4. The letters in the left-hand column are the question code number. You only need to answer the items in the right-hand column.

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	<b>Questionnaire Part 1: please fill out this part before you come to Pine Street Foundation to provide your exhaled breath sample.</b>	
Date	Please write the date on which you are filling in Questionnaire Part 1:	
Age	Your age:	
Ethnicity	Please circle your ethnic group: Caucasian      African American      Asian      Hispanic	
Family history 1	Do you have any sisters with ovarian cancer? No	Yes
Family history 2	Do you have any sisters or brothers with breast cancer? No	Yes
Family history 3	Did your mother have ovarian cancer? No	Yes
Family history 4	Did your mother or father have breast cancer? No	Yes
Diagnosis	Please circle if you have one or more of the following:  <div style="display: flex; justify-content: space-around; text-align: center;"> <div>ovarian cancer</div> <div>endometriosis</div> <div>polycystic ovarian syndrome</div> </div>	
Age at menopause	If you are in menopause, at what age did this happen:	
Age at first menstruation	How old were you when you began to have your menstrual periods (if you remember):	
Height	Please tell us your height:	
Height unit	Is that in feet and inches, or in centimeters? centimeters	Feet/inches
Weight	Please tell us your body weight:	
Weight unit	Is that in pounds or kilograms? kilograms	Pounds
Alcohol current	Do you currently drink alcohol?	Yes    No
Alcohol month	Please tell us how many days per month you have alcohol, on average:	
Alcohol daily	Please tell us on the days you have alcohol, how many drinks daily, on average:	
Alcohol history	Did you used to drink alcohol, but no longer do?	Yes    No
Alcohol duration	For how long did you used to drink alcohol?	
Smoking current	Do you currently smoke tobacco?	Yes    No
Smoking month	Please tell us how many days per month you smoke tobacco, on average:	
Smoking daily	Please tell us on the days you smoke, how many cigarettes daily, on average:	
Smoking history	Did you used to smoke tobacco, but no longer do?	Yes    No
Smoking duration	For how long did you used to smoke tobacco?	

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Smoking second 1	Are you now frequently exposed to secondhand smoke?    Yes    No
Smoking second 2	Were you in past frequently exposed to secondhand smoke? Yes    No
Smoking second 3	For how many years were you exposed to secondhand smoke?
Exercise	Physical activity (duration and type)
ZIP code	Please tell us your ZIP code:
Education	Please tell us the highest level of education you have completed: high school            undergraduate school            graduate college            professional/trade school
Other diseases	Please circle yes or no, about whether or not you have any of the following: chronic obstructive pulmonary disease            Yes    No periodontal disease            Yes    No rheumatoid arthritis            Yes    No asthma            Yes    No rhinitis            Yes    No diabetes            Yes    No renal disease            Yes    No cardiovascular disease            Yes    No GERD            Yes    No Dental, tooth decay, mouth infections            Yes    No
Medications	Please list all prescriptions, OTC medications you are currently taking:
Herbs and vitamins	Please list herbs and vitamins you are currently using:

After we have scheduled your study visit, please bring this section along to fill out on that day.

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	<b>Questionnaire Part 2: please fill in on the day of your breath sampling</b> <b>The following questions refer to your most recently eaten meal</b>		
Vegetarian	Are you vegetarian?	Yes	No
Beef	Did you eat beef?	Yes	No
Pork	Did you eat pork?	Yes	No
Lamb	Did you eat lamb?	Yes	No
Fish	Did you eat fish?	Yes	No
Fruit	Did you eat fruits?	Yes	No
Vegetables	Did you eat vegetables?	Yes	No
Spicy	Did you eat hot spices?	Yes	No
Sweets	Did you eat sweets?	Yes	No
Garlic	Did you eat garlic?	Yes	No
Onions	Did you eat onions?	Yes	No
Alcohol	Did you drink alcohol?	Yes	No
Coffee	Did you drink coffee?	Yes	No
Tea	Did you drink tea?	Yes	No

	<b>Questionnaire Part 3: you not need to answer these questions.</b> <b>This information will be provided by the technician who helps you</b> <b>provide the breath sample, or will come from your medical record</b>
Samples	Number of samples collected
Time	Time collected
Histology	Cellular pathology
Stage	Staging
Differentiation	Degree of cellular differentiation
BRCA 1 status	(if known)
BRCA 2 status	(if known)
Date diagnosis	Date of Diagnosis