Protocol Title: Gene Sequence Variants in Fibroid Biology

Principal Investigator: Cynthia C. Morton, Ph.D.

Site Principal Investigator: Cynthia C. Morton, Ph.D.

Description of Subject Population: Women with fibroids

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form. If you have any questions about the research or about this form, please ask us. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a copy of this form to keep.

Why is this research study being done?

The purpose of the study is to understand how fibroids (benign uterine tumors) form and develop. Specifically, current scientific research indicates that many women with fibroids may have certain genes, which predispose them to the development of fibroids. We have been searching for these genes, and have identified a number of good candidates. We want to look more closely at these candidate genes to understand the mechanism by which they contribute to the formation and development of fibroid tumors. Ultimately, we hope to use this information to design better treatment options for women with fibroids.

To achieve these goals, we want to recruit up to 200 women that are patients at Brigham and Women's Hospital to participate in our study. You are being asked to participate in this study because of your decision to have surgery (myomectomy or hysterectomy) to remove your fibroids. The scientist in charge of this study is Dr. Cynthia Morton with funding provided by the NIH (National Institutes of Health). To contact study staff regarding information about the study, administrative questions, and/or requests for withdrawal of your study materials see pages 6-7 below.

How long will I take part in this research study?

The study involves signing a consent form and filling out two questionnaires. The expected time commitment to complete this study is about 30 minutes.

What will happen in this research study?

If you agree to participate, we will ask you to fill out a single detailed questionnaire along with this consent form during your pre-surgery doctor's appointment in Obstetrics and Gynecology at Brigham and Women's Hospital. You will have approximately one week, the time between the pre-surgery appointment and the day of surgery, to decide if you wish to participate. This questionnaire should take 20-30 minutes of your time to complete if you choose to do so, and it can be mailed to the study staff using a pre-paid envelope provided with the questionnaire or brought in person to your doctor at any time prior to surgery. Since the questions on the questionnaire cover a range of personal information, it is important that you know you can skip and not answer any questions that make you too uncomfortable. If there is illegible or incomplete information on the questionnaires, we may send them back requesting you to provide the necessary information.

Upon receiving the signed consent form and completed surveys, on the day of admission for fibroid surgery in the pre-surgery area, we will collect 27 ml (about 5½ teaspoonfuls) blood and a urine sample. The blood and urine samples will allow us to maximize our chance of exploring relationships that may exist between environmental exposures and fibroids. The blood will be used to isolate your DNA as well as to study various proteins in your blood. DNA is the genetic material from which genes are made: we will use the DNA to study genes that may be associated with fibroids. All living things are made of cells. Genes are the part of cells that contain the instructions which tell our bodies how to grow and work, and determine characteristics such as hair and eye color. Genes are inherited (that is, passed from parent to child). We will use this DNA to study fibroid-associated candidate genes.

We also seek your permission to be allowed to study the fibroid tumors that you are having removed, and that are normally discarded as medical waste after your surgery. The fibroid tumors may be used to examine the chromosomes in the tumor and to isolate the RNA in the tumor. RNA is a molecule that provides the information to the cell to make proteins. A portion of the fibroid tissue will also be frozen. In addition, we will want to review the portion of your

medical records that involves your diagnosis of fibroids. This information is helpful in connecting our research results with specific medical findings. To this end, we will ask you to fill out a medical records release form, which is attached behind this consent form. Importantly, confidentiality is maintained regarding the information we collect from you. All information and samples obtained for this study are permanently stored, assigned a code, and entered into a database. No names are entered into this database, only the codes assigned to the research record. Similarly, no names or other identifiers will be used on samples to link information to a specific person. A key to the code will be kept in a separate locked file in Dr. Morton's office. Only the study investigators will have access to the key to the codes and the keys to the data files. Your samples will also not be used for unrelated research and will not be shared with others outside our research group.

Furthermore, because at this time no clinically or diagnostically relevant information may be learned from this research, the results from this study will not be shared with you. Instead, this research is a stepping-stone toward understanding the causes and biology of uterine fibroids. Therefore, it is possible that relevant general information about uterine fibroids may be learned from this study. Whenever general information is learned, a newsletter that discusses the new findings can be sent to you. If you choose to receive similar newsletters, it will be addressed to you, but no information regarding your genetic study participation or results will be in the newsletter. If you wish to receive this newsletter, initial the line marked "YES" below.

I wish to receive the Newsletter if general information is learned about uterine fibroids:

_____ **YES, send the Newsletter** Initials

_____ **NO, do not send the Newsletter** Initials

In addition, you may be contacted in the future and asked for further samples to continue research in this area. You may choose whether or not you wish to participate in additional research. If you wish to be contacted about participation in future research, initial the line marked "YES" below.

I wish to be contacted about participation in future research:

_____ **YES, contact me** Initials

_____ **NO, do not contact me** Initials

Also, as mentioned above, a portion of your fibroid tissue will be frozen. May we use this tissue for future studies that are focused on understanding the biology of uterine fibroids? If you wish to allow your tissue to be used in additional fibroid-related research, initial the line marked "Yes" below.
I wish to allow use of my tissue for future research to understand the biology of uterine fibroids:

_____ **YES, use the tissue** Initials

_____ **NO, do not use the tissue** Initials

Lastly, we have enclosed two copies of the Consent Form. Please sign and date **both** copies, and keep the **"Participant Copy"** of the Consent Form for your records. We ask that you return the other copy along with your questionnaires in the enclosed pre-paid envelope or bring it in person to your doctor at any time prior to surgery. As you have received the **"Participant Copy"** of the Consent Form, please initial the line marked "YES" below.

_____ **YES, I received a copy of this Consent Form for my records, which I have signed** Initials

_____ **NO, I did not receive a copy of this Consent Form which I need to sign for my records** Initials

What are the risks and possible discomforts from being in this research study?

An unlikely but potential risk concerns disclosure of research results. In general, information about a person's participation in a genetic study may influence insurance companies and/or employers regarding one's health status. Therefore, the following safeguards are in place to prevent unintentional disclosure. First, genetic information gained from this study does not have medical or treatment implications at this time, and no diagnostic information can be learned from the results. Therefore, neither information about your study participation nor the results of the research will be placed in your medical records. Your samples will be coded and stored permanently; the key to the code will be kept in a separate, locked file. Similarly, no results from this study will ever be released to a family member or to you, or published in a way that will identify you as a specific participant. If you choose to receive the newsletter, no remarks or statements will be made that indicate that you participated in a genetic study. Any materials mailed to you will not identify you as a patient or participant in a genetic study. Finally, by not

sharing information about your participation in this study with others, you will further minimize the risk of unintentional disclosure. Although we will make every reasonable effort to keep your participation confidential, we cannot guarantee absolute confidentiality.

A second risk is that you may feel discomfort from the personal nature of the questions on the questionnaire. Although there is a scientific purpose behind each of the questions we ask you, you may leave unanswered any questions that make you feel uncomfortable.

What are the possible benefits from being in this research study?

There are no direct benefits to you from participation in this study. It is our intention to understand the genetic basis of fibroids with the ultimate goal in mind to use this information to design better treatment options for women with fibroids.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

It is possible that we will have to ask you to drop out before you finish the study. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

What will I have to pay for if I take part in this research study?

No charges will be billed to your insurance company or to you for this study. A pre-paid mailing envelope has been included with this consent form and questionnaire for the free return of these completed materials. Please keep in mind that the surgery (myomectomy or hysterectomy) is

independent of this study and you or your insurance company will remain responsible for all surgery-related costs. You will not be financially compensated for participation in this study.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them.

Giving you care does not mean that Partners hospitals or researchers are at fault, or that there was any wrongdoing. There are no plans for Partners to pay you or give you other compensation for the injury. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Study Contacts:

Raghava Shree Kavalla M.B.B.S., M.P.H
Study Coordinator
Center for Uterine Fibroids
Brigham and Women's Hospital
77 Avenue Louis Pasteur, New Research Building, Room 160D, Boston, MA 02115
Phone: 617-525-4434 or 1-800-722-5520 and ask operator for 525-4434 (U.S. only)
Email: fibroids@rics.bwh.harvard.edu
Website: www.fibroids.net

Cynthia C. Morton, Ph.D.
Principal Investigator
Center for Uterine Fibroids
Brigham and Women's Hospital
77 Avenue Louis Pasteur, New Research Building, Room 160D, Boston, MA 02115
Phone: 617-525-4535
Email: cmorton@partners.org

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 617-424-4100.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

Federal law requires Partners (Partners HealthCare System and its hospitals, health care providers and researchers) to protect the privacy of health information that identifies you. This information is called Protected Health Information. In the rest of this section, we refer to this simply as "health information."

If you decide to take part in this research study, your health information may be used within Partners and may be shared with others outside of Partners, as explained below.

We have marked with a ☒ how we plan to use and share your health information. If a box is not checked ☐, it means that type of use or sharing is not planned for in this research study.

We will also give you the **Partners Notice for Use and Sharing of Protected Health Information.** The Notice gives more details about how we use and share your health information.

- **Health Information About You That Might be Used or Shared During This Research**

  ☒ Information from your hospital or office health records within Partners or elsewhere, that may be reasonably related to the conduct and oversight of the research study. If health information is needed from your doctors or hospitals outside Partners, you will be asked to give permission for these records to be sent to researchers within Partners.

  ☒ New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study

- **Why Health Information About You Might be Used or Shared with Others**

  The reasons we might use or share your health information are:

  - To do the research described above
  - To make sure we do the research according to certain standards - standards set by ethics and law, and by quality groups
  - For public health and safety - for example, if we learn new health information that could mean harm to you or others, we may need to report this to a public health or a public safety authority
  - For treatment, payment, or health care operations

- **People and Groups That May Use or Share Your Health Information**

  1. People or groups within Partners

  ☒ Researchers and the staff involved in this research study

  ☒ The Partners review board that oversees the research

  ☒ Staff within Partners who need the information to do their jobs (such as billing, or for overseeing quality of care or research)

  2. People or groups outside Partners

  ☒ People or groups that we hire to do certain work for us, such as data storage companies, our insurers, or our lawyers

  ☒ Federal and state agencies (such as the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health,

and/or the Office for Human Research Protections) and other U.S. or foreign government bodies, if required by law or involved in overseeing the research

☒ Organizations that make sure hospital standards are met

☐ The sponsor(s) of the research study, and people or groups it hires to help perform this research study

☒ Other researchers and medical centers that are part of this research study

☐ A group that oversees the data (study information) and safety of this research study

☐ Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow. We share your health information only when we must, and we ask anyone who receives it from us to protect your privacy. However, once your information is shared outside Partners, we cannot promise that it will remain private.

- **Time Period During Which Your Health Information Might be Used or Shared With Others**
  - Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

- **Your Privacy Rights**
  - You have the right **not** to sign this form permitting us to use and share your health information for research. If you don't sign this form, you can't take part in this research study. This is because we need to use the health information of everyone who takes part in this research study.
  - You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing.

    If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. This includes information used or shared to carry out the research study or to be sure the research is safe and of high quality.

    If you withdraw your permission, you cannot continue to take part in this research study.

- You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study.

  In this research study, you may only get such health information after the research is finished.

- **If Research Results Are Published or Used to Teach Others**

  The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Consent/Assent to take part in this research study, and authorization to use or share your health information for research

Statement of Subject or Person Giving Consent/Assent

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other options for treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.

If you understand the information we have given you, and would like to take part in this research study, and also agree to allow your health information to be used and shared as described above, then please sign below:

Signature of Subject:

_____ _____

Adults or Minors, ages 14-17 Date/Time

OR

If you understand the information we have given you, and would like to give your permission for your child/the person you are authorized to represent to take part in this research study, and also agree to allow his/her health information to be used and shared as described above, then please sign below:

Signature of Parent(s)/Guardian or Authorized Representative:

_____ _____
Parent(s)/Guardian of Minor Date/Time

OR

_____ _____
Court-appointed Guardian or Health Care Proxy Date/Time

OR

_____ _____
Family Member/Next-of-Kin Date/Time

Relationship to Subject:_____

Signature of a Witness:

_____ _____
Witness (when required by the PHRC or sponsor) Date/Time

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject, and
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent _____ Date/Time _____

In certain situations, the Partners Human Research Committee (PHRC) will require that a subject advocate also be involved in the consent process. The subject advocate is a person who looks out for the interests of the study subject. This person is not directly involved in carrying out the research. By signing below, the subject advocate represents (or "says") that the subject has given meaningful consent to take part in the research study.

Statement of Subject Advocate Witnessing the Consent Process

- I represent that the subject or authorized individual signing above has given meaningful consent.

Subject Advocate (when required by the PHRC or sponsor) _____ Date/Time _____

Consent Form Version Date: 6/30/2008