Consent for Participation in a Research Study

Title of Research Study: TAP 0307.5.31: A sub-study of Genotype and Phenotype (GAP) to understand the role of stem cells in endometriosis and other diseases (functioning under the North Shore – LIJ Tissue Donation Program, Global Collection Protocol)

Principal Investigator: Peter K. Gregersen, MD (Feinstein Institute for Medical Research)
Sponsors: Endometriosis Foundation of America
Diva International Inc.

Introduction

You are being asked to join a research study. The purpose of a research study is to answer specific questions.

This consent form will explain:

- the purpose of the study
- what you will be asked to do
- the potential risks and benefits

It will also explain that you do not have to be in this study to receive medical care. You should ask questions before you decide if you want to participate. You can also ask questions at any time during the study.

Why is this research study being done?

The purpose of this research study is to learn more about stem cells found in the endometrium (uterine lining), how they act during normal tissue repair and growth, and how they may contribute to endometriosis and other diseases.

Stem cells are unspecialized cells that can be 'pushed' to become more specialized cells such as nerve cells or heart muscle cells. Specialized cells, such as heart or nerve cells, are generally not able to replicate themselves, so if they are injured the entire organ may not be able to function well. Because stem cells can be 'pushed' to become specialized cells, they have been shown to help repair injured organs. We are interested in studying stem cells found in menstrual blood.

Endometriosis occurs when the tissue that normally grows and lines the inside of the uterus (the endometrium) escapes the uterus and grows within the abdomen (outside of the uterus). Endometriosis can cause a variety of symptoms including painful menstrual cramps, abdominal pain when a woman is not menstruating and infertility. Stem cells in menstrual blood are thought to be involved in this condition.

To do this we will establish a tissue bank. We will collect and store stem cells from menstrual blood, plasma (the liquid part of menstrual blood), and DNA (the genetic material in your cells). Cells obtained from your samples may be grown in the lab for either a short period of time or indefinitely. The samples will be used for future genetic research as well as other types of research, to learn more about endometriosis as well as possibly other diseases. We will also collect information about your age, ethnicity and medical/history. We hope future studies using the tissue bank sample will lead to improved understanding of endometriosis.

Genotype and Phenotype Registry (GAP): This study is part of another study called the Genotype and Phenotype (GAP) Registry. This means that you must be enrolled in the GAP study to participate in this study. This is because we will use the genetic sample collected when you joined the GAP to study how the genetic information (contained in the DNA and RNA) affects the characteristics of stem cells. If you wish to join the GAP study, we will provide you with the details for participation. You will have to sign another consent form specifically for the GAP study.

Tissue Donation Program (TDP): This study is also part of the Tissue Donation Program, at The Feinstein Institute for Medical Research, in the North Shore-LIJ Health System. The Tissue Donation Program (TDP) oversees a data and specimen bank, developed to support research on different diseases and conditions. The TDP collects and stores many types of samples, along with health history information from participants. These samples and data are made available to scientists for use in medical research studies that may or may not be related to endometriosis.

Before banked samples can be used in a research project, the proposed research study will be reviewed and approved by the Committee for Participant Protection (COPP). This committee reviews research projects that request banked samples and assures that they are ethical and appropriate research.

The COPP may allow your samples to be given to researchers in the North Shore- LIJ Health System, as well as researchers at other academic institutions or for-profit companies that do biomedical research. The TDP may receive compensation to cover the cost of collection, storage and shipping of samples to researchers outside of the North Shore-LIJ Health System.

You are being asked to join a research study because you are a female over the age of 18, who is still menstruating and does not have endometriosis. You cannot participate in this study if you are currently breastfeeding or if you are currently using an internal birth control device such as an IUD.

How many people will take part in this study?
We expect to enroll about 200 women per year over the next 5 years.

How long will you be in this study?
Answering the questionnaire will take about 15 minutes. Collection menstrual blood samples will take between 12 – 48 hours. Your samples and information will be kept indefinitely, for use in future research. Once the menstrual blood sample has been collected and you have completed the questionnaire, your active participation in this research will be over.

The time period in which we may re-contact you to request another sample or additional health information is indefinite, as this study will go on for many years and it is not possible to know when we may want to re-contact you, if ever.

Your samples and information will be kept indefinitely for use in future research.

What will happen in this research study?
If you agree to participate in the study, you will be asked to complete the following:

1. You will collect a sample of menstrual flow, using a reusable menstrual cup (The DivaCup). This is a flexible healthcare grade silicone cup worn inside the vagina to collect menstrual blood. You are asked to do this during the first three days of your period, at a time and place convenient for you. You will be asked to collect menstrual flow with a menstrual cup for a 12 hour period. Some women may be asked to collect for up to 48 hours. The DivaCup holds up to 1 ounce (2 tablespoons). The entire, average monthly menstrual blood flow is approximately 1 to 2 ounces (2 -4 tablespoons). The DivaCup can be worn up to a maximum of 12 consecutive hours before removing, washing and re-inserting. By monitoring the fullness of the cup, you will learn how often to empty it according to your needs. The DivaCup should be washed with a mild, unscented soap and warm water before reinserting.

   You will need to place the menstrual blood collected each time the cup is removed into a sample collection container(s) we will provide. We will provide a kit containing a re-usable menstrual cup, along with instructions for use and return shipping materials or instructions for having the sample returned to us via courier.

   You will receive a copy of the manufacturer's User Guide regarding menstrual cup use and are responsible to read it before using the cup. We encourage you to speak with a Customer Care representative from The DivaCup if you have questions about how to use the DivaCup. You should also consult your physician with any gynecological /medical questions.

2. Complete a questionnaire about your gynecological medical history.

3. Allow us to re-contact you to request another sample of menstrual flow or additional health information. You are free to refuse to provide any additional samples or information. You will be compensated for each sample you provide.

What are the risks of the research study? What could go wrong?

Menstrual Cup: Collecting a sample of menstrual blood via a menstrual cup is safe when used as directed. You will be asked to collect menstrual flow with a menstrual cup for a 12 hour period. Some women may be asked to collect consecutive samples, for up to 48 hours. There is a low occurrence rate of vaginal or urinary tract infections in women using a menstrual cup, similar to women who use tampons.

Sometimes a woman may have difficulty removing the DivaCup after insertion. This can cause anxiety and make it more difficult to remove. Rarely medical assistance may be required to remove the cup. It is important to read the DivaCup User Guide thoroughly before trying the DivaCup. You may want to consult with your doctor or the Customer Care Team at DivaCup (support@divacup.com) for questions or concerns before trying the DivaCup.

Genetic Research: You will not receive individual results of genetic research that might be done on your samples. Researchers must study samples and information from many people over many years before they can know if the results have meaning. We will send a newsletter once a year

to people who take part in the study. The newsletter will give general updates about the studies being done.

You should know that there might be social or economic burden associated with the genetic research results of this study, if they were to become known by unauthorized individuals. To prevent this, we will not give research test results to anyone including you, your family members, your health care providers, insurance companies and/ or employers. In addition, we have strong measures in place to prevent other unauthorized individuals from gaining access to your genetic research results; however even with strong protections there is a small risk the information could be inappropriately accessed.

Interviews/Questionnaires: Some of these questions may seem very personal or embarrassing. You may skip any question that you do not want to answer.

What are the benefits of this research study?
You will not benefit directly from participating in this study. However knowledge may be gained that could increase the understanding of endometriosis and possibly other conditions and benefit others in the future.

Are there any costs for being in this research study?
There will be no costs to you for participating in this research. The DivaCup used to collect the menstrual flow sample(s) will be provided at no cost to you.

Will you receive any payments for participating in this research study?
You will receive $50 for your time required for the collection of each 12 hour menstrual blood sample. If the total payment you receive from Northwell Health, during this year, is equal to $600 or more, the payment is required to be reported to IRS. Although this study does not pay $600, if you participate in other Northwell Health studies, it is possible your payment could end up totaling $600. If this occurs, the payment you receive on this study will be reported to the IRS. In this case, you will be issued a 1099 form and be required to provide your social security number at that time for reporting purposes. You will also be responsible for reporting this income while filing your tax return.

If the research procedures marketable procedures, will you receive any payment?
If this research project, or the operation of the data and tissue bank, results in the development of any marketable product, there are no plans for you to share in any profits.

What are your rights as a research participant?
Your participation in this project is voluntary. The quality of your medical care will be the same, whether you join, refuse to join, or decide to leave the study.

If you do not join the study you will not be penalized or lose benefits to which you are entitled. If you join the study you may withdraw at any time without prejudice to your future care at Northwell Health. Follow-up examinations may be needed to assure your well-being.

Could you be taken off the study before it is over?
It is also possible that your participation in this study may end without your consent. This decision may be made by a researcher or the Institutional Review Board (IRB- the committee that oversees research at this institution).

Reasons for withdrawal may include:

- failure to follow instructions,
- it is not in your best interest to continue on this study, or
- the study is stopped.

If you withdraw from this study or if you are withdrawn from the study, any data or samples already collected will continue to be used. However, no new data will be collected.

What happens if new information is learned?
You will be told of any new findings that may change your decision to continue to participate. Your consent to continue to take part in this study may be obtained again.

What information will be collected and used for this study?
If you agree to be in this study, we will collect health information that identifies you. We may collect the results of questionnaires and interviews. . We will only collect information that is needed for the research. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information. This permission is called authorization. If you do not want to provide authorization, then you cannot participate in this research study.

Who else will see your information?
Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside Northwell Health.

Investigators will share information collected from this research study with:

- Other researchers.

The following reviewers may access your study record to make sure that this study is being done properly:

- Representatives from federal and state government oversight agencies.
- Representatives from Northwell Health's Institutional Review Board (IRB - the committee that reviews research at this institution)

We will do our best to protect the privacy of your records but it is possible that once information is shared with people listed on this form, it will be released to others. If this happens, your information may no longer be protected by the federal law.

In the future, we may publish results of this study in scientific journals and may present it at scientific meetings. If we do we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Will you be able to access your records?
You have the right to know who has and who will see your records. To request this information, or for any questions related to your health information, you may contact the Research Privacy Officer at 516-321-2100.

How long will your health information be kept?
There is no limit on the length of time we will keep your information for this research because it may be analyzed for many years. We will keep it as long as it is useful, unless you decide you no longer want to take part or we close the study. You are allowing access to this information indefinitely.

Can you change your mind?
If you change your mind about being in the study, you may withdraw at any time. If you want us to stop collecting your health information, you need to send a letter to the researcher at the following address:

Dr. Peter K. Gregersen
The Feinstein Institute for Medical Research
350 Community Drive
Manhasset, NY 11030

Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information or samples any further. You may also need to leave the research study if we cannot collect any more health information. We will destroy your sample to the best of our ability, but it may not be possible to retrieve information or samples that have already been used in the research, prior to your request to stop using them.

Certificate of Confidentiality
To help us protect your privacy, we have obtained a Certificate of Confidentiality from the U.S. Department of Health and human Services (DHHS). This means that the researchers cannot be forced to identify you or turn over any information contained in our research record, even under a court subpoena. The Certificate does not mean the Secretary of DHHS approves or disapproves of the project. It adds special protection for the research information about you. However, researchers may provide information to appropriate authorities if harm to you, harm to others, or child abuse becomes a concern. In addition the federal agency funding this research may see your information if it audits us.

A Certificate of Confidentiality does not prevent you from voluntarily giving information about yourself or your involvement in this research to other people. However, if you agree that an insurer, employer, or any other person may receive your research information, then the researchers may not use the Certificate to withhold that information.

Does the investigator of this study receive money if you take part?
Funding for this research study is provided by Endometriosis Foundation of America. The funding is used to support the activities of the Division of Genomics and Human Genetics and to pay back the Division for the costs of the conducting the study, including paying personnel. Compensation is not based on the number of people enrolled in the study.

Who can answer your questions about the study?
If you have any questions about this study, you may call the principal investigator, Peter Gregersen, MD at (516) 562-1542. If you have questions about side effects or injury caused by this research you should

call, Peter Gregersen, MD at (516) 562-1542. If you have questions regarding your rights as a research subject or concerns about the research project, you should call the Office of the Institutional Review Board at 516-321-2100. A signed copy of this consent form will be given to you.

Summary:

You have read the above description of the research study. You have been told of the risks and benefits involved and all your questions have been answered to your satisfaction. A member of the research team will answer any future questions you may have. You voluntarily agree to join this study and know that you can withdraw from the study at any time without penalty. By signing this form, you have not given up any of your legal rights.

Subject's printed name	Subject's signature	Date
Witness's printed name	Witness's signature	Date

☐ *Witness signature waived if mailed consent.*

Investigator's Statement:

In addition to advising the above subject about this research, I have offered an opportunity for further explanation of the risks and discomforts which are, or maybe associated with this study and to answer any further questions relating to it.

Investigator's signature	Investigator's printed name	Date