Kisspeptin Physiology in the Human

NCT05901467

November 3, 2023

Mass General Brigham

Research Consent Form
Certificate of Confidentiality Template
Version Date: November 2022

Subject Name:

MRN or DOB:

Subject Identification

Protocol Title: Kisspeptin Physiology in the Human

Principal Investigator: Stephanie Seminara, MD

Site Principal Investigator:

Description of Subject Population: Adult men (ages 18-60 years) and adult women (ages 18-40 and 50-60 years)

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 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 signed copy of this form to keep.

Key Information

We are asking you to be in a research study. This form will tell you what you should expect if you agree to be in the study. You will find more information about each of the following points later in this form.

It is your decision whether or not to join the study. We are asking you to be in this study because you are either a healthy volunteer or are enrolled in the Mass General Brigham Biobank study. We are doing this research to learn more about how the hormones kisspeptin and gonadotropin-releasing hormone (GnRH) affect the human reproductive system. If you agree, you will come to Massachusetts General Hospital (MGH) for up to three study visits. During one or two of those visits you may receive kisspeptin and GnRH through an IV, and we will take small amounts of blood to see how your hormone levels change over time or in response to GnRH and kisspeptin. The amount of time you spend on the study will depend on your availability to schedule the visits. However, we do not expect it will take more than six months if you decide to stay for the whole study.

The main risks of being in the study are associated with the administration of study drugs and frequent blood sampling.

You will be paid up to $2,070 by check for taking part in this research study. You will find more information about the payment amount for each visit and a plan if you do not complete all study visits later in this form.

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

Dr. Stephanie Seminara, MD is the person in charge of this research study. You can call her at [redacted] (Monday-Friday, 9am-5pm). You can also call Dr. Margaret Lippincott, MD at (Monday-Friday, 9am-5pm) or page her ([redacted] pager #[redacted]) 24 hours a day, 7 days a week with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call the study [redacted].

If you want to speak with someone **not** directly involved in this research study, please contact the Mass General Brigham IRB. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Why is this research study being done?

We are doing this research study to learn more about the human reproductive system and the hormones that it uses to communicate. A hormone is a chemical that the body makes naturally.

We know that a specific part of the brain called the hypothalamus makes the hormone GnRH (short for "gonadotropin-releasing hormone"). Women need GnRH to make estrogen, to have normal menstrual cycles, and to become pregnant, and men need GnRH to make testosterone and to father a child. The purpose of this study is to understand how another hormone called kisspeptin affects GnRH levels. Kisspeptin is involved in reproduction and is made in very high levels in women during pregnancy.

We will give you kisspeptin and GnRH as part of this study and take small amounts of blood to see how your hormone levels change in response to kisspeptin and GnRH.

Kisspeptin is not approved by the U.S. Food and Drug Administration (FDA). This means that kisspeptin can only be used in research studies.

GnRH has been approved by the FDA for clinical use; however, it is only sold outside the United States. This means that GnRH used in research studies must be under an investigational drug application monitored by the FDA; we have been approved by the FDA to use GnRH in our research studies.

Who will take part in this research?

We are asking you to take part in this study because you:

- are a healthy volunteer; or
- are an enrolled participant in the Mass General Brigham Biobank study.

About 80 healthy men, 240 healthy cycling women, 20 healthy postmenopausal women, and 120 genetically characterized men and women will take part in this research study. All subjects will participate at MGH.

The National Institute of Child Health and Human Development (part of the National Institutes of Health) is paying for this research to be done.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Screening
The purpose of screening is to see if you qualify for the research study. The screening for this study will be done either at MGH or remotely. If you come to MGH for a screening visit, it will take about one hour. Remote activities may take place over the phone or at a local blood drawing laboratory.

At this visit, we will:

- Ask you about your health history
- Give you a physical exam, including an exam of your testicles if you are male and a breast exam if you are female
- Draw blood to measure your blood count, hormones, and to make sure you are generally healthy
- Administer a pregnancy test, if you are able to become pregnant; if you are pregnant, you cannot take part in this research study

We may also ask you to complete a questionnaire about your health and your family history.

The study doctor will review the information collected during screening. If you don't qualify, the study doctor or a study team member will tell you why.

Stopping Your Current Medications ("The Washout Period")
If you are on any hormonal medication (such as birth control pills [also known as oral contraceptives] or hormonal replacement), we may ask you to stop taking it for several weeks. Stopping the medicine means not taking any tablets, patches, creams, or using vaginal rings. This "washout period" allows these hormone medications to leave your body before you begin taking the study drug. We suggest that you discuss the washout with your prescribing physician before you stop taking your medication. Without your regular medications, certain medical conditions or symptoms may get worse. If this happens, please call the study doctor at the phone number provided in this consent form. If you stop taking birth control, your chances of becoming pregnant increase. As described later in this document, you will need to use alternate forms of birth control to participate in the study.

In addition to hormone medications, there are other, *non-hormone* medicines that can also affect the reproductive system. For example, certain types of pain medicines can suppress reproductive hormones. If you would like to washout of one of those medicines to participate in this study, please let the study team know. The doctors for this study, in most circumstances, will not be part of your regular health care team. Therefore, the study doctors will need to speak with your prescribing physician(s) to determine if it is appropriate for you to stop taking any medication.

Sex Steroid Replacement
If you are a woman who qualifies for the study, we may ask you to start taking one or more hormone medications (estradiol or medroxyprogesterone) for up to two weeks. This may cause one to two days of light menstrual bleeding.

Translational and Clinical Research Centers Visit(s)
If your screening results tell us that you are eligible to participate, we will ask you to come to the Translational and Clinical Research Centers (TCRC) at MGH for one or two visits. We will let you know during screening how many TCRC visits we would like you to attend. While you are at the TCRC, we will:

- Administer a urine pregnancy test, if you are able to become pregnant. If you are pregnant, you cannot take part in this research study.
- Place a thin, plastic tube called an intravenous line (IV) in your arm. The IV allows us to take many blood samples without having to use a needle each time. The IV will stay in your vein for the whole study visit.
- Draw a small amount of blood every 10 minutes for 2-19 hours. These blood samples will be used to measure hormones such as luteinizing hormone (LH), follicle stimulating hormone (FSH), estrogen, and testosterone.
- We may administer kisspeptin and GnRH boluses through the IV or subcutaneously (SC), an injection method under the skin. Injections are most likely to occur in the abdomen but may also occur in the leg or arm.
- We may ask you to complete a questionnaire about your health and your family history.

After the last blood draw we will remove the IV and you can go home.

We will call you within five to seven days after you leave the hospital to check if there are any problems, and to see if you have any questions or concerns. If you are having any problems, we may ask you to come for a follow-up visit.

Stopping the Study Early
You may decide to stop taking part in the study for any reason. The study doctor may also take you out of the study without your permission. You might be asked to stop taking part because:

- The study doctor thinks it is best for you to stop taking the study drug
- The study doctor thinks it is best for you to stop participating in the study
- You can't make the required study visits
- We stop doing the study for other reasons

If this happens, the study doctor will explain why you need to stop taking part in the study. We may ask you to come in for a final study visit.

Follow Up Visit
Within a month after the telephone call or stopping the study early, you may return for a short physical exam and blood tests to check your blood count. If your blood count is low, we will ask you to take iron tablets and to return for repeat checks until your blood count is back to normal levels.

Review of Medical Records from Hospital Admissions or Emergency Department Visits
Mass General Brigham has an electronic system that lets your study doctors know if you are admitted to a Mass General Brigham Hospital, or if you visit a Mass General Brigham Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study.

We will also review your medical records to collect information about your health. We may ask you to provide medical records from outside hospitals or doctors. We will ask you to sign a medical record release form to allow the outside hospital or doctor to send us records.

Study Information Included in Your Electronic Medical Record
A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

Use of Your Samples and Research Information
All your samples will be stored in our research lab and labeled with a code that links the sample to you, but not labeled with your name. Your samples will be saved indefinitely.

If you participate in other research studies in the Reproductive Endocrine Unit (past or future), we may access information from that study to better understand data generated from this study.

Research is an ongoing process, and we will continue to use your samples and data in the future. We cannot give you an exact date when we will either destroy or stop using your samples and data.

In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that analyze data and collect the results of whole genome studies. These banks may also analyze and store DNA samples, as well. These central banks will store your genetic information and samples and give them to other researchers to do more studies. We do not think that there will be further risks to your privacy and confidentiality by sharing your samples and whole genome information with these banks. However, we cannot predict how genetic information will be used in the future. The samples and data will be sent with only your code number attached. Your name or other directly identifiable information will not be given to central banks. There are many safeguards in place to protect your information and samples while they are stored in repositories and used for research.

Research using your samples and whole genome information is important for the study of virtually all diseases and conditions. Therefore, the sample/data banks will provide study data for researchers working on any disease.

How may we use and share your samples and health information for other research?

The samples and information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

No. The research study we are doing is only a steppingstone in understanding human reproduction. Therefore, no information about the results of this research study or the results of your individual participation in the research study will be given to you or your doctor. Tests done for the research using your samples will not be useful in directing your medical treatment. The results of the tests will not be placed in your medical record.

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

Risk of Allergic Reaction
With any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.

Risks of Taking Kisspeptin
Kisspeptin is naturally made in the human body. In research studies, this study drug has been given to healthy reproductive-age men and women, older men, menopausal women, and people with reproductive disorders, including people with infertility and children with delayed puberty. We also studied the effects of high doses of kisspeptin on rats and dogs. There have been no negative side effects seen in either the animal or human studies.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant
We do not believe that kisspeptin has any risk to an embryo or fetus (unborn baby in the womb). This is largely based on studies showing very high levels of kisspeptin during pregnancy. However, there may be harmful risks that are unknown. Therefore, women cannot take part in the study if they are:

- pregnant
- trying to become pregnant
- breastfeeding

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you are unable to get pregnant due to any well-documented method of surgical sterilization, you will not need to have a pregnancy test. Some methods of surgical sterilization include having had a hysterectomy (removal of the uterus), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female participants must have a negative pregnancy test before starting the study drug.

If you are sexually active and you or your partner(s) are able to become pregnant, you must agree to use two forms of birth control for the entire study.

Acceptable birth control methods for use in this study are:

- barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- intrauterine device (IUD)
- abstinence (no sex)
- partner(s) of male participants may use hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants

The study investigator will discuss your choices for birth control during the study.

If you think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and stop taking part in the study. The study doctor may ask for your permission to collect information about the outcome of your pregnancy and the condition of your newborn.

Risks of Gonadotropin-Releasing Hormone (GnRH)
GnRH has been given to patients for more than 30 years and it is approved by the FDA for ovulation induction in women. There have been no serious side effects that were felt to be related to GnRH in human studies aside from a single report of a possible allergic reaction.

Unknown Risks of Kisspeptin and GnRH
There may be other risks of kisspeptin and GnRH that are currently unknown, including side effects that may happen when taking kisspeptin and/or GnRH with other drugs.

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

Risks of Estradiol (Estrogen) (Applicable to Women Only)
Common undesirable effects of estradiol include tenderness or enlargement of the breasts, nausea, and headache.

Long term use of estrogens such as estradiol has been associated with rare but serious side effects that include abnormal vaginal bleeding, and increased risk of breast cancer, heart attack and blood clots. Because of the short period of time that you will receive the estradiol, these side effects are extremely unlikely.

An earlier research study, called the Women's Health Initiative (WHI), showed that the benefits of oral (by mouth) estrogen alone, or estrogen and a progestin together, were not greater than the

possible risks. There is no evidence for any increased risk associated with short periods of use as in this study.

Risks of Medroxyprogesterone Acetate (Progestin) (Applicable to Women Only)
Common undesirable effects of medroxyprogesterone acetate include bloating, stomach discomfort, nausea, breast tenderness, headache, and dizziness or drowsiness.

Long term use of medroxyprogesterone acetate has been associated with rare side effects that include blood clots, changes in weight or mood, and discharge from the nipple.

If you take estradiol as a part of this study and have an intact uterus, you may be given 10 days of medroxyprogesterone acetate (5-10 mg) around one of the TCRC visits. You may have one to two days of light menstrual bleeding after finishing this low dose progestin.

Risks of Iron Supplements
Iron supplements may occasionally cause mild gastrointestinal (stomach and digestion) problems, including constipation and darkening of the stool.

Risks of Stopping Current Medications
If you stop taking your current medications, you might experience the return of some symptoms that the medication lessened. If this happens, tell the study doctor. If you stop taking oral contraceptives, or another form of birth control, the likelihood of becoming pregnant increases, unless you are abstinent or use another highly effective form of contraception. If you take hormone medication and stop taking it, you may have symptoms of low sex hormone levels. These symptoms include decreased energy level, decreased libido (sex drive) and occasionally hot flashes.

Risks of Blood Draws and Intravenous (IV) Lines
You may have a bruise (a black and blue mark) or pain where we take the blood samples or where we put in an IV. There is also a small risk of infection, lightheadedness, and/or fainting. There is a slight chance that an IV line may stop working. If an IV line stops working, we will put in a new one.

You may feel fatigued after blood drawing. Also, it is possible that you could develop anemia from blood drawing. To lower the chances you will develop anemia we take less than two and a half cups (550 mL) of blood over the course of the study. A healthy person will normally replace this amount of blood in about eight weeks. You should not donate blood or have large amounts of blood drawn for eight weeks before or after the study.

Risks of Subcutaneous (SC) Administration of Kisspeptin and GnRH
There is a possibility of a reaction at the site of SC study drug administration including: pain, tenderness, warmth, itching, swelling, irritation, redness, or bruising.

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

You will not benefit from taking part in this research study. However, people with reproductive disorders may benefit in the future from what we learn in this study.

Can you still get medical care within Mass General Brigham if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Mass General Brigham 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.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the 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.

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

Will you be paid to take part in this research study?

We will pay you:

- Screening: $40
- Health questionnaire: $30
- TCRC visit(s): up to $2,000 (amount will be variable depending on the length of stay)

This means that you will be paid up to $2,070 if you complete all possible parts of this study. Depending on the timing and length of your visit, we may give you meals during your time at the TCRC.

We will pay for parking in the hospital garage during study visits. If you are traveling from a distance, we may also defray transportation and hotel costs.

If there is a follow-up visit because you have a problem during the study, we will not pay you for the extra follow-up visit.

We may use your samples and information to develop a new product or medical test to be sold. The hospital and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

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

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are 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. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. 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 beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why:

- Mass General Brigham researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)

- Other researchers within or outside Mass General Brigham, for use in other research as allowed by law.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate, unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Mass General Brigham, we cannot control all the ways that others use or share it and cannot promise that it will remain completely private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

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

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable 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. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable 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. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

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

Signature of Subject:

I give my consent to take part in this research study and agree to allow my identifiable information to be used and shared as described above.

_____

Print Name

_____ _____ _____

Subject Signature Date Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

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

_____
Print Name

_____	_____	_____
Signature of Study Doctor or Person Obtaining Consent	Date	Time (optional)

Permission for Future Contact

We may want to contact you about additional studies in the future. Do you give permission for us to contact you about future studies?

☐ **YES, I give permission to be contacted about future studies.**

☐ **NO, I do NOT wish to be contacted about future studies.**

_____	_____	_____
Subject	Date	Time (optional)

Consent Form Version Date: October 11, 2023