Clinical Research Consent Summary
Oocyte Donation

TITLE: Evaluation of in vitro gene correction techniques in germ cells

PRINCIPAL INVESTIGATOR: Shoukhrat Mitalipov, Ph.D. (503) 418-0196

You are being asked to join a research study. You do not have to join the study. Even if you decide to join now, you can change your mind later.

1. The purpose of this study is to learn how well gene correction techniques work and what problems it might cause in human eggs, sperm, & embryos. In vitro experiments (experiments performed outside of the body) will be conducted to test these techniques. Inherited genetic diseases are caused by mutations in genes found in egg & sperm cells which may be passed from parent to child. We will try to correct these mutations by conducting in vitro experiments in fertilized eggs and make embryonic stem cell lines to study the outcomes. A stem cell line is a cell line with the potential to grow into many different types of cells. Stem cell lines may allow scientist to develop personalized medical therapies.

2. This project is a collaboration between the Knight Cardiovascular Institute and the Center for Embryonic Cell and Gene Therapy. This study is being funded by Oregon Health & Science University.

3. We do not know if the techniques we are testing will work. This science will not result in any pregnancies or births. The embryos and stem cell lines will only be used for research.

4. If you choose to participate, we will collect blood, egg cells, and possibly a skin sample from you. The study will produce preimplantation embryos and stem cell lines that will be used for research purposes only.

5. The length of active participation is roughly two months (two menstrual cycles). You will be required to come to the Center for Health and Healing approximately every other day for a two-week period during your Ovarian Stimulation.

6. There are risks involved in participating in the study.

7. Samples collected during the study will be used for genetic research. All samples and embryonic stem cell lines will be saved for future research purposes only.
Clinical Research Consent and Authorization Form
Oocyte Donation

TITLE: Evaluation of in vitro gene correction techniques in germ cells

PRINCIPAL INVESTIGATOR: Shoukhrat Mitalipov, Ph.D. (503) 418-0196

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FUNDED BY: Oregon Health & Science University (OHSU)

PURPOSE:
You have been invited to participate in this research project because you:
- Are a healthy woman between 21 - 35 years of age OR
- Are a woman between 21 – 37 years of age who is a carrier of an inherited gene mutation listed below:
  - mutations in MYH7 gene (c.2605 C>T) causing Familial Hypertrophic Cardiomyopathy
  - mutations in MYBPC3 gene causing Familial Hypertrophic Cardiomyopathy
  - LDLR AND LDLRAP1 gene mutations causing Familial Hypercholesterolemia (FH)
- Are not pregnant
- Are in good general health
- Have regular menstrual cycles and
- Are interested in donating egg cells, blood and a skin cell sample for research.
The purpose of this study is to test new techniques for correcting a gene mutation in egg & sperm cells in a laboratory experiment. We need to see if this technique works to correct the gene mutation and test what other problems this technique might cause. Genetic disease is the result of changes or mutations in your DNA. When these changes occur in the letters that make up a gene (DNA sequence) a severe illness can occur. These changes are passed from parent to child during human reproduction. Genes are the units of DNA—the chemical structure carrying your genetic information—that determine many human characteristics that make us who we are. A copy of each parent’s DNA is passed on to the child when the egg (female reproductive cell) and sperm (male reproductive cell) combine to form the embryo (a collection of cells developed from a fertilized egg).

Germline gene editing is currently being discussed by a range of stakeholders; including scientists, national leaders, ethicists, academics, and many more individuals. A consensus report was published upon the conclusion of the International Summit on Human Gene Editing which supports basic science experiments to be conducted in order to provide sufficient evidence regarding the safety and efficacy of gene editing tools. The knowledge gained from basic research studies, like this one, will add scientific data to the continued discussion of whether gene editing tools should be used in a clinical setting.

During this study, your donated eggs, cumulus cells (the cells that surround your eggs), a possible skin biopsy, and blood cells will undergo genetic testing. These tests will help researchers better understand human reproduction and development as it relates to embryonic stem cell research.

Researchers will try to correct the faulty gene mutations in reproductive cells, including eggs, sperm, or early embryos provided by people carrying genetic mutations. This involves putting genes, gene products (a biochemical material, either proteins or RNA, which is made when a gene is turned on) or chemicals into human reproductive cells. The researchers will then create human embryonic stem cells from the proposed corrected reproductive cells. An embryonic stem cell line is a cell line that has been developed from a human embryo.

The embryonic stem cell lines that researchers create have the potential to grow into many different types of cells. This research may lead to new knowledge about developing gene therapies.

At no time during this study will the reproductive cells you donate for research be used to establish a pregnancy. The donated cells will be used to develop basic knowledge about the genetic cause of disease and ways of fixing disease-causing gene mutations.

Your blood/tissue samples, as well as stem cells created from your donations, will be stored indefinitely and may be used in future research. All reproductive cells donated will be used at the Center for Embryonic Cell and Gene Therapy only; DNA, stem cell lines, and/or established cell lines from your blood and skin donations may be used in future IRB approved collaborations outside of OHSU. This research may involve genetic and/or stem cell research. Your donations will be used specifically for research purposes; none of your donations will result in an embryo being transferred with the intent of producing a viable fetus, nor will the stem cells created from your donation be used for therapeutic purposes.

Donated samples will not be used to create a pregnancy and will not be available to you for future fertility treatments.
PROCEDURES:
If you are eligible to enroll in the study, and agree to donate eggs, skin cells, cumulus cells and blood, your active participation will last for approximately two months (two menstrual cycles). Your donation will be for research purposes only, no portion of your donation will be used for fertility treatment or the creation of children.

All of the procedures that you will undergo in this study represent the normal standard of care for women undergoing infertility treatment with In Vitro Fertilization (IVF) and for women donating eggs to infertile couples. None of the procedures are experimental. To minimize risk of unintended pregnancy, you will be required to use barrier contraception (i.e. condoms) if you are heterosexually active during the course of the study and two weeks afterwards.

Your eggs will be used in experiments to create embryos, embryonic stem cells, and genetic testing. This involves fertilizing your donated eggs with sperm donated separately for this research. The developing fertilized egg (embryo) will be used to evaluate the correction of mutated DNA using gene correction tools. Researchers will derive stem cells from the embryos and perform genetic tests which requires the destruction of the embryos. This means that the embryo made will be destroyed for purposes of this study. You will have no opportunity to use this embryo for any reproductive or other purposes.

Please see Appendix A on the last page of this form for a chart of the procedures described below.

Pre-Screening (1 visit):

The one-hour group informational night session will include presentations that describe in detail the research focus of the Center for Embryonic Cell and Gene Therapy, fertility egg donation, and research specifics related to the donation process. A fertility physician will cover the process of egg donation from start to finish and discuss potential risks of egg donation; including, but not limited to potential impacts on future fertility and potential health risks. The research coordinator and study team member will present information specific to this study. Time will be provided for open discussion to answer any and all questions that may arise by potential participants.

At the conclusion of this meeting you will be asked if you would like to be included in further screening. If yes, you will be sent home with a copy of the consent form to review. The research coordinator will contact you via phone or email to schedule continued screening.

Screening (1-2 visits):

This screening visit will include a review of your medical history (e.g. if applicable, to check if you have children or parents with genetic diseases, to check what type(s) of DNA mutations and syndromes you and/or your family members may have, etc.), demographics (date of birth, race and ethnicity), and any current medications you may be taking. We will also ask you to sign a release that permits review of your medical records. You may be asked to provide health information about your relatives. Any information you provide will be kept confidential. We will not contact your relatives without your permission.

We will perform a full physical examination (including a breast exam). A vaginal ultrasound will be performed in order to estimate the number of eggs in your ovaries. Blood will be drawn from
a vein in your arm (about 2 tablespoons) to check your hormone levels. A portion of the blood collected for these hormonal assays will be used for genetic analysis. An additional blood draw may be required during the period of the hormone treatment to obtain an adequate amount of blood cells for this study.

You will also be asked to attend one brief counseling session with a mental health counselor. We will try to schedule this session the same day as your health exam. However, you may be required to return for a second visit in order to meet with the counselor.

If you are an egg donor with a known DNA mutation you will also be required to have additional consults, for added safety measures, with Internal Medicine, Anesthesia, and/or any other consult deemed necessary during your initial physical exam. This set of consults will be in addition to the standard procedures for healthy donors.

The screening process should take approximately 2 hours to complete.

**Blood Draw (1 visit, or combined with screening visits):**
We will draw blood from a vein in your arm. We will collect about 2 tablespoons of blood. Your sample may be frozen and later thawed and used for future experiments. Genetic tests will be conducted.

**Skin Biopsy (1 visit, or combined with screening visits):**
If you are a patient diagnosed with an inheritable DNA mutation disorder and agree to participate in this study, you will also undergo a skin biopsy procedure. If you do not have a diagnosed DNA mutation, we may ask you to donate a skin sample depending on our research needs. During this procedure, an area of skin will be cleaned with an alcohol swab. A solution of diluted lidocaine (a drug that will numb the surrounding skin) will be injected. The provider will use a small tool called a core punch biopsy to remove a piece of skin about 1-3 mm in size (about the size of a small pencil eraser). A Band-Aid will be applied to the wound to prevent infection. This visit should take approximately 1 hour.

After your skin cells have been collected, they will be transferred to the OHSU Center for Embryonic Cell and Gene Therapy, located on the 13th floor of the Center for Health and Healing and used for this research study. Your samples may be frozen and stored in liquid nitrogen and later thawed and used for future experiments. Genetic tests will be conducted.

In the future, samples of your tissue and genetic information may be given to other researchers as part of a search for genetic disorders, or for other research purposes. The samples will be labeled as described in the **CONFIDENTIALITY** section.

**Enrollment and Ovarian Suppression (2-3 visits):**
Research providers will review the results of your screening exams to make sure you are healthy enough to undergo egg donation. They will also look at you blood tests to see if your eggs can be used in this research. If the results of your screening process allow you to continue in the study, you will be asked to return for enrollment.

You will be assigned to one of two protocols that are commonly used in egg donation. The first protocol uses a medication called Gonadotropin Releasing Hormone (GnRH) agonist, leuprolide. Leuprolide is used to prevent the body from releasing hormones that could stimulate ovulation or allow premature ovulation. The other protocol uses a GnRH antagonist, ganirelix.
Ganirelix also helps to prevent premature ovulation. The infertility physicians involved in this study will determine which protocol you will follow based on your age, hormone blood levels, and number of follicles seen on your ovaries during scans. For both protocols, you will be given oral contraceptives to suppress your ovaries.

**GnRH antagonist protocol:** If you are assigned to the GnRH antagonist protocol, you will start the ovarian stimulation process (see below) right after you complete the course of oral contraceptives.

**GnRH agonist protocol:** If you are assigned to the GnRH agonist protocol, you will also be instructed on how to give yourself subcutaneous (i.e. under the skin) injections during your first enrollment visit. You will start giving yourself daily injections approximately 14 days after starting birth control pills. You will continue to take this medication for one to two weeks, at which point you will return for a blood test and vaginal ultrasound. These tests will determine whether your ovaries are suppressed and that you can move on to the ovarian stimulation process (see below).

**Ovarian Stimulation Visits (Approximately 4-5 visits):**

Once we have established that your ovaries have been suppressed, you will be instructed to stop taking the oral contraception and begin injections (shots) of follicle-stimulating hormone (FSH) and/or human menopausal gonadotropins (hMG) that will stimulate the production of eggs. These medications must be injected into a specific part of your body (generally the stomach region) in order to be effective. You or a friend will be instructed on how and where on your body to properly administer these injections so that you can take them at home. You will be taking these injections daily for approximately 10 – 14 days.

During this time, you will need to come in for frequent office visits so that we can monitor your hormone levels and follicle development. At each visit, a blood test and vaginal ultrasound will be performed. You will return to the office 3-4 days after starting hormone injections. Your next visit will occur 2-3 days after the first visit of this section (or 5-7 days after the start of hormone injections). You will then return for visits approximately every other day until your follicles are the right size and your hormone levels are adequate.

Once we can see by ultrasound that the eggs have matured, you will be instructed to stop all medications and take a one-time injection of hCG, with or without leuprolide, (a different hormone that helps your eggs separate from the wall of your follicles). Your egg retrieval appointment will be scheduled to be approximately 36 hours after you have taken this injection.

(If you are assigned to the GnRH antagonist protocol, you will follow the ovarian stimulation process as described above. However, you will also be instructed to begin taking an injection of ganirelix (Antagon or Cetrotide) once your ovarian follicles have become 12-14 mm in size. This medication helps prevent premature ovulation.)

**Egg Retrieval (1 visit):**

Your egg retrieval appointment will be scheduled 35 hours after your final hCG injection. This visit will take up to two hours. Eggs are retrieved through transvaginal ultrasound aspiration, a surgical procedure performed under conscious sedation.
Conscious sedation means that although you will receive sedating drugs and pain killers, which will be given to you by an anesthesiologist, you will probably not be completely asleep. You may remember part or all of the procedure, and you may feel some discomfort.

Prior to the beginning of the procedure, you will meet with an anesthesiologist. The anesthesiologist will ask you questions about your medical history, examine you, and discuss how you will be sedated during the egg retrieval. This will include receiving intravenous fluid and anesthesia drugs through an IV cannula (where a needle, attached to a flexible plastic tube, is placed in your vein in order to deliver medications or fluids). The anesthesiologist will place some standard monitors on you to monitor your blood pressure, your heart and your breathing during the procedure. You will also receive oxygen through tubing going to your nose. The details of this process and any additional risks associated with anesthesia will be explained to you prior to the procedure.

The drugs you may receive include midazolam, alfentanil, or fentanyl. Midazolam is a sedating drug which makes you sleepy and forgetful, and alfentanil and fentanyl are strong pain killers. The risks of these drugs are described in the RISKS AND DISCOMFORTS section of this form. However, the decision as to what you receive will be made by the anesthesiologist. You will also receive an IV antibiotic and some anti-nausea medications.

Using a tube attached to an ultrasound probe, a physician guides a suctioning needle into each ovary and removes mature eggs with surrounding cumulus cells. The procedure takes approximately 45 minutes. Following egg retrieval, you will remain in the clinic for approximately 30 minutes to 1 hour and then return home for further recovery. We will send you home with written instructions about the signs and complications to be aware of, antibiotics to minimize the risk of infection and with pain medication to use if you experience discomfort. You will need to have a friend accompany you to the clinic whom will provide a ride home after your procedure. You will not be allowed to undergo the egg retrieval procedure without a ride home from a known companion on site – no taxi and/or rideshare programs.

After your egg(s) and cumulus cells have been collected, they will be transferred to the OHSU Center for Embryonic Cell and Gene Therapy located on the 13th floor of the Center for Health and Healing. Your samples, including the eggs and cumulus cells, will be used in experiments to create embryos and embryonic stem cells as described above and may be frozen for use in the future.

Follow-up (1 visit):
You will be asked to return for one follow-up visit after your egg retrieval procedure. This visit is to check on your health following the egg donation process. During this visit, a vaginal ultrasound may be performed to verify that there were no complications from your procedure.
## Schedule of Events

<table>
<thead>
<tr>
<th>Study Section</th>
<th>Screening</th>
<th>Ovarian Suppression</th>
<th>Ovarian Stimulation</th>
<th>Egg Retrieval</th>
<th>Follow-up</th>
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<td>2.2</td>
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### SUBJECT ACCESS TO GENETIC INFORMATION:

The results of these studies will not be made available to you because the research is still in an early phase and the reliability of the results is unknown.

If we discover new information that is important for your health care, either in this study or the future, you will be asked whether you wish to receive the results. You will be required to have the test repeated in a clinical laboratory; results from your donation are performed in a research laboratory and therefore are not considered a clinical diagnostic tool. If you choose to receive these results they will be presented to you by one of the physicians approved in this research protocol; because genetic information is complex and sensitive, the results should further be discussed with a genetic counselor or your primary care provider who can answer your questions or discuss your concerns.

If you consent to this study, we may contact you again in the future to update your information or inquire about your specific healthcare history.

_______ Yes, I would like to receive the non-clinical research only findings if it is deemed important for my health care. I understand this is not a clinical diagnosis and must be repeated in a clinical laboratory. I understand all costs incurred for healthcare services are my responsibility.

_______ No, I would not like to receive non-clinical research only findings.

IRB Approved: 3/15/2018
Approval Expires: 2/1/2019

MED. REC. NO.:______________________
NAME:______________________
RISKS AND DISCOMFORTS:
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects.

Blood draws:
We will draw blood from a vein in your arm. You may feel some pain when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, an infection, or fainting.

Pelvic exam and vaginal ultrasounds:
The examinations in this study are of a personal nature and may cause you to feel embarrassed. Most women feel pressure, but not pain when these exams are being performed.

There are no risks to vaginal ultrasound but you may experience some slight discomfort. A female chaperone will be provided during the entire examination for your comfort if you desire.

Oral Contraceptives:
For the majority of women, oral contraceptives can be taken safely. However, there are some women who are at high risk of developing certain serious diseases that can be life threatening or may cause temporary or permanent disability or death. The risks associated with oral contraceptive use increase significantly if you smoke, have high blood pressure, diabetes, high cholesterol, have or have had a clotting disorder, heart attack, angina pectoris (severe pain and constriction around the heart), cancer of the breast, jaundice (yellowness of the skin and eyes), or malignant or benign liver tumors.

The most common side effects are nausea, vomiting, bleeding between menstrual periods, vaginal discharge and discomfort, menstrual cramps and pain, headache (including migraine), weight gain, and breast tenderness. Less common side effects include jaundice, mood changes, and decrease in desire to engage in sexual activity, intolerance to contact lenses, changes in your liver and/or kidney functions, acne, and changes in your hair patterns. You should not take oral contraceptives if you suspect you may be pregnant, or if you are breastfeeding. Oral contraceptives do not protect against sexually transmitted diseases such as herpes, chlamydia, syphilis, genital warts, gonorrhea, hepatitis B and HIV (AIDS).

Certain drugs may interact with birth control pills to make the birth control pills less effective. These drugs include phenobarbital (which treats epilepsy, insomnia, and anxiety), Dilantin (which treats epilepsy and seizures), and Butazolidin (which treats arthritis) and possibly some antibiotics. If you need to use any of these medications, or if you have any questions, you can contact the study investigator or study staff.

Hormonal Fertility Injections:
While serious complications to fertility medications are unlikely, donors commonly experience abdominal swelling, tension and pressure in the ovarian area, mood swings, and bruising at injection sites as a result of fertility drugs. Temporary menopause-like symptoms, including vaginal dryness and hot flashes, may result. Unintentional pregnancy is another potential complication due to enhanced ovulation. To avoid unintentional pregnancy, you must agree to be heterosexually abstinent or, if heterosexually active, must be in a monogamous relationship with a vasectomized partner or be willing to use a barrier method of contraception (i.e. condoms) if you are sexually active during the course of the study and two weeks afterwards.
A less frequently occurring risk is ovarian hyperstimulation syndrome (OHSS), a serious complication marked by chest and abdominal fluid buildup and cystic enlargement of the ovaries that can cause permanent injury and even death. According to one study, severe OHSS affects approximately 1 percent of donors depending on the drug regimen used. Patients with OHSS may experience dehydration, blood clotting disorders, and kidney damage.

Less than one percent of the time, ovarian stimulation can also cause adnexal torsion, a condition that results when a stimulated ovary twists on itself and cuts off its blood supply. Surgery is required to untwist and in some cases to remove the ovary.

You may also experience specific side effects with the different types of injections. These side effects are outlined below:

**Gonadotropins**

**Common:**
- Breast tenderness
- Constipation
- Decreased sex drive
- Difficulty sleeping
- Hot flashes/sweating
- Impotence
- Infection (fever, chills, sore throat)
- Nausea or vomiting
- Pain
- Swelling
- Urination problems

**Uncommon:**
- Dizziness or lightheadedness
- Fast or irregular heartbeat
- Increase in bone pain
- Severe drowsiness
- Severe headache
- Vision changes

**Rare but serious:**
- Severe allergic reactions (rash; hives; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue)
- Blood in urine
- Chest pain
- Swelling of the lungs
- Unusual or one-sided weakness

**Ganirelix**

**Common:**
- Headache
- Mild pain, redness, pain or swelling at injection site

**Uncommon:**
- Nausea
- Vaginal bleeding
• stomach pain
• bloating, or swelling
• sudden weight gain
• unusual cough
• dark urine
• decreased urination
• diarrhea
• dizziness

**Rare but serious:**
• Abdominal pain (severe)
• nausea and vomiting
• weight gain (rapid)
• Severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue)
• Shortness of breath

**hCG**

**Common:**
• Bloating (mild)
• stomach or pelvic pain

**Uncommon:**
• Abdominal or stomach pain (severe)
• bloating (moderate to severe)
• Decreased amount of urine
• Feeling of indigestion
• Nausea, vomiting, or diarrhea (continuing or severe)
• Weight gain (rapid)
• Skin rash - hives or welts, itching or redness of skin; unusually warm skin
• Severe, sudden headache
• Vision changes
• Wheezing
• Discouragement, feeling sad or empty, irritability, loss of interest or pleasure
• Enlargement of breasts
• Headache
• Lack of appetite
• Pain at place of injection
• Trouble concentrating
• Trouble sleeping and tiredness

**Rare but serious:**
• Pelvic pain (severe)
• Shortness of breath
• Swelling of feet or lower legs
• Difficult or labored breathing
• Large, hive-like swelling on face, eyelids, lips, tongue, throat, hands, legs, feet, sex organs
• Pain in chest, groin, or legs, especially the calves
• Slurred speech
• Sudden loss of coordination
• Sudden, severe weakness or numbness in arm or leg
• Sudden, unexplained shortness of breath
• Tightness in chest

Egg retrieval:
Pain medication: You will also be given a medication such as hydrocodone for pain both before and after your procedure. The prescribing physician will explain the risks and side effects of the specific medication you are given.

Other risks associated with the egg retrieval include intra-abdominal or vaginal bleeding, infection, possible injury to bowel or urinary tract and potential psychological risks. If there is a complication with your procedure, or you develop an infection, there is also a remote risk to future fertility.

Anesthesia:
The risks of anesthesia include some very serious complications such as death, heart attack, stroke and brain damage, although these problems are very rare in healthy people. You may experience nausea and vomiting after the procedure. This can last for several hours.

You may feel pain while the IV cannula is placed. You may have pain, bruising or infection at the IV site afterwards. You may also experience some discomfort with the cuff used to monitor your blood pressure, and the oxygen tubing going to your nose.

You will receive an antibiotic IV, which may cause pain in your arm as it is administered. Rarely, the antibiotic can cause a severe allergic reaction called anaphylaxis, which can be a life-threatening emergency.

The anesthetic drugs that you will receive will make you sleepy. Some people feel that they are not sleepy enough with these drugs, while others become very sleepy. Sometimes these drugs will stop your breathing, and the anesthesiologist will need to help you to breathe.

The side effects associated with the anesthetic drugs commonly used are listed below:

Midazolam:

Common:
• Blurred vision
• changes in blood pressure, breathing, and heartbeats
• coughing;
• dizziness or drowsiness
• dry mouth
• headache
• hiccups
• nausea or vomiting
• pain, redness, or tenderness at the injection site

Rare but serious:
• short-term memory loss
• slurred speech
• Severe allergic reactions (rash; hives; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue);
• agitation or combativeness
• chest pain
• irregular breathing patterns
• unusual or involuntary muscle movements or muscle tremor

Alfentanil:
Common:
• Muscle stiffness
• Nausea or vomiting
• pruritus (itchiness)
• confusion, somnolence or agitation
• dizziness or drowsiness
• Blurred vision

Rare but serious:
• Severe allergic reactions (rash; hives; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue);
• pain, redness, or tenderness at the injection site
• irregular breathing patterns
• hypotension
• bradycardia
• hypertension
• arrhythmia

Fentanyl:
Common:
• anxiety or confusion
• constipation
• difficulty walking
• dizziness or drowsiness
• dry mouth
• headache
• indigestion, nausea or vomiting
• itching

Rare but serious:
• Severe allergic reactions (rash; hives; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue)
• hallucinations
• muscle rigidity
• seizures
• slow or irregular heartbeat
• slowed or trouble breathing
• weakness

If you have any further questions about side effects, please ask one of the investigators.
Skin Biopsy:
Prior to biopsy, the skin will be cleaned with an alcohol swab, and then a few milliliters of 1% lidocaine with epinephrine diluted 1:100,000 will be injected to achieve local anesthesia. Some people (fewer than 1 in 10,000) have an allergic reaction to lidocaine, the numbing medicine used in the shot. A 1-3 mm core punch biopsy instrument will be used to remove a piece of skin and the specimen will be placed on saline. You may experience some pain or discomfort from the biopsy procedure. Heavy bleeding from a skin biopsy is rare. There is a small chance, about 10%, that you may get an infection from the biopsy. Sterile conditions will be used to minimize any risk. A small scar will form at the biopsy site. The scar is usually much smaller than the original biopsy.

The side effects associated with the lidocaine and epinephrine used are listed below:

**Lidocaine and Epinephrine:**

**Common:**
- Bruising, redness, itching or swelling at injection site
- Dizziness
- Nausea

**Rare but serious:**
- Fainting
- Signs of infection in the affected area (e.g. oozing, pus discharge)
- Depression
- Drowsiness
- Vomiting
- Seizures
- Fast heart rate
- Slow heart rate
- Severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips or tongue)
- Blurred vision
- Chest pain

**Genetic Testing:**
Although we have made every effort to protect your identity, there is a small risk of loss of confidentiality. If the results of these studies of your genetic makeup were to be accidentally released, it might be possible that the information we will gather about you as part of this study could become available to an insurer or an employer, or a relative, or someone else outside the study. Even though there are discrimination protections in both Oregon law and federal law, there is still a small chance that you could be harmed if a release occurred.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for most insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that this new Federal law does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination if you have already been diagnosed with the genetic disease being tested.
BENEFITS:
You will not personally benefit from participating in this study. However, by serving as a subject, you may contribute new information which may benefit patients in the future.

ALTERNATIVES:
You may choose not to participate in this study.

CONFIDENTIALITY AND PRIVACY OF YOUR PROTECTED HEALTH INFORMATION:
We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. Neither your name nor your identity will be used for publication or publicity purposes. As part of this study we may share a small amount of information about your genetic code and mutation in papers we publish about this study. This could mean that others could identify that you were in this study, but they could only do so if they also had your DNA so that they could “match” your genetic code to what was published. Other people would not be able to tell anything about you (such as your hair or eye color) from the small amount of your genetic code that we may publish.

We will create and collect health information about you as described in the Purpose and Procedures sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study and store in a repository for future research.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The Food and Drug Administration
- The Office for Human Research Protections, a federal agency that oversees research involving humans

Those listed above may also be permitted to review and copy your records, including your medical records.

We may also share your information with other researchers, who may use it for future research studies. A code number will be assigned to you, your cells and genetic information, as well as to information collected about you. Only the investigators named on this consent and authorization form and their research staff will be authorized to link the code number to you.

Other investigators who may receive samples of your tissue and genetic information for research will be given only the code number which will not identify you.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

When we send specimens or information outside of OHSU, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used and re-released without your permission.
We may continue to use and disclose protected health information that we collect from you in this study indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

If you have any questions, concerns, or complaints regarding this study now or in the future, contact the principal investigator, Shoukhrat Mitalipov (503) 418-0196, or the clinical coordinator for this project at (503) 494-4831.

COMMERCIAL DEVELOPMENT:
Samples and information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

COSTS:
There will be no cost to you or your insurance company to participate in this study. If the results are deemed important for your health care, you may have the tests repeated in a clinical laboratory at your own expense. The costs of the testing and the counseling necessary to be certain that you understand what the results mean may be billed to you or to your third party carrier. Note that this will probably make the results available to the third party carrier and to your clinical record.

During your participation, an insurance policy will be purchased by the researchers to cover any side effects that may occur as a result of the research experience. The coverage will include the possibility of hospitalization in the rare case that ovarian hyperstimulation or other complications occur. The policy will not extend beyond your participation in this study.

Upon full completion of this study you will be paid $5000 for egg donation and $50 for skin donation (if applicable) as compensation for your time and costs related to this study. If you stop participating or are removed from the study before all your visits are complete, a pro-rated portion of this amount based on the number of visits completed following enrollment, will be paid to you. Please see the table at the end of this form for details on how compensation will be pro-rated. For patients diagnosed with a DNA mutation enrolled in the current study, reimbursement for travel expenses incurred during the study participation period is negotiable and can be discussed and agreed upon during the initial screening process. No other compensation is offered.

You may receive payment via a debit card. There may be fees (for example, if the card is inactive for more than six months), which will be deducted from the balance on your card. Details on how to use the card and any fees are included in the separate card member agreement and FAQ sheet.
Payment received as compensation for participation in research is considered taxable income for a research subject. If payments are more than $600 in any one calendar year, OHSU is required to report this information to the Internal Revenue Service (IRS). Research subject payments exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the research subject and a copy will be sent to the IRS.

**LIABILITY:**
If you believe you have been injured or harmed while participating in this research and require immediate treatment, contact Dr. Paula Amato (503) 418-3700 or (503) 494-8311 and ask to have the “on call” Reproductive Endocrinologist paged. If you have other questions or concerns that do not need immediate medical treatment, please contact your research coordinator (503) 494-4831 or (503) 360-6705.

You have not waived your legal rights by signing this form. If you are harmed by the study procedures, you will be treated. Oregon Health & Science University does not offer to pay for the cost of the treatment. Any claim you make against Oregon Health & Science University may be limited by the Oregon Tort Claims Act (ORS 30.260 through 30.300). If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887. Oregon Health and Science University is also subject to the Oregon Genetic Privacy law (ORS 192.531 through ORS 192.549) and its requirements concerning confidentiality and the legal remedies provided by that law for breach of its requirements. You have not waived your legal rights by signing this form. For clarification on this subject, or if you have further questions, please call the OHSU Research Integrity Office at (503) 494-7887.

**PARTICIPATION:**
This research is being overseen by an Institutional Review Board ("IRB"). You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:
- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

The participation of OHSU students or employees in OHSU research is completely voluntary and you are free to choose not to serve as a research subject in this protocol for any reason. If you do elect to participate in this study, you may withdraw from the study at any time without affecting your relationship with OHSU, the investigator, the investigator’s department, or your grade in any course. If you would like to report a concern with regard to participation of OHSU students or employees in OHSU research, please call the OHSU Integrity Hotline at 1-877-733-8313 (toll free and anonymous).
If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study.

You may withdraw your consent to donate at any time up until the samples have been used for the purpose of research. If you withdraw your consent prior to the usage of your donated material by the researchers, your unused samples will be destroyed. Your identity and the data obtained from this study will be kept strictly confidential. Only the investigators listed above and their research staff will have access to identifying information and the data will be maintained indefinitely.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

The Center for Embryonic Cell and Gene Therapy
3303 SW Bond Ave
Portland, OR 97239
koskia@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

Paula Amato, MD (503) 418-3700 and Shoukhrat Mitalipov, Ph.D., (503) 418-0196 have offered to answer any other questions you may have about this study.

Your health care provider may be one of the investigators of this research protocol, and as an investigator is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time, you may ask for a second opinion about your care from another doctor. You do not have to be in any research study offered by your physician.

Your donated material may be developed into cell lines that researchers manipulate using the cell lines from animals. This means that the cells lines created from your sample may be combined with the cells of animals as part of this research. These cell lines will not be used for fertility purposes in either human or animal.

In the future, the cells derived from your donation may be used to develop treatments for other individuals. By signing this consent and authorization form, you agree to donate without restriction or indication for who may receive these treatments.

The lab responsible for the collection and storage of your sample has been certified by the Food and Drug Administration (FDA) and follows the Good Laboratory Practices required by that certification. The laboratory in which the research of your samples will take place has agreed to follow the National Institute of Health (NIH) guidelines for human stem cell research.

You may be removed from the study if the investigator stops the study, if you develop serious side effects or if you do not follow study instructions. We will give you any new information
during the course of this research study that might change the way you feel about being in the study.
SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

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Social Security number (for tax purposes, we must have this in order to pay you)

Address (we must have this in order to pay you and send your check)

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Complete if the participant is not fluent in English and an interpreter was used to obtain consent. Participants who do not read or understand English must not sign this full consent form, but instead sign the short form translated into their native language. This form should be signed by the investigator and interpreter only.

Print name of interpreter: _______________________________________

Signature of interpreter: ________________________________ Date: ______

An oral translation of this document was administered to the subject in ______________ (state language) by an individual proficient in English and ______________ (state language).

See the attached short form for documentation.