Purpose of the Study

We are asking you to be in this research study because you asked for carrier testing to find out if you are a genetic carrier of an inherited condition or disease such as cystic fibrosis. You asked for this testing before getting pregnant or during pregnancy. Genetic testing involves looking at genes, which are made up of DNA and are the “instruction book” for the cells that make up our body.

Genetic research involves looking at genes, which are made up of DNA and are the “instruction book” for the cells that make up our body.

The purpose of this study is to compare a new type of genetic testing against the standard genetic test that you requested. Standard carrier tests look at one gene or a small number of genes. The new test is called Genome Sequencing. This new technology is different from standard carrier tests because:

1) It looks at more genes
2) For each gene, it looks at many more changes than just the most common ones
3) It also looks at genes that may be important for your health, not only the one for which you requested testing.

Research Consent and Authorization Form

Female Participants

NextGen: Clinical Implementation of Carrier Testing Using Genome Sequencing

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Clinical Trials Required by Law to Be Registered at www.ClinicalTrials.gov

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.

What if I have questions?

You can talk to the study staff about any questions or concerns you have about this study. You can call:

Mari Gilmore at 503-331-6325
Pat Himes at 503-331-6328 or
Katrina Goddard at 503-528-6361

If you have questions about your rights as a research subject, or about research-related injuries, contact the Human Subjects Institutional Review Board (IRB): Caroline Miner, the Director of Research Subjects Protection, at 503-335-6725.

CONSENT SIGNATURES

My signature below means that:

- I have read this consent form,
- I agree to take part in this study,
- This consent form has been explained to me,
- All of my questions have been answered,
- I understand the benefits, risks, and alternatives to being in this study, and
- I understand that I will receive a copy of this consent form after I sign it.

PARTICIPANT SIGNATURE

YOUR NAME | PRINT

________________________________________________________

YOUR SIGNATURE | DATE

NAME OF STUDY STAFF OBTAINING CONSENT | PRINT

________________________________________________________

SIGNATURE OF STUDY STAFF OBTAINING CONSENT | DATE

THANK YOU!

Kaiser Permanente Northwest (KPNW) Region

Female Participants

Carrier testing looks for changes called mutations in your genetic material (DNA), which can cause the condition you are being tested for. Every body has mutations, but only some mutations cause disease. Genetic carriers of recessive conditions do not show symptoms, but can pass the mutation(s) on to their children. Children only develop the condition if they also get a second mutation in the same gene from their other parent. It is very unlikely that a mother and father would have mutations in the same genes that can cause a disease.

Women can also be carriers of x-linked recessive conditions. If the mother passes on the x-linked mutation to her sons, they will have the condition even if the father does not carry a mutation in this gene. Daughters must receive an x-linked mutation from both parents in order to have the condition. Parts of a cell, called mitochondria, are passed onto children from their mothers. You could be found to carry a change in your mitochondrial DNA. You may pass along the change to your child, which could cause disease.
You could get your information on about 700 conditions that could affect your future children and 150 conditions that could affect you.

How long will the study last?
You will be enrolled for up to 4 years.

Which group will I be in?
If you agree to be in this research study, you will be assigned randomly (by chance), to one of the study groups:

- **Usual Care Group**: standard carrier testing only (which is the way we usually provide care). About 250 women will be assigned to the Usual Care group.

- **Genome Sequencing Group**: standard carrier testing plus Genome Sequencing testing. About 150 women will be in the Genome Sequencing group.

It is important to remember that neither group is known to be better than any other. You should be willing to be in either group before you agree to be in this study.

Study Procedures
In both groups you will get the standard clinical test for carrier status for the condition you requested as part of your usual medical care. This test has already been ordered by your regular doctor, and the results will be or have already been returned to you.

For both groups, we will:
- Put the test results into your medical record, so that any Kaiser Permanente provider can use the information to help provide you medical care.
- Have you complete a survey on your thoughts about genetic testing (about 30 minutes).
- Contact you 6 months after you get your results to complete a survey about your experience and about the testing and how you used the test result (about 30 minutes). We will send a link to complete the survey to your personal email account.
- Collect data from your medical record about how you use health care after this testing.
- If you have a male partner, we will ask you to give him information about being in the study so we can ask him to get the same testing that you had. He will only be eligible if you were found to be a carrier. He does not have to be tested or be in the study for you to be eligible. If he chooses to be tested, he does not need to be a Kaiser Permanente member in order to get the testing. The testing will be provided to him at no charge.

For the Usual Care Group
In this group, you will need to provide a blood sample for the standard genetic test if you haven’t already done so. No additional blood is taken as no added testing will be done.

For the Genome Sequencing Group
- You will need to provide two tubes of your blood (about 3 teaspoons) for the Genome Sequencing. In rare cases we may need to ask you back for a second blood draw (about 2 teaspoons) to double any other personally identifying information.

The researchers in this study will be looking at your personal health information and may need to disclose it to others. Whenever possible, your samples and data will be labeled with a code and not your name, SSN, or other easily identifi- cation. However, we cannot promise total privacy. Information about you and your health, which might identify you, may be given to:
- National Institutes of Health (NIH) (funder who maintains dbGaP repository of de-identified genetic information)
- Commercial laboratory vendor who performs DNA sequencing
- University of Washington (collaborators who perform DNA testing and analysis)
- Oregon Health & Sciences University (collaborators who will confirm DNA testing and analysis of laboratory tests completed by University of Washington)
- The Institutional Review Board (IRB), a committee of scientific, nonscientific, and community members who review research to protect the rights and welfare of participants.

Kaiser Permanente has agreements with other organizations to protect your health information. If this information is given to an organization not covered by these policies and laws, Kaiser Permanente cannot guarantee the privacy and confidentiality of your personal health information. By signing this consent form you agree to let us use and disclose your personal health information. If you do not agree to this, we cannot include you in the study. This agreement will not expire.

How long will my blood and health information be stored?
If you decide to be in this study, your blood and health information will be stored and possibly used in future approved research. If you decide now that your blood and health information can be used for research, you can change your mind at any time and we would remove your blood and health information from our research database. You can do this even if you are no longer a Kaiser Permanente member by contacting the investigator at the end of this consent form.

Reasons why you might want to participate in this study:
1. Research is important before introducing new technologies, such as genome sequencing, in clinical practice.
2. Learning about carrier status before pregnancy is an important topic to you.
3. Participation in research allows others to benefit from your experience.

May I withdraw or cancel (revoke) my permission?
Yes. You do not have to be in this research study and you can quit at any time. If you decide not to be in this study or to withdraw from it will not affect your regular medical care or health care benefits, and your doctor’s attitude toward you will not change. If you do not want to be in the study, the alternative is to receive usual care from your doctor.

If at any time you want to withdraw this agreement, you must notify Katrine Goodard, PhD in writing or by phone at the Center for Health Research, 3800 N. Interstate Avenue, Portland, OR 97227 or 503-335-6361.

After we receive your request, only data that has already been looked at or disclosed will continue to be used, unless we need to monitor your data for your safety. No further blood or data will be collected, and we will destroy any remaining samples at your request.
Kaiser Permanente is committed to protecting your personal health information.

Confidentiality
Kaiser Permanente is committed to protecting your personal health information. State and federal laws also require Kaiser Permanente to maintain privacy and security of your information in this study. In order to do this study we will be looking at or collecting information about you and your health, including reviewing your medical record.

To protect your confidentiality we will use a study assigned number whenever possible and use only secure computers or locked files. If you receive genetic testing through the study, those tests will include your name, date of birth, and health record number so the results can be returned to your medical record. If information from this study is presented publicly or published in a medical journal, you will not be identified by name, picture, or other identifiers.

We will ask you to complete a second survey about your experience and opinions after you get your carrier status results (about 30 minutes). We will send you a link to complete the survey to your personal email account.

If there are any results about disease that could affect you, we will return them to you at an in-person meeting with a genetic counselor about a month after your visit to get your results on carrier status. We call these results “incidental findings” because they are not related to the reason you asked for genetic testing. We will only analyze and confirm information from your genome about certain conditions.

We will only give you information that is “medically actionable,” which means that it is about a medical condition you have that can be treated OR it is about a condition you may develop that can be prevented. For example, we would not give you information about a mutation for Alzheimer Disease, because there is no treatment.

We would give you information about a mutation that makes you more likely to get breast cancer, because you could get early screening or choose to have surgery before you would possibly get cancer. We don’t think it is likely that your test will find this type of information. If the test does not find anything, we will notify you by phone or mail and you will not need to meet with a genetic counselor.

We will ask you to complete a survey about your experience and perceptions after your medically actionable incidental findings results are returned (about 30 minutes). We will send you a link to complete the survey to your personal email account.

We will look again at the mutations in your sequence about once a year until the study ends in 2017. Your genetic information will not have changed over time, but there may be new ways to interpret it that we want to share with you. What we know about genomics is changing all the time, and new, medically actionable incidental information may become available during the study. If there are changes that would affect your medical care, you will be contacted for a follow-up visit as part of the study.

If you have a meeting with a genetic counselor, our study staff would like to observe that meeting. This will help us learn how you understand
In the event that your genetic results may be shared, and if it were linked with a medical condition, this could affect your ability to get some kinds of insurance. If family members were to see this information, it could also affect them, and it could hurt family relationships. It is possible that you could be identified from the sample if someone has another DNA sample from you or a relative. The two samples could be matched to identify you from the sample given for this study.

Your samples and information will be shared with researchers from KPNIW and elsewhere (such as universities, companies, or non-profit organizations) for research studies that have been approved by an Institutional Review Board. Your coded (anonymous) genetic and other health information may be disclosed to these approved researchers to increase the chances of new discoveries. You will not get any genetic results from these other research studies.

There are many safeguards in place to protect your information while it is stored in repositories and used for research. The National Institutes of Health (NIH) has developed a federally funded database called dbGaP that collects the genetic test results of research studies. Qualified researchers from government, academic, or commercial institutions worldwide can access the databases. Your coded genetic and health information will be stored in an NIH database without your name or other information that could identify you. We do not think there are further risks to your privacy and confidentiality by sharing your genetic information in these databases; however, we cannot predict how genetic information will be used in the future.

To help us protect your privacy, we have applied for a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

However, you or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, we may disclose medical information in cases of medical necessity, or take steps (including notifying authorities) to protect you or someone else from serious harm, including child abuse. Additionally, if you request the release of information about you in writing (through, for example, a written request to release medical records to an insurance company), the Certificate does not protect against that voluntary disclosure. This Certificate does not prevent the researchers from releasing information about you to prevent serious harm to you or someone else. Moreover, federal agencies may review our records under limited circumstances, such as a Department of Health and Human Services request for information for an audit or program evaluation.

**Pregnancy**

A small percentage of women (7-8%) may become pregnant while the testing is underway and if this happens to you, this may cause you some anxiety. There are fewer options available for reproductive decision-making once you become pregnant. You can still be in the study if you get pregnant, and you can decide not to learn the results of your carrier status after becoming pregnant. Before each study visit, we will ask if you have become pregnant, and give you the chance to not get your test results. However, if the testing has been performed, the results will still be placed in your medical record and can be viewed by any of your care providers. If you decide that you want to get your carrier status results after becoming pregnant, standard genetic counseling will be made available to you.

**Upsetting Information**

Learning about your risks for a genetic disease or carrier status could be upsetting. Not knowing exactly how the genetic risk will affect you or your offspring may be stressful to you. Learning that a condition runs in your family might cause some tension among family members. Genetic counseling will be available to help you understand what this genetic information means to you and your family. If at any point we think that you are having too much anxiety or stress, we will offer you a referral for mental health counseling through Kaiser Permanente. Talking about private matters and feelings may make you feel uncomfortable. You can choose not to answer any question or stop an interview at any time.

**Unknown Risks**

There may be unknown risks, stresses, or discomforts that we don’t know about in this new research. You should tell us about any concerns that you have.

**Potential Benefits**

You may or may not personally benefit from participating in this research. Your participation will help us understand how to use these new genetic tests in the future and help us learn how people respond to receiving different kinds of information from this kind of genetic testing.

**Blood Draws**

The risks of the blood drawing procedures may involve pain or bruising from the insertion of the needle, fainting, and very rarely, swelling or clotting of the vein, or infection where the needle enters the skin. Should you experience any discomfort during the blood draw, please inform the staff member working with you.

**Costs**

**Costs covered by the research study**

The sponsor of this study, the National Human Genome Research Institute, will pay for any study procedures, including Genome Sequencing, conducted for research purposes. You or your health insurance including Kaiser Permanente will not be billed for any extra visits that are part of the study.

**Costs not covered by the research study**

The initial genetic testing that you requested and was ordered by your provider for carrier status before getting pregnant, such as for cystic fibrosis, will be charged to you based on your insurance.