Frequently Asked Questions about Multi-Gene Panel Testing

This information will help you learn more about multi-gene panel testing. **It is not a cancer screening plan.** Before making any decisions about cancer screening, speak with your healthcare provider or a genetic counselor. They will help you make a cancer screening plan based on your personal and family history of cancer and your genetic testing results.

**What causes cancer to develop?**

Most cancers develop by chance. There are a number of things, called risk factors, which can increase the chance that a person will get cancer. Different cancers have different risk factors. Aging is the biggest risk factor for all types of cancer. Another risk factor is having a family member with cancer. If one person in a family has a particular type of cancer, close relatives of that person are often at higher risk for the same kind of cancer.

Most people with cancer have no family history of the same type of cancer. However, in some families there are several people who have the same type of cancer, often at young ages. These families may have a “hereditary” or “inherited” risk. About 10% of all cancers are hereditary. Hereditary cancers occur when a change in a particular gene (known as a mutation) is passed down from parent to child. Different gene mutations cause an increased risk of developing different types of cancer. In families that have a gene mutation, family members who inherit the mutation will often develop the same or related types of cancer, at earlier ages than usual. These families are said to have “hereditary cancer syndromes.”

**What causes hereditary cancer syndromes?**

Hereditary cancer syndromes are caused by mutations in certain genes. Genes
are the blueprints for the substances, called proteins, that make up our bodies and keep them working normally. Genes are in every cell in our bodies. Genes come in pairs. One member of each pair comes from our father, and the other from our mother. Genes are composed of DNA and contain carefully spelled-out instructions for making the proteins that help our bodies function properly. A change in the spelling of the gene can cause the gene to work abnormally or stop working all together. These changes in the spelling of a gene are called mutations.

Each person has about 20,000 genes. Mutations in different genes can cause different diseases. At the end of this resource, there is a list of some genetic mutations that cause different hereditary cancer syndromes. The list shows what kinds of cancer can be caused by each genetic mutation.

What is the chance of inheriting a mutation that causes a hereditary cancer syndrome?

Hereditary cancer syndromes are rare. Less than 1 in 10 cases of cancer are caused by inherited mutations. The chance of finding a mutation is higher in people who have cancer at a young age, people who have had more than one type of cancer, and people who have several family members affected by the same type of cancer.

Genetic counselors and doctors can often identify families with a pattern of different cancers that suggests a specific hereditary cancer syndrome. Certain groups of people are at increased risk for mutations in some genes. For instance, people of Ashkenazi Jewish ancestry (from Eastern or central Europe and Russia) are at increased risk for certain mutations in the \textit{BRCA1} and \textit{BRCA2} genes, which cause hereditary breast and ovarian cancers.

Both men and women can pass down a genetic mutation that causes a hereditary cancer syndrome. It usually only takes one mutation to cause the increased risk for the associated cancers. If you have a parent with a genetic mutation, you may or may not inherit it. You would have a 50% chance of inheriting the mutated gene from your parent. You would also have a 50% chance of not inheriting the mutated gene.
How are mutations found in genes that cause hereditary cancer syndromes?

It is possible to test for mutations in genes that cause hereditary cancer syndromes. Genes are made up of “bases,” which are like letters. These letters are arranged in a particular order, or sequence, much like the way letters are arranged in a particular order to form words. Genetic testing “spells out” the letters in your genes, and compares them to what is thought be the “normal” spelling. Mutations are differences from the “normal” spelling of a gene.

Genetic mutations can be detected in blood or saliva samples. It is best to start testing with a member of the family who has or has had cancer. Once a mutation has been found, the same mutation can be looked for in other family members.

What is multi-gene panel testing?

Mutations in different genes can cause the same type of cancer. These genes can be looked at either one at a time, or a number of genes at the same time. By testing a number of genes all at once, it may be possible to find the cause of cancer in a family more quickly. Your genetic counselor will tell you about the genes that are on the panel that you are having.

What are the possible risks and benefits of genetic testing?

Risks and benefits should be considered before genetic testing. There are no risks of physical harm from testing other than that of a blood draw. However, genetic testing can have emotional effects, especially if a mutation is found. If a mutation is found, it can impact other family members. Some may not want to know these results.

There is a chance that someone could use your genetic test results against you. This is considered discrimination. The federal government and some states have laws that forbid using genetic tests results against you. Under these laws, insurance companies cannot use your test results to deny you health insurance. They also cannot use your test results to raise the cost of your current health insurance. Some laws also prevent employers from using your test results as a
reason not to hire or to fire you.

Despite these laws, we cannot promise that no one will ever try to use your genetic test results against you. We do not know of any insurance or work problems for those who have had gene testing at MSK. Most insurers have covered the costs of genetic testing with no penalty (e.g. no risk of increased premiums or no risk to be dropped by the carrier).

There are many possible benefits of genetic testing. It can give you and your family members a better understanding of your cancer risk. The results can help your doctor design a personal cancer screening program. They can also help you decide about options for reducing cancer risk, including preventative surgeries.

This is a personal choice, but your doctor, genetic counselor, and other healthcare professionals can help you make your decision. Regardless of whether you decide to have genetic testing, please feel free to contact us at the number at the end of this resource with any questions that you may have.

What does a positive test result mean?

If a gene mutation is identified, it means that that person has an increased risk for certain types of cancer. Different mutations are linked to increased risks for different types of cancers. The risks for cancer may differ for the different mutations. For some mutations, the risks of specific cancers may be very high. For other mutations, the risks may be lower, although still more than the risk of someone who does not have a mutation.

A person with a mutation may be offered special or more frequent cancer screening exams to try to find any cancers that develop as early as possible. The exact exams will depend on the gene that is mutated. For some mutations on multi-gene panels, there are no clear guidelines about the best screening exams to use, or how often. The list at the end of this resource gives examples of the kinds of exams that may be offered to people with different mutations identified through the multi-gene panel test. A person with a mutation may also be offered certain types of surgeries that may help reduce his/her risk of developing cancer.

If a person has a genetic mutation, family members may also carry this same
mutation. If they do, they will have an increased risk for the types of cancer linked to that mutation. Your genetic counselor can help identify who in the family is at risk of having the mutation, who should be tested, and when is the right time (age) for them to be tested. Before you have gene testing, family members should be consulted as to whether or not they would like to know the results, as these results may impact them.

**What does a negative test result mean?**

A negative test result means that no mutation was found. This can happen for several reasons, including:

- You could have a mutation in the gene(s) that was tested, but the mutation cannot be found by the current testing method. No one form of genetic testing can find all mutations in a gene.
- You may have a mutation in a different gene. For example, you could carry either a mutation in a gene that has not yet been discovered or a very rare genetic mutation. We suggest that you speak with your genetic counselor about this when you receive your test results.
- Your personal or family history of cancer could have happened by chance. Some types of cancer may occur in several people in a family without being caused by a genetic mutation.
- There may be a genetic mutation in other members of your family, but you did not inherit it.

**What does a variant of uncertain significance mean?**

Genes are written in letters called bases. A wrong spelling of a gene can cause an increased risk of cancer. However, changes in the spelling of a gene bases may differ in people without cancer. We are still learning which spellings are normal (harmless) and which can cause an increased risk for disease. These kinds of uncertain changes are called “variants of uncertain significance.”

If you have a variant of uncertain significance, we may not be able to tell you whether or not you are at increased risk for cancer. We will make cancer screening recommendations for you based on your family history. We may
suggest testing certain relatives to learn more about the variant but this information will probably not be helpful in predicting cancer risks for your relatives. Future research may make it clearer whether or not a variant of uncertain significance leads to increased risks of cancer.

**If someone doesn’t want to have genetic testing, how can they manage the risk of cancer?**

If a person doesn’t want to have genetic testing, we will recommend a personalized risk assessment and screening plan. The cancer screening recommendations would depend on a number of factors including family history of cancer as well as other risk factors.

**If I have a genetic mutation, what are the risks to my children?**

If you carry a mutation in a gene that causes a hereditary cancer syndrome, each of your children (or future children) has a 50% (1 in 2) chance of sharing that mutation. A child who inherits the mutation will also inherit the cancer risks associated with that mutation. It is important to remember that just inheriting the mutation does not automatically mean that a person will develop cancer.

Most genes that cause hereditary cancer syndromes do not increase the risks for cancer in children. However, some of genetic mutations for which we test in the multi-gene panel, are tied to increased risks of certain kinds of childhood cancer. Your genetic counselor can help determine the risk for your family members and will also determine what would be an appropriate age for your family members to have their own genetic testing. In some circumstances, it may be appropriate to test individuals before they reach their 20s.

Some of genes on multi-gene panels cause disease in children who inherit abnormal copies of the gene from both parents. This is rare, because mutations in these genes are rare in the general population. We will help you find a reproductive genetic counselor if you are considering having children and if testing shows that you have a mutation in a gene than can cause disease in children who inherit abnormal copies from both parents.
If I have a genetic mutation, what are my options for having children?

If there is a genetic mutation identified in your family, you may want to learn about family planning options (starting a family or having more children). For example, embryos can be tested for the family’s genetic mutation before they are even implanted in a woman’s uterus. This process is called preimplantation genetic testing (PGT). PGT is performed with in vitro fertilization, and may be an option for families who wish to have children without the hereditary cancer risk. To learn more, ask for a referral to a specialist before attempting pregnancy.

Having children with the assistance of donor eggs or donor sperm and adoption are two other possible family planning options.

Will the information about my genetic testing be kept private and confidential?

Yes, your genetic test results and your medical record will be kept private and confidential. When you registered at MSK, you were given a Notice of Privacy Practices. That document explains who has access to your medical record and what reasons they have to access your record. If you would like to know more about MSK’s privacy practices, or if you would like another copy of the privacy notice, please let us know.

Will my insurance cover genetic counseling and testing?

Many insurance companies and managed care plans pay for genetic counseling and testing. Check with your insurance provider before having genetic testing to see what it will cover.

Who should I contact if I have questions?

If you have questions, call MSK’s Clinical Genetics Service at 646-888-4050.