RAD51D Gene Information

The RAD51D gene plays a role in preventing people from developing tumors or cancer. Everyone has two copies of RAD51D – one copy of the gene inherited from each parent. If you inherit one copy of a RAD51D gene with a mutation (likely pathogenic/pathogenic variant) in the genetic code that prevents the gene from working properly, this leads to increased chances to develop cancer. Medically significant changes in the genetic code are called “mutations” or “pathogenic variants.” Not everyone who is born with a RAD51D mutation will develop cancer – many will not.

Cancer Risks

The table below shows the risks of cancer for people with RAD51D mutations compared to people in the general population. These are cancer risk estimates over a lifetime and do not reflect yearly risks. Certain interventions may be able to lower these risks.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>RAD51D Gene-Associated Risk</th>
<th>General Population Risk</th>
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</thead>
<tbody>
<tr>
<td>Female breast cancer</td>
<td>20-40%</td>
<td>12-13%</td>
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<tr>
<td>Ovarian cancer</td>
<td>10-20%</td>
<td>1-2%</td>
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1Female and male refer to sex assigned at birth, and these risks are based on data from mostly cisgender populations. In addition, general population cancer risks may vary by ancestry and other factors.

- Male breast cancer has not been associated with inherited mutations in RAD51D.

It is possible that the information about cancer risks associated with RAD51D could change over time as our knowledge about this gene expands.

Medical Recommendations

The recommendations below are meant as general guidelines and may change based on other personal risk factors or family history. To make an appointment to discuss personal recommendations with a Cancer Genetics Physician at Dana-Farber, please call 617-632-2178.
• **Ovarian cancer** is very hard to find in the early stages, and available screening tests are not able to reliably find ovarian cancer when it is most treatable. Because of this, it is recommended that individuals have surgery to remove the ovaries and fallopian tubes around ages 45-50. This surgery is called risk-reducing salpingo-oophorectomy (RRSO). This surgery reduces the risk for ovarian cancer by about 90%.

• **Breast cancer** screening is recommended to begin at age 40 with annual mammograms, with consideration of annual breast MRI imaging as well. Screening may be considered at earlier ages, especially if there is a family history of breast cancers at a young age, and should be discussed individually.

These recommendations are based on our current understanding of the *RAD51D* gene and may change over time. Recommendations are also influenced by other factors, including but not limited to: cancer treatments, family history of cancer, personal preference and gender affirming care. You should discuss personalized recommendations with your physician.

**Inheritance and Meaning for Your Family**

It is important that you share your test results with your biological (blood-related) relatives. Your close relatives, including parents, siblings, and children, have a 50%, or 1 in 2 chance, to have inherited the *RAD51D* mutation as well. All individuals in the family can inherit and pass along *RAD51D* mutations to their children. Mutations in *RAD51D* do not skip a generation. If someone in your family did not inherit the *RAD51D* mutation, they cannot pass it along to children.

We recommend that young adults wait until they are at least 18 years old before seeking genetic testing. However, people may wait to do testing until the age their medical care would change if they carried a *RAD51D* mutation, and/or they feel emotionally ready to learn this information.

**Family Planning**

Rarely, a child can inherit two copies of the *RAD51D* gene with a mutation, one from each parent. Children who are born with two non-working *RAD51D* genes may have a condition called Fanconi anemia. Fanconi anemia can be a serious childhood condition associated with multiple issues, including physical differences and an increased risk for childhood cancer. Fanconi anemia is a rare condition, and the *RAD51D* gene is not a common cause for this disorder. We recommend that if a parent is found to have a *RAD51D* mutation, that their reproductive partner also consider genetic testing. A child can only inherit two copies of a *RAD51D* mutation if both parents carry a mutation in this gene.

Further information about this, including options for lowering the chance of having a child with Fanconi anemia, can be discussed with a genetic counselor.

**Glossary of Cancer Genetics Terms**

- **Early detection**: The process of finding cancer when it is just starting to develop.
- **Carrier**: A person who has a single mutation in a gene.
- **Gene**: A small piece of DNA that gives instructions for a specific trait.
● **Heterozygous**: Having a single mutation in a gene.

● **Inherited**: Passed from biological parent to child (through egg and/or sperm).

● **Lifetime cancer risk**: The chance that a person will develop cancer in their life. This is sometimes defined as the chance of developing cancer by the age of 75 or 80.

● **Mutation**: A change in a gene that prevents it from working correctly. Also called likely pathogenic/pathogenic variant.

● **Risk-reducing surgery**: Surgery to remove healthy tissue or organs before cancer develops. Also called prophylactic surgery.

● **Surveillance**: Screening tests or procedures to look for early signs of cancer development or cancer returning (recurrence).

● **Female**: Refers to sex assigned at birth.

● **Male**: Refers to sex assigned at birth.

● **Cisgender**: A person whose sex assigned at birth matches their gender.