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Genomic
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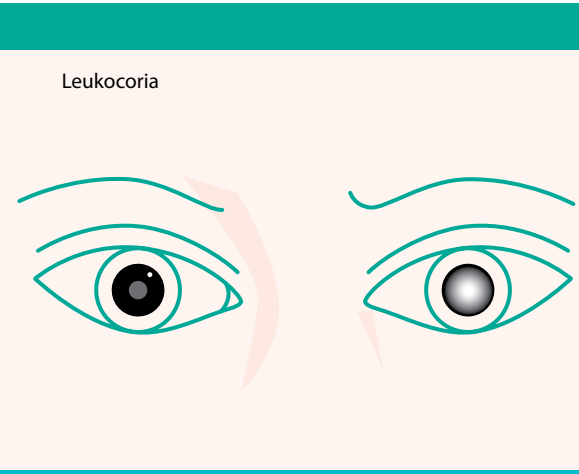
Heritable Retinoblastoma



SingHealth

What is heritable or hereditary cancer?

Heritable or hereditary cancer makes up about 5-10% of all cases of cancer. Some genes function to protect us from cancer. When they are not working well, it causes hereditary cancer. We refer to genes that are not working well as faulty genes.

Individuals who carry a faulty cancer gene(s) have a higher chance of developing certain cancers over their lifetime compared to the general population. The types of cancers that they may be at increased risk of will depend on the gene(s) involved.

If you have a faulty cancer gene, you may be at increased risk of developing certain cancers. As genes are shared among family, other family members may have inherited the faulty gene and may be at increased risk of cancer too.

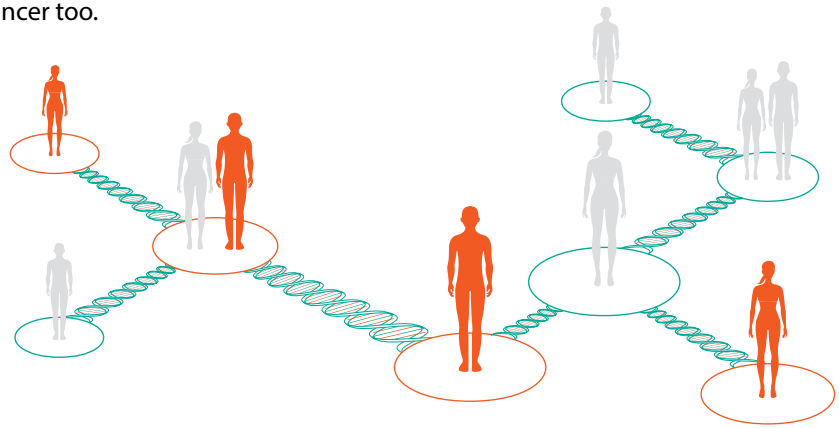
What is genetic testing?

Genetic testing is offered to individuals where a hereditary cause of their personal and/or family history of cancer is suspected.

Genes contain the instructions that our body reads to carry out different functions. Genetic testing involves analysing your genes to understand if there are faults (i.e., mutations) that may increase the risk of diseases like cancer.

How is genetic testing done?

- Genetic testing is typically a one-time blood test.
- If a blood sample cannot be taken, other sample sources (e.g., skin or saliva) may be used.



What are the possible results of genetic testing?

There are 3 types of results you may receive:

Positive

Faulty gene(s) identified

General Population Risk — Elevated Risk

Increased risk of developing certain tumours and cancers (depends on faulty gene(s) involved)

Your family (parents, siblings, children and extended relatives) may have inherited the faulty gene(s) and should consider genetic testing to clarify this

Uncertain

Variant of Uncertain Significance (VUS)

Uncertain gene change(s) identified, unclear if these change(s) increase risk for tumours and cancers

General Population Risk — Elevated Risk

May be clarified by testing other family members

May be reclassified over time as 'positive' or 'negative' when more information is known

Negative

No faulty gene(s) identified

General Population Risk — Elevated Risk

Tumour and cancer risk is similar to that of general population

Test limitations will be explained in the context of your personal and family history of tumours and cancers

What is retinoblastoma?

Retinoblastoma is a rare form of eye cancer typically diagnosed in children before 7 years of age. It develops in the retina, a vital part of the eye that enables us to see colour and light.

It can occur in one (unilateral) or both (bilateral) eyes, though only one eye is affected in around two-thirds (60%) of all cases.

The diagnosis of retinoblastoma in young babies and toddlers may be made during routine eye examinations, following which the child should be referred to an eye specialist (ophthalmologist).

What are the features of retinoblastoma?

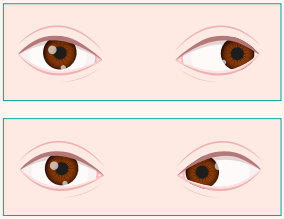
If parents notice one or more of the following features suggestive of retinoblastoma, they should consult an eye specialist as soon as possible.

- Leukocoria or a white pupil, especially with flash photography

Leukocoria (white pupil)

- Vision problems
- Red or irritated eyes
- Strabismus or misaligned eyes (one eye turns in/out/up/down when the child is looking straight ahead)

Strabismus (misaligned eyes)



Can retinoblastoma be cured?

Retinoblastoma can be cured in most cases, especially for those in which the disease is confined within the eye.

If left untreated, the cancer can spread out of the eye and to other parts of the body, where it becomes much harder to treat or may even result in loss of life. This is why early reporting of unusual symptoms is important.

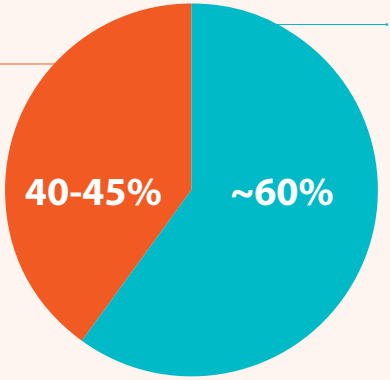
How common is retinoblastoma?

Retinoblastoma is not common. It makes up 2-3% of cancers diagnosed in children. It affects about **one in 15,000 to 18,000 children**.

What is heritable retinoblastoma?

There are two types of retinoblastoma

Heritable
Caused by a faulty *RB1* gene that was inherited, or could have developed at birth. It is found in every cell of the body.



Non-inheritable
Caused by chance events and/or environmental factors that resulted in a faulty *RB1* gene that is only found in the tumour cells of the eye.

It is important to identify and differentiate between non-inheritable and heritable retinoblastoma as the heritable form carries other health risks that are not found with the non-inheritable form. Family members may also be at risk if the heritable form is identified.

Differences between heritable and non-inheritable retinoblastoma

Heritable retinoblastoma	Non-inheritable retinoblastoma
• Faulty *RB1* gene present in all cells in the body • Usually affects both eyes (bilateral), though about 10% may only have one eye affected • Usually diagnosed at 1 year of age • Can be passed down in families	• Faulty *RB1* gene present only in tumour cells • Affects only one eye (unilateral) • Usually diagnosed at 2 years of age • Not passed down in families

Differences between heritable and non-inheritable retinoblastoma (continued)

Heritable retinoblastoma	Non-inheritable retinoblastoma
Children with heritable retinoblastoma are at an increased risk of: • Developing new retinoblastoma tumours • Developing other cancers • Passing down the condition to their future children Their other family members may also be at risk.	Children with non-inheritable retinoblastoma are usually not at risk of passing down the disease to their children, and their family members are not at risk. They also have a much lower risk of developing a second retinoblastoma tumour or other cancers, compared to those with heritable retinoblastoma.

What are the tumour and cancer risks associated with heritable retinoblastoma?

Heritable retinoblastoma is associated with a faulty *RB1* gene present in every cell of the body, which increases the lifetime risk of developing other tumours or cancers.

Tumour and cancer risks associated with heritable retinoblastoma as compared to the general population

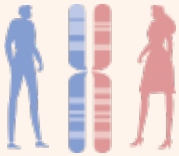
Tumour / cancer type	*RB1* faulty gene carrier risk *(50-60 years after diagnosis)*	General population risk
Soft tissue cancer (soft tissue sarcoma)	7 - 9%	0.4%
Bone cancer (osteosarcoma)	4 - 7%	0.1%
Brain tumour	4%	0.6%
Skin cancer (melanoma)	3 - 4%	2.3%

Note: The conditions associated with a faulty RB1 gene and their risk estimates may change as more information is available.

How is heritable retinoblastoma inherited?

Heritable retinoblastoma follows a **dominant inheritance pattern**. This means that having one faulty copy of the *RB1* gene can result in an increased risk of cancer. It can affect both males and females.

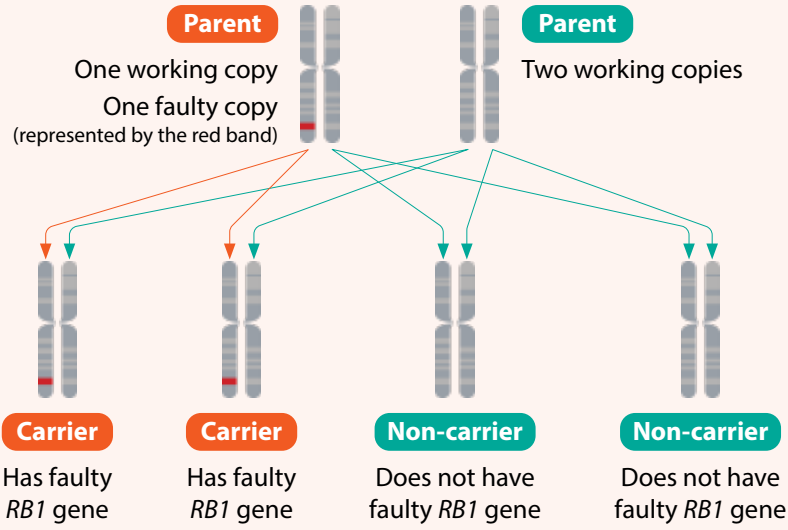
Everyone has 2 copies of each gene in their body's cells:



1 copy comes from our father

1 copy comes from our mother

Dominant inheritance pattern



- A parent with a faulty *RB1* gene has a 50% chance of passing down their faulty gene to their children.
- A child carrying the faulty *RB1* gene also has a 50% chance of passing down the faulty gene to each of their future children.
- Relatives of the carriers of the faulty *RB1* gene may have also inherited the same faulty gene.

Not all children with heritable retinoblastoma inherited the faulty *RB1* gene from one of their parents.

Often, both parents are not carriers but the child has acquired a faulty *RB1* gene *(de novo)* at conception. As this child carries the faulty gene, they can pass it on to their future children, but their other family members would not be at risk.

While most people who have a faulty *RB1* gene develop retinoblastoma, some individuals who carry the faulty gene may not develop retinoblastoma or other cancers. Therefore, the disease may present differently among family members.

Who should undergo genetic testing for heritable retinoblastoma?

You should consider genetic testing if you meet one or more of the following criteria:

- Diagnosis of retinoblastoma at any age
- A family history of retinoblastoma
- A previously identified faulty *RB1* gene in a family member

How can your genetic test result help you / your family?

The genetic test result can help determine if the retinoblastoma is heritable or not.

1. Medical implications

If heritable, it will guide screening for other cancers you may be at risk for.

2. Familial implications

Your genetic test result can also help you understand if other family members are at risk of heritable retinoblastoma. They can subsequently consider their own testing (predictive testing) to clarify their carrier status to determine tumour and cancer risks.

Family members who ***have inherited*** the same faulty *RB1* gene may be at increased risk of tumours and cancer and can benefit from management options such as screening (to detect tumours and cancer at an early and manageable stage). Family members who ***did not inherit*** the faulty *RB1* gene can avoid unnecessary screening and worry. Their children will also not be at risk.

3. Family planning

Individuals with a faulty *RB1* gene can also consider reproductive options and antenatal screening when planning a pregnancy/family.

What can I do to manage my increased risk of cancer?

Screening

Retinoblastoma

- Regular eye examinations by an eye specialist

Skin cancer (melanoma)

- Regular self-examination of skin
- Note and discuss any new naevi (moles) with unusual or changing appearance with a skin specialist

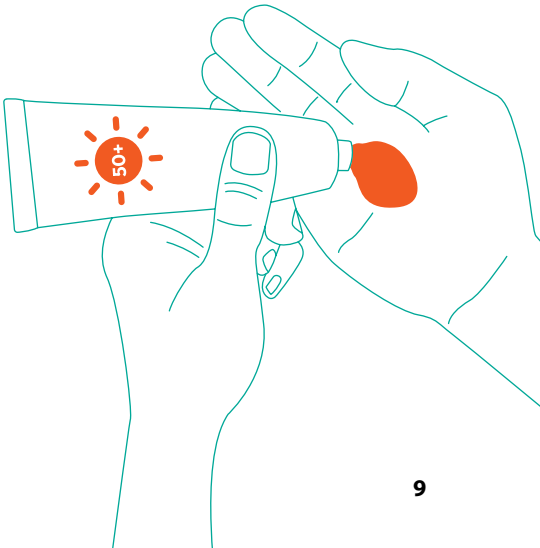
Other cancers
(brain tumours, bone cancer, soft tissue cancer)

- Brain or whole-body magnetic resonance imaging (MRI) scans may be recommended

Your managing doctor(s) will discuss screening recommendations with you in greater detail. The age, onset and frequency of screening may depend on your personal and/or family history of cancer. Screening guidelines may change as more information is known.

Lifestyle adjustments

- Avoid unnecessary radiation exposure where possible (including X-ray, CT scans and external beam radiation)
- Avoid smoking
- Practice sun-smart behaviour (e.g., wearing sunscreen)



Common Myths & Misconceptions

If my genetic test result is positive, it means that I have or will have retinoblastoma, or my retinoblastoma will recur.

FALSE. The genetic test result cannot determine the likelihood of cancer recurrence or the presence of cancer. A positive result only indicates an increased risk of getting cancer or a new cancer developing.

If my child tests positive, it means that my grandchildren will also have retinoblastoma.

FALSE. If your child has a positive genetic test result where a faulty *RB1* gene is identified, it means each of his/her future children has a 50% (1 in 2) chance of inheriting the faulty *RB1* gene.

My child looks a lot like me, so he/she must have inherited the faulty gene(s) since I have it.

FALSE. Genes that govern your appearance are different from the genes that determine the risk of retinoblastoma like *RB1*.

My child has heritable retinoblastoma and I have two other children, so one will inherit the faulty gene(s) and one will not, because there is a 50% chance.

FALSE. It is recommended for parents of a child with heritable retinoblastoma to undergo predictive testing to determine if he/she has a faulty *RB1* gene as well.

If a parent does carry a faulty *RB1* gene, all his/her children have a 50% (1 in 2) chance of inheriting the faulty gene. The genetic test result of one child does not impact the chances of the other child having heritable retinoblastoma.

If you have any questions, please contact:

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Weekends and Public Holidays: Closed

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