

This fact sheet describes the way in which some cancers can occur in a family because of a genetic factor. It provides an overview of how all cancer develops and describes when cancer is considered to be an inherited or familial condition.

### In summary

- **Cancer is very common in the community and mostly occurs just by chance**
- **Sometimes cancer occurs in families because of a shared environment such as high sun exposure or cigarette smoke**
- **Some rare families have an inherited faulty gene that increases the likelihood of developing cancer.**

### WHAT IS CANCER?

Cancer occurs when cells in the body continue to divide uncontrollably. This can happen in any tissue or organ in the body. A group of cells that has resulted from uncontrolled cell division and growth is called a tumour.

Tumours can be *benign* (not cancer) or *malignant* (cancer). *Metastatic* cancer occurs when cancer cells spread into other surrounding tissues or enter the circulatory system and travel to other parts of the body, producing new tumours.

### CELLS, DNA AND GENES

Our bodies are made up of millions of cells. Each cell contains a complete copy of our genetic information or DNA. Our DNA contains the instructions for growth and development and is packaged into chromosomes that contain all our genes. Genes provide a code for the proteins our body needs to function.

We all have two copies of every gene, one that is inherited from the mother, and one from the father. As we age and grow, our cells are continually dividing to form new cells by the process of cell division. This means our DNA is copied over and over again.

Some genes work together to instruct each cell how to copy its genes properly, and how to divide and grow in a controlled and orderly manner. They are known as growth control genes. There are many different ones in the body. For example, growth control genes that are active in the cells of breast tissue may be different to growth control genes that are active in the cells of the bowel.

### CANCER PROTECTION GENES

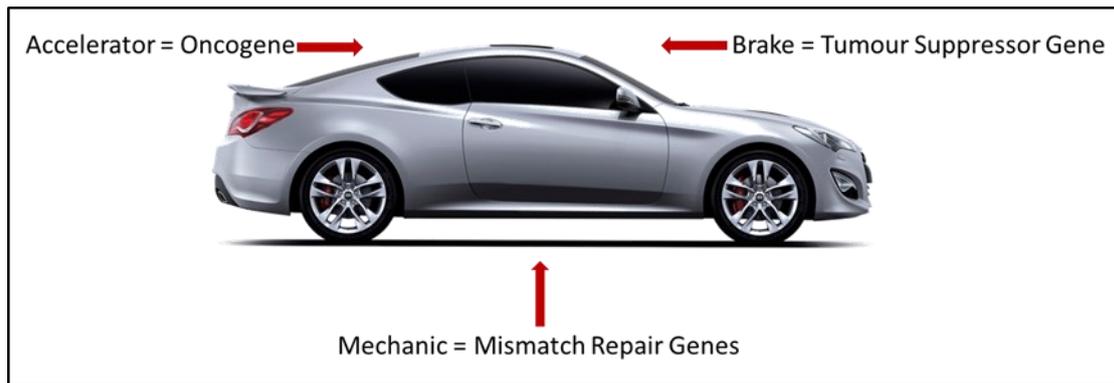
Since the growth control genes normally provide information to prevent uncontrolled cell division, they can be thought of as '**cancer protection**' genes.

There are different types of 'cancer protection' genes:

- **Tumour suppressor genes** are genes that act as the 'brakes' on uncontrolled cell growth. Cancer may occur when both copies of a tumour suppressor gene (both 'brakes') fail to work properly
- **Oncogenes** are the accelerators of cell division (they increase the rate of cell division). Cancer may occur when these genes are switched on inappropriately (too much accelerator)
- **Mismatch repair genes** help find and repair mistakes in the genetic information that can occur during cell division. The mismatch repair gene acts just like a 'spell checker' on the computer. Cancer may occur when changes to these genes results in failure to repair mistakes in the DNA.

Another way of thinking about how these genes work in the cells is to imagine that the genetic control of cell division is a car that is working well (see *Figure 31.1*).

For the car to work, the mechanisms to make the car move (the accelerator or oncogenes) and stop (the brakes or tumour suppressor genes) must be in balance. Also the mismatch repair genes are like the mechanic who keeps the car running smoothly.



**Figure 31.1:** The balance of cell growth and division is maintained by the ‘cancer protection’ genes just like a well-maintained car.

### HOW DOES CANCER DEVELOP?

Changes to the information in a ‘cancer protection’ gene in a cell of a body such as a breast or bowel cell may cause the process of cell division to be less well controlled. There will be a variation in the usual information in the gene and therefore the gene may be unable to issue its normal instructions to the cell. Cells that normally divide and grow in an orderly manner may grow and divide abnormally when their ‘cancer protection’ genes become faulty. A variation that makes the gene faulty is called a **mutation** or a **pathogenic variant**.

The cycle of cell division and growth continues throughout the lifespan and mutations can build up over this time. All cancers can, therefore be considered genetic in origin because they arise from accumulated changes in the normal ‘cancer protection’ genes that we all have.

A normal cell does not become a cancerous cell just because one copy of one ‘cancer protection’ gene becomes faulty. Mutations have to occur in a number of different ‘cancer protection’ genes in a cell, building up over time, before that cell becomes cancerous.

One way of representing this process is as a staircase where the bottom of the staircase represents a normal cell and the top a cancerous cell (*Figure 31.2*).

The steps of the staircase represent a progression of changes to the information that may occur in one or both copies of a number of different ‘cancer protection’ genes in a cell. Some of these changes will be mutations.

So for a normal cell to become cancerous, both copies of a number of different ‘cancer protection’ genes in the cell of a tissue or organ must become faulty over time.

### HOW DO MUTATIONS OCCUR?

Mutations can occur in a number of ways in a person. They can come about in the body over time (**acquired**), they can be **inherited** from one or both parents, or they can occur for the first time in a person for no apparent reason (**sporadic**).

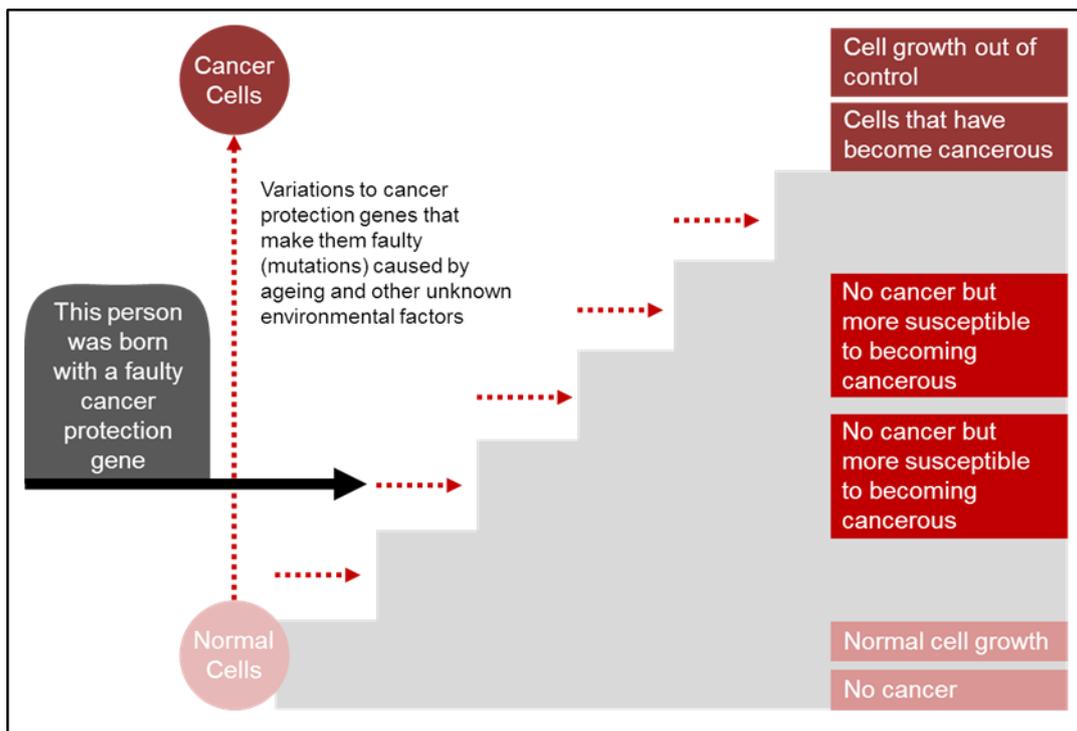
#### Acquired Mutations

DNA changes can come about due to things we experience during our life, for example radiation produced by the sun, certain chemicals, or other environmental factors. DNA changes may also occur as our cells are copied to enable us to grow or repair damaged cells throughout life as we age.

Although the body has an efficient system to repair these variations in the DNA as they occur, sometimes there is a breakdown in the cell’s repair system.

If a variation to the DNA occurs and is not repaired, it will be copied into all the cells arising from that cell. As with other DNA variations, if the gene message becomes faulty, a mutation is said to have occurred.

Body cells (not the egg or sperm) are called ‘somatic cells’ and therefore a mutation that occurs in a somatic cell is called a **somatic mutation**.



**Figure 31.2:** Changes build up in the different ‘cancer protection’ genes in the cells over time due to ageing and other environmental factors. Some of these changes make the ‘cancer protection’ genes faulty. Each step on the staircase to becoming cancerous cells represents a change in a copy of one of the many ‘cancer protection’ genes in the cells.

A somatic mutation will only affect the part of the body in that particular individual (*Figure 31.3*). Somatic cells are therefore not passed down to children or inherited.

Research is continuing to more fully understand the cause of specific mutations in the ‘cancer protection’ genes. However it is clear that ageing and our environment play major roles

### Inherited Mutations

Everyone is born with several gene mutations in their 20,000 or so total number of gene pairs. These are usually passed down in the father’s sperm or the mother’s egg.

Once that child has the mutation, they will have it for life and can also pass it on to their future children. This is an **inherited mutation**.

Inherited mutations can be passed down by only the father, only the mother or by both parents. The way in which the mutation/s will affect the child will depend on other factors as well as the mutation/s themselves.

Sperm and egg cells are called ‘germ cells’ and therefore mutations that are present in the genes of the egg or sperm are called germ cell or **germ-line mutations**.

### Sporadic Mutations

When a health condition is caused by a gene mutation that appears for the first time in a family, it is said to be **sporadic**. Sporadic genetic conditions come about when a spontaneous mutation occurs in the egg or sperm that went on to become that person.

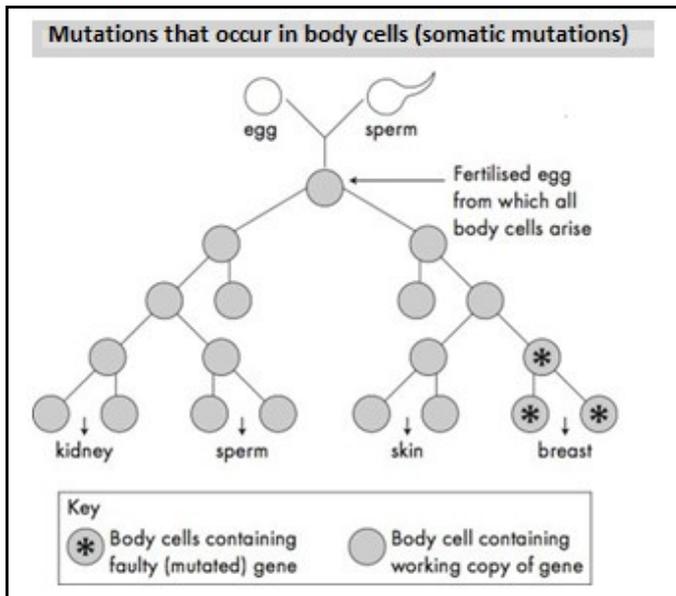
If a sporadic gene mutation occurs at the time of fertilisation but is not inherited from one of your parents, you can still pass it on to your future children. Your sperm or eggs will now contain this mutation.

### INHERITED PREDISPOSITION TO CANCER

In a small number of cancer cases (about 5%), a mutation in a ‘cancer protection’ gene is present in **all** the cells of a person from birth. This is due to an inherited or sporadic mutation.

As shown in *Figure 31.4*, if a mutation in a ‘cancer protection’ gene is in the egg or sperm (**germ cell mutation**), it will then be present in all the cells of the body of the individual arising from the fertilised egg.

When mutations in ‘cancer protection’ genes are present in the germ cells, the mutation can be passed on to a child.



**Figure 31.3:** Mutations in ‘cancer protection’ genes that occur in the body cells (somatic mutations) during life such as in the breast cells are confined only to the breast tissue. The cancer protection genes are normal in that person’s egg or sperm and therefore they will not pass on the gene mutation.

Most people are born having two working copies of each of the different ‘cancer protection’ genes in their cells. So that means that most people have not inherited a genetic predisposition to developing cancer.

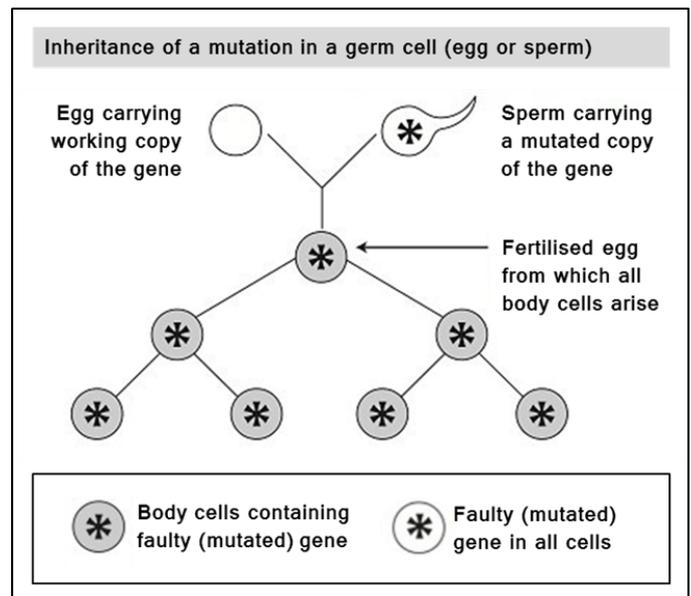
A small number of people inherit from a parent a mutation in one of the copies of their ‘cancer protection’ genes.

If a child is born with a mutation in one copy of a ‘cancer protection’ gene, the child has a higher than average risk of developing cancer in their lifetime. They are already a step up in *Figure 31.2*.

These individuals are carriers of a mutation in a ‘cancer protection’ gene and have inherited a predisposition to develop cancer.

A carrier may never develop cancer unless other cancer protection genes in the cells become faulty over the individual’s lifetime.

If cancer does develop, however, it may tend to do so earlier in their life. For the same reason, new cancers can develop in more than one place in the body.



**Figure 31.4:** Inheritance of a mutation in a ‘cancer protection’ gene in a germ cell (egg or sperm). The egg (from the mother) is carrying a working copy of the gene. The sperm (from the father) is carrying a faulty copy of the gene. Their offspring will have both a faulty copy and a working copy of the ‘cancer protection’ gene in all the cells of their body. This may also occur in the reverse situation

If someone does not carry a mutation in a ‘cancer protection’ gene, they still have the same chance of developing cancer as anyone else in the community

### A FAMILY HISTORY OF CANCER

Some families have a number of blood relatives who have been affected by cancer. A family history of cancer can be due to:

- Chance, because cancer is common
- Common environmental influences among family members
- An inherited gene mutation.

There are Australian guidelines for doctors that indicate for certain cancers, where there is a strong family history, the likelihood of the cancer being due to an inherited mutation in a ‘cancer protection’ gene. In these families, genetic counselling at a family cancer clinic can provide the most up to date information about determining if the cancer does involve an inherited faulty ‘cancer protection’ gene and discussion about genetic testing.

## WHAT IF YOU HAVE A FAMILY HISTORY OF CANCER?

### Compile a family health history

Documenting the health history of family members (blood relatives) over several generations is important in determining if a condition is running in the family. Ask about the family history of cancer on both your mother's and father's side of the family. It is important to note:

- How the individual is related to you
- The type of cancer they have or had
- The age of the individual when they was first diagnosed or when they died from the cancer.

### Discuss your family history with your Doctor

Many cancers can be cured if picked up at the earliest stage. Discuss your personal and family history of cancer with your GP.

### Genetic counselling and risk management

Some individuals with a strong family history may require referral by their GP to their local genetic counselling service or a specialist family cancer clinic (if available). Their risk of developing cancer, based on their family history, can be estimated and discussed in more detail.

The genetic counselling team may be able to:

- Clarify their chance of developing cancer based on family history
- Answer any questions they have about their family history of cancer
- Discuss what medical check-ups are appropriate
- Discuss the limitations, potential benefits, disadvantages and appropriateness of genetic testing
- In some cases, preventive surgery is considered. Research is continuing to investigate cancer prevention with drug therapy.

**Genetic testing** for mutations in the 'cancer protection' genes is complex.

First, the mutation has to be identified in a family member who has or had the cancer. This is called a **mutation search** and may take considerable time.

Second, and only if a mutation is found, other family members without cancer can be tested to determine if they have inherited the faulty gene. This is called **predictive genetic testing**.

### Lifestyle may help

The progression to cancer requires mutations to build up in a number of the 'cancer protection' genes in the cells over time. The reason why these mutations occur is thought to be a combination of genetic factors, environmental factors and the process of ageing. Research is currently being undertaken to more fully understand the cause of specific gene mutations.

However researchers do believe a balanced diet high in fibre and low in fat, no smoking and living a healthy lifestyle will reduce the chance of developing cancer.