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Important points

- A family history of cancer can occur:
 - Just by chance, because cancer is common
 - Because family members are exposed to the same environmental factors
 - Because a predisposition to cancer is running in the family, though this is rare
- We all have in our cells two copies of a number of different genes that control orderly growth and division of our cells throughout life (growth control genes)
- When these growth control genes become faulty in cells in a particular part of the body, eg breast tissue, the cells divide and grow out of control and accumulate to form a cancer
- Cancer occurs as a result of uncontrolled cell division and growth. These growth control genes can therefore be thought of normally acting as ‘cancer protection’ genes
- All cancers can be considered genetic in origin because they arise from changes in the normal ‘cancer protection’ genes that we all have. A change in the information in a ‘cancer protection’ gene that makes the gene faulty is called a mutation
- The cause of the changes that make the ‘cancer protection’ gene faulty is unknown, but may be due to a combination of genetic factors, environmental factors, and the process of ageing
- The development of cancer is not a quick or simple process. It is a progression involving a build-up of changes in a number of different ‘cancer protection’ genes in the cells of the body tissues over a lifespan. This is why the development of cancer can take many, many years and is more often seen in older people
- Most people are born having two working copies of each of the different ‘cancer protection’ genes in their cells. This means that most people have not inherited a genetic predisposition to developing cancer
- A small number of people inherit from a parent a change in one of the copies of one of their ‘cancer protection’ genes that make the gene copy faulty. These people are carriers of a faulty ‘cancer protection’ gene and have inherited a predisposition to develop cancer ie. are at increased risk
- The pattern of inheritance of predisposition to cancer in the family can be different depending on which gene is involved
- A carrier of a faulty ‘cancer protection’ gene may never develop cancer unless other cancer protection genes in the cell become faulty over that 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
- If someone does not carry a faulty ‘cancer protection’ gene they still have the same chance of developing cancer as anyone else in the community
- Genetic counselling can clarify a individual’s risk and discuss their options for genetic testing, its limitations, advantages and disadvantages and available prevention and early detection strategies

What is cancer?

Each cell contains a copy of the genetic plan for our growth, development and health. This genetic plan comes in the form of the genes, located on chromosomes that we inherit from our parents. The genes contain the information for the body to make all the necessary structural components and chemicals to ensure normal function.

There are two copies of every gene, one inherited from our mother and one inherited from our father. For more information on genes, see Genetics Fact Sheet 1.

As we go through life our cells are continually growing and being replaced. New cells are formed from existing cells by a process called cell division. Each time a cell divides it has to make a copy of all of its contents, including its genes, so that the new cells have the same genes or information as the old.

A number of different genes act together to instruct each cell how to copy its genes properly, and how to divide and grow in a controlled and orderly manner (ie. *growth control genes*). Different

growth control genes work in the cells of different organs and tissues in the body ie. 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 occurs when cells in the body become abnormal and grow out of control and they have the ability to spread to other parts of the body (metastasise). Cancer is a result of uncontrolled cell division and growth.

Uncontrolled cell division and growth leading to cancer can occur in any tissue or organ in the body. Cancer is named according to the place where it starts growing: for example, when it occurs in the breast it is called breast cancer.

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 cancerous cells spread into other surrounding tissues, or enter the circulatory system and travel to other parts of the body, producing new tumours

‘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. We all have two copies of a number of different ‘cancer protection’ genes in our cells, one copy inherited from our mother and one copy inherited from our father.

There are different types of ‘cancer protection’ genes:

- **Tumour suppressor genes**
- 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**
- Oncogenes are the accelerators of cell division (ie. they increase the rate of cell division). Cancer may occur when these genes are switched on inappropriately (too much accelerator)
- **Mismatch repair genes**
- These are genes that are involved in finding and repairing mistakes in the genetic information that can occur when the genes are copied to make new cells. The mismatch repair gene acts just like a ‘spell checker’ on the computer. Cancer may occur when damage 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 47.1).

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.

Changes in the ‘cancer protection genes’

If a change occurs in the information in one of these ‘cancer protection’ genes in a cell of a tissue or organ such as a breast or bowel tissue, the prostate or skin, that cell’s division may be less well controlled.

Some of these changes will make the gene unable to issue its normal instructions for the cell to divide in an orderly manner ie. the gene becomes faulty. A change that makes the gene faulty is called a mutation (see Genetics Fact Sheets 4 & 5).

Cells that normally divide and grow in an orderly manner may grow and divide abnormally when their ‘cancer protection’ genes become faulty.

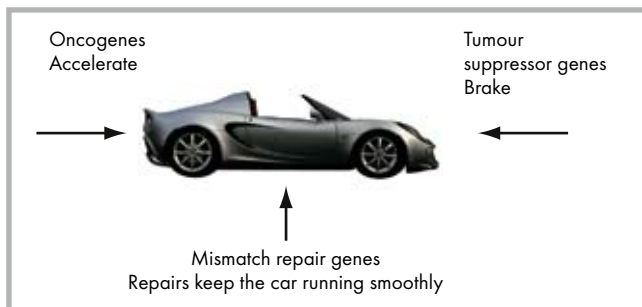


Figure 47.1: The balance of cell growth and division is maintained by the ‘cancer protection’ genes just like a well-maintained car.

What role do faulty ‘cancer protection’ genes have in the development of cancer?

The cycle of cell division and growth continues throughout the lifespan. Changes (*mutations*) in the ‘cancer protection’ genes that make them faulty and impair their ability to protect against cancer 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 in the cells of the tissues of the body.

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 to think of the path to cancer as a staircase where the bottom of the staircase represents a normal cell and the top a cancerous cell (Figure 47.2).

The steps of the staircase represent a progression of changes 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 that make the ‘cancer protection’ gene faulty.

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

What causes mutations to build up in the ‘cancer protection’ genes over our lives?

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

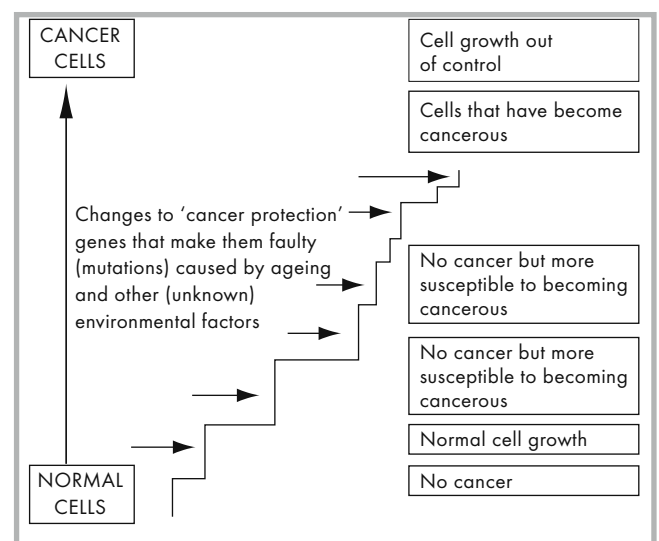


Figure 47.2: Changes build up in the different ‘cancer protection’ genes in the cells over time due to ageing and other environmental factors. Some of these changes make the ‘cancer protection’ genes faulty. Each step on the staircase to becoming cancerous cells represents a change in a copy of one of the many ‘cancer protection’ genes in the cells.

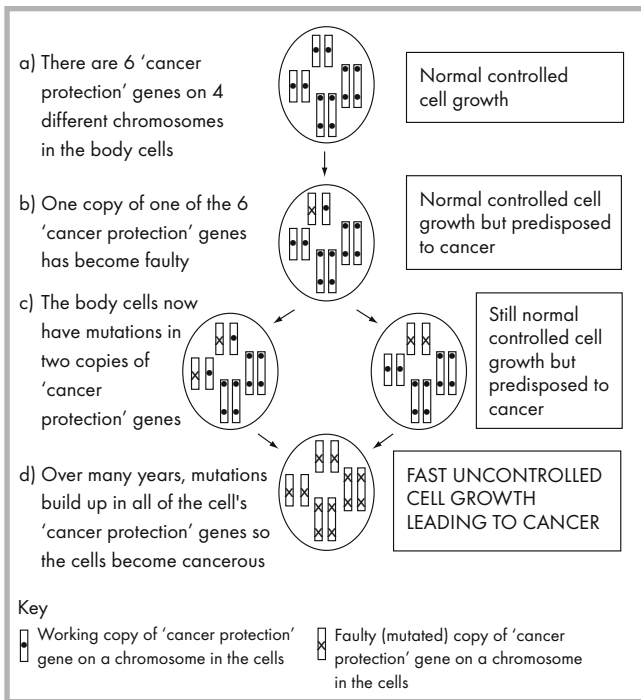


Figure 47.3: Mutations that build up in the 'cancer protection' genes in cells.

Ageing

Changes build up in our genes as we age, most likely due to mistakes in the repair process as 'spelling mistakes' are made in the copying of the cells during our lives.

Environmental factors

One example of an environmental factor that can damage our DNA is sun exposure. Other environmental factors include exposure to various toxins and radiation, lifestyle and diet.

When faulty 'cancer protection' genes occur in our body cells

All the cells of the body contained in the tissues and organs, other than the egg or sperm cells, are called **somatic cells**. The progression to cancer in a somatic cell over an individual's lifetime is represented in Figure 47.3.

- (a) While there are 46 chromosomes (23 pairs) in each cell, only four chromosome pairs are represented on which are located six different 'cancer protection' genes. There are two copies of each gene on the chromosomes in the cell. The first step up the staircase to cancer in the cell occurs when a change occurs in one of the copies of a 'cancer protection' gene in these cells making the copy of the 'cancer protection' gene faulty. This change is a mutation.
- (b) Because the other copy of this 'cancer protection' gene is still working properly, the rate of cell division and growth remains basically unaltered but the cells are now more susceptible to becoming cancerous.
- (c) A mutation occurs in either the second copy of the 'cancer protection' gene on its partner chromosome or in a copy of an additional other 'cancer protection' gene on a different chromosome. Either way, the cells have taken another step

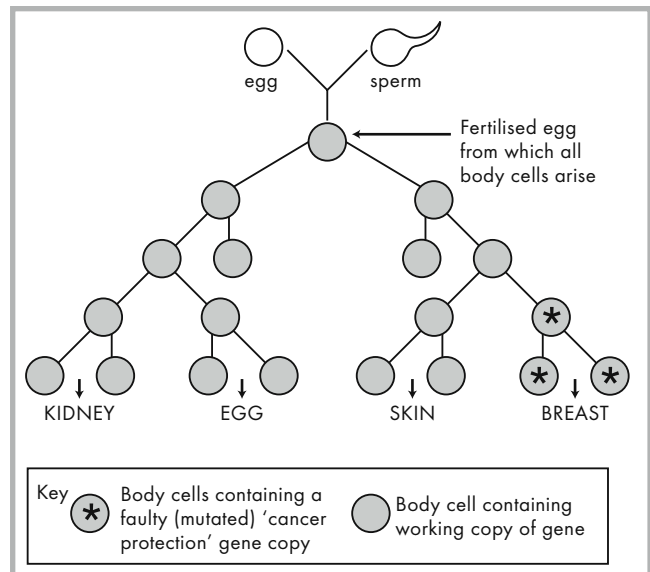


Figure 47.4: Mutations in 'cancer protection' genes that occur in the body cells (somatic mutations) during life such as in the breast cells are confined only to the breast tissue.

up the staircase to becoming cancerous. Normal controlled growth, however, is still occurring and the cells are simply more susceptible to cancer.

- (d) Over time, mutations have built up in all the represented six different 'cancer protection' genes in these cells. It is only now that the cells have become cancerous as all the 'cancer protection' genes in these cells are no longer working properly. Most people are born with somatic cells that have the right information in both copies of each of their different 'cancer protection' genes as in Figure 47.3a.

When a mutation occurs in one copy of a 'cancer protection' gene in any of these body cells (a **somatic mutation**), the cell in which it occurs is now predisposed to becoming cancerous (Figure 47.3b).

- As that cell continues to divide, the mutation is also copied into the new cells
- When other mutations occur in the other 'cancer protection' genes in the cell over time, the faulty genes are also passed to the new cells

Over time, sometimes many years, further mutations may occur in the other copy of the same gene, and in other additional 'cancer protection' genes (Figures 47.3c and 47.3d), leading to uncontrolled cell growth and division. The cells now grow out of control in that tissue and become cancerous.

The mutations in the 'cancer protection' genes will only affect the cells in a particular tissue eg breast tissue of an individual (Figure 47.4) and these mutations cannot be passed to the man or woman's children.

Faulty 'cancer protection' genes in the egg and sperm cells

The egg and sperm cells are called the **germ cells**. In a small number of cases of cancer, for example, about 5% of the common cancers, a faulty 'cancer protection' gene is present in **all** the cells of a person ie. their somatic cells as well as their egg or sperm cells.

There are several possible reasons why a faulty ‘cancer protection’ gene is present in both the somatic and germ cells of a person. This may occur because it has been passed down through the family from generation to generation (**inherited**). Alternatively, it may have occurred for the first time in the egg or sperm from which that person arose.

Inherited predisposition to cancer

As shown in Figure 47.5, 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 faulty ‘cancer protection’ gene can be passed on to a child.

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 change in one of the copies of one of their ‘cancer protection’ genes that makes the gene copy faulty.

- If a child is born with one copy of a ‘cancer protection’ gene that is already faulty, the child has inherited from a parent a higher than average risk of developing cancer in their lifetime. They are already at step ‘b’ in Figure 47.3
- These individuals are carriers of a faulty ‘cancer protection’ gene and have inherited a predisposition to develop cancer
- A carrier of a faulty ‘cancer protection’ gene 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
- If someone does **not** carry a faulty ‘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 or had cancer. They are said to have a family history of cancer.

The cancer in the family can be due to:

- Chance, because cancer is common
- Common environmental influences among family members
- An inherited faulty ‘cancer protection’ gene running in the family

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 predisposition. In these families, genetic counselling (see Genetics Fact Sheet 3) can provide the most up to date information about determining if the cancer does involve an inherited predisposition and appropriateness and availability of genetic testing.

What can be done if cancer is running in the family?

See the following Genetics Fact Sheets for more information about some different types of cancer where a small number of cases involve an inherited predisposition:

- Genetics Fact Sheet 48: Breast and Ovarian Cancer
- Genetics Fact Sheet 49: Bowel Cancer
- Genetics Fact Sheet 50: Melanoma
- Genetics Fact Sheet 51: Prostate Cancer

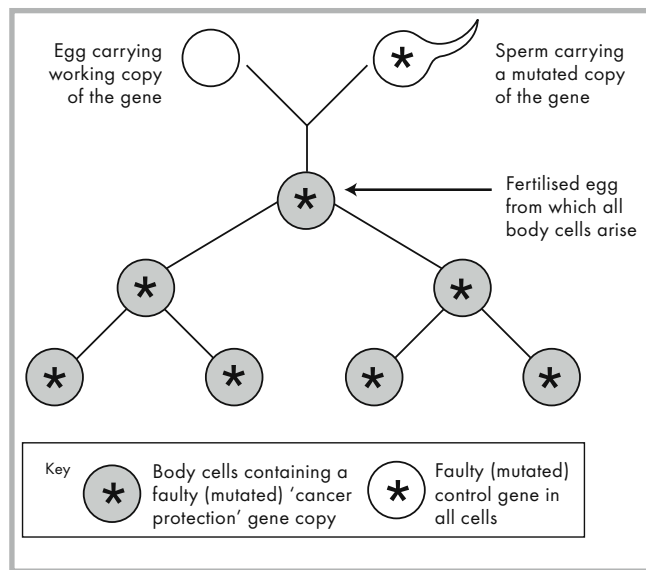


Figure 47.5: Inheritance of a mutation in a ‘cancer protection’ gene in a germ cell (egg or sperm). The egg (from the mother) is carrying a working copy of the gene. The sperm (from the father) is carrying a faulty copy of the gene. Their offspring will have both a faulty copy and a working copy of the ‘cancer protection’ gene in all the cells of their body. This may also occur in the reverse situation.

(a) 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 it was first diagnosed or when they died from the cancer

A guide to documenting a family health history is available from the Centre for Genetics Education.

Anyone with concerns about a family history of cancer can seek advice from their doctor. It is important to keep the family health tree up-to-date as family members are born, die or develop new conditions.

(b) Genetic counselling

Some individuals with a strong family history may require referral 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 (see Genetics Fact Sheet 3).

The genetic counselling team may be able to:

- Clarify their chance of developing cancer based on his/her 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 (see Genetics Fact Sheet 21)

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** (see Genetics Fact Sheet 21)

(c) Prevention

In some cases, preventive surgery is considered. Research is continuing to investigate cancer prevention with drug therapy.

The progression to cancer requires mutations to build up in a number of the 'cancer protection' genes in the tissues over time. If the environmental factors could be identified that cause these mutations, preventive strategies could be implemented.

As yet, there is limited understanding of these factors although a 'best bet' may include a healthy diet and a healthy lifestyle.

(d) Detecting cancer early

The earlier a cancer is found, the more successful the outcome of treatment is likely to be.

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 3, 4, 5, 21, 48, 49, 50, 51

Information in this Fact Sheet is sourced from:

National Health and Medical Research Council. (1999). *Clinical Practice Guidelines Familial aspects of cancer: a guide to clinical practice* [online]. Available from: <http://www.nhmrc.gov.au/publications/synopses/cp67syn.htm>. [Accessed June 2007]

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