Fact sheet **02**

VARIATIONS IN THE GENETIC CODE

DNA stands for DeoxyriboNucleic Acid and forms the 'instruction book' of our bodies.

IN SUMMARY

- DNA contains the instructions for growth and development and is in cells that make up the body
- Everyone's DNA is somewhat different; variations in our DNA make us unique
- Some DNA variations are inherited from our parents, some appear from birth while others are picked up throughout life
- Generally, DNA variations that have no impact on our health are called benign variants or polymorphisms. These variants tend to be more common in people.
- A variation in a gene that causes a health or developmental condition is called a **pathogenic variant** or **mutation**.

DNA AND GENES

Our DNA is made up of sections that code for proteins and sections that do not code for proteins. Genes are sections of DNA that code for the proteins that the cells of our body needs to work properly. Proteins are important for the cells and our body to work properly and to prevent problems with health or development.

Our protein coding DNA, our genes, contain less variation. Sections of our DNA that do not code for protein contain more variation. Some non-coding DNA separate genes from each other along the chromosomes and there is increasing evidence that it has a role in turning genes **on** and **off**. This non-coding DNA may therefore control how the genome works.

People generally have the same number and sequence of protein coding genes so that the same messages are sent to the body. There can, however, be small variations between individuals in the DNA code. Members of the same family tend to be more similar in their DNA code than unrelated individuals.

An example of this is eye colour. Everyone has genes that determine eye colour, but changes in these genes can make eye colour vary. This is why some people have blue eyes, some brown and some hazel. The same gene can send different messages because of variations in the messages.

Similarly, there may be small variations in our DNA that may affect how our bodies grow and develop.

DNA VARIATIONS

Variations in the DNA code can happen during our life for a variety of reasons including exposure to radiation, certain chemicals, by chance or other unknown factors. Ageing is one of the most common causes of genetic variation. Throughout our life, our cells are continually being replaced. This means cells and their DNA are copied over and over again. DNA variations accumulate and can have an impact on our health.

The genes in our DNA provide the instructions for proteins, which are the building blocks of the cells that make up our body. Although we all have variation in our genes, sometimes this can affect how our bodies grow and develop. Generally, DNA variations that have no impact on our health are called **benign variants** or **polymorphisms**. These variants tend to be more common in people. Less commonly, variations can change the gene so that it sends a different message. These changes may mean that the gene does not work properly or works in a different way that is harmful. A variation in a gene that causes a health or developmental condition is called a **pathogenic variant** or **mutation**.

Content updated July 2020

GENE VARIANTS

Everyone is born with several pathogenic variants in their 20,000 or so total number of gene pairs. Depending on other factors, these variants may or may not cause health conditions.

Most of the time, pathogenic variants cause no problem because genes come in pairs. This means that even when one gene copy has a variant that makes the gene not work properly, the other gene copy is working and can still send the right message to the body. These are known as **recessive gene variants**.

In some cases, however, it is important to have both gene copies working correctly. So, in these cases, even though only one copy of the gene is not working properly, and the other is working, a health condition may still happen. These are known as **dominant gene variants**.

Other gene variations may make a person susceptible to particular conditions but they will never develop the condition unless they are exposed to particular environmental or other genetic triggers. These are known as **multifactorial** *or* **susceptibility gene variants**.

In some cases, having a particular change in your DNA can be beneficial to a person. For example, in regards to the condition called thalassaemia, people who have one copy of their thalassaemia gene working and the other copy of the gene is not working, are less likely to develop malaria, than people who have two working copies of the gene.

INHERITED, SPORADIC AND ACQUIRED VARIANTS

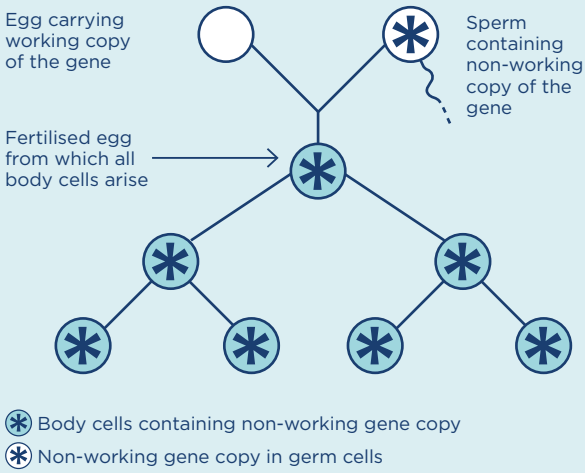
Variants can happen in a number of ways in a person. They can be **inherited** from one or both parents, they can happen for the first time in a person for no known reason (**sporadic**) or they can come about in the body over time (**acquired**).

Inherited

Variants may be passed down in the father's sperm or the mother's egg.

Figure 2.1:
Inheritance of a variant from 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 copy of the gene that has a variant, making it not work properly (a pathogenic variant). Children inheriting this will have both a non-working copy of the gene with the variant and a working copy of the gene in all the cells of their body. This may also happen in the reverse situation.

Inheritance of a pathogenic variant in a germ cell (egg or sperm)



If a variant is **inherited**, that person will have it for life and may also pass it on to their future children.

Figure 2.1 shows a variant being passed down through the sperm only. Inherited variants can be passed down by only the father, only the mother or by both parents. The way in which the variant(s) will affect the child will depend on other reasons as well as the variant(s) themselves.

Sperm and egg cells are called 'germ cells' and therefore variants that are present in the genes of the egg or sperm are called germ cell or germ-line variants.

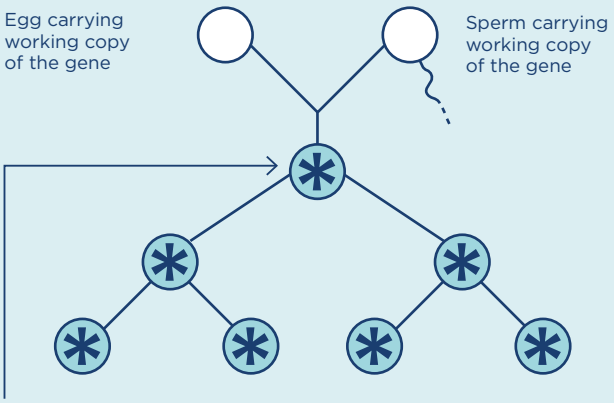
If you have inherited a gene variant from one or both of your parents, you will also possibly pass it on to your future children.

Sporadic

When a health condition is caused by a gene variant that appears for the first time in a family, it is said to be **sporadic**.

Figure 2.2:
Variations in genes that make the gene not work properly can happen very early during fertilisation of the egg and sperm. The variant is not inherited from a parent but all future cells of the baby have the variant.

Variation developing after fertilisation (non-inherited)



Fertilised egg develops a new variation in a gene that makes it not work properly (pathogenic variant), causing all of the **baby's cells** to carry the copy of the gene with the variant

- Body cells containing non-working gene copy
- Germ cells (egg and sperm) containing working copy of the gene

Sporadic genetic conditions come about when a **spontaneous** variant in a gene that makes it not work properly happens at the time of fertilisation. Although it 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 variant (see *Figure 2.2*)

Acquired

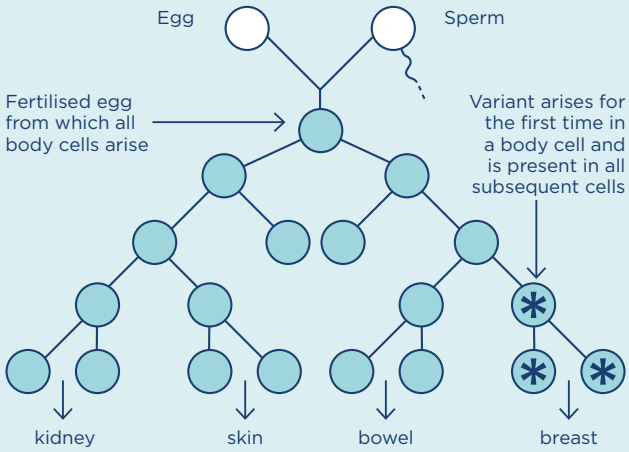
Variations in the DNA code can happen during our life for a variety of reasons including exposure to radiation, certain chemicals or other unknown environmental factors.

DNA variations may also happen as our cells are copied to enable us to grow or repair damaged cells throughout life.

As with other DNA variations, if the gene sends a message that is not working properly, a pathogenic variant has happened.

Figure 2.3:
Variants in somatic cells (body cells) may only affect one specific area, such as the breast tissue.

Variants that happen in body cells (somatic variants)



- Body cells containing the non-working gene copy
- Body cells containing working copy of the gene
- Germ cells (egg and sperm) containing working copy of the gene

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

If a variation in the DNA happens and is not repaired, it will be copied into all the cells arising from that cell (see *Figure 2.3*).

Body cells (not the egg or sperm) are called 'somatic cells' and therefore a variant that happens in a somatic cell is called a **somatic variant**.

In *Figure 2.3*, the somatic variant has arisen in a gene within a cell of the breast tissue only, and so cannot be passed on to a child.

A somatic variant may only affect the part of the body in that particular individual. Somatic cells are therefore not passed down to children or inherited.