

Genes contain the instructions for growth and development. Some gene variations make the gene faulty so that the message is not read correctly or is not read at all by the cell. A variation in a gene that makes it faulty is called a **mutation** or **pathogenic variant**.

In summary

- A mutation alters the gene message so that it no longer sends the correct information to the cells
- Mutations are present in all of us however, there are other factors which affect how they impact on our health
- Some mutations are passed down through a family, while others may be acquired throughout life
- Genes are made up of a DNA code
- There are different types of mutations when you look closely at the DNA code.

Our body is made up of millions of cells, and in each cell there are instructions, called **genes**, that make all the necessary structural components and chemicals for the body to function. These genes are packaged onto long strands known as **chromosomes**.

We all have 46 chromosomes arranged into 23 pairs. One copy of each pair is inherited from our mother and the other from our father. The first 22 chromosome pairs are numbered and are known as **autosomal chromosomes**. The 23rd pair is made up of the **sex chromosomes** called X and Y. Males have an X and a Y chromosome and females have two copies of the X chromosome.

A CLOSE LOOK AT DNA, GENES AND CHROMOSOMES

DNA is found along the chromosomes and can be thought of like an extremely long thin string, made up of a sequence of chemical units called bases. There are four different types of bases, **Adenine (A)**, **Cytosine (C)**, **Guanine (G)**, and **Thymine (T)**.

The bases that form DNA are grouped together in batches of three, which makes it possible for the cell to read the instruction sequence.

Each three letter sequence forms what is called a **codon**. An example of the code in a very small part of a gene may be TAC GCC CAG CAG TCA CTG.

When these codons are read as part of a gene, they provide the cell with the instructions to build a **protein**.

Proteins are important in controlling specific functions in the cells, muscles, organs and many other parts of the body.

It is important that the correct gene message is read in order for the correct protein to be built.

The way that a protein is made depends on the DNA messages in the gene.

The three letter codons *code* for specific amino acids. It is these amino acids which build up to form the proteins.

Codons do not always code for an amino acid.

Some have other specialised messages for the cell such as *stop* or *start* and help the cell recognise where the actual gene messages begin and end.

Only about 2% of the entire DNA in the human cell (the human genome) is made up of genes that contain the information for making proteins.

The coding DNA sequence within a gene is called an **exon** (because it is expressed).

Other sections of DNA do not code for proteins and are referred to as *non-coding DNA*.

Genes are strings of codons arranged in a specific order.

- Just like in a recipe for a cake, the ingredients must be right and added together in the right order. A codon is therefore like a word in a recipe for a protein

- If the recipe does not work properly or is faulty, the protein may not be produced in the right amount or it may not be able to function as it should in the cell. In some cases, this can cause a genetic condition.

The sequence of letters in a gene, in sets of three, contain the instructions for our cells to start making a protein, to put the amino acids into the protein in the right order and to stop when the protein is complete.

LOOKING FOR MUTATIONS IN THE GENETIC CODE

If the sequence of DNA letters in a gene is not able to be read in the correct way, the protein:

- May not be produced in the right amount
- May be produced in a form that will not function
- Is not produced at all.

This can lead to health concerns and may be recognised as a genetic condition.

The first step in determining the cause of a genetic condition is to locate the gene involved. The location of many of the genes in humans is now known.

The next step is to study the sequence of letters in the gene or surrounding the gene in a person's cells. It is important to determine if the sequence of codons in the recipe of that gene is correct.

Genetic testing aims to determine whether a person has or does not have a mutation in a particular gene. This can be important information for both that person and their family for a number of reasons:

- Genetic testing can lead to the diagnosis of a genetic condition in that individual or other members of their family
- For some common conditions, the results of a genetic test may show that a person is at an increased chance of developing a particular condition. This is known as *predictive testing* for conditions such as familial breast cancer

- More rarely, a genetic test can determine whether a person will develop a condition, based on the presence of a mutation. This can be identified long before any symptoms are present, and is called *presymptomatic genetic testing*. An example of a condition where this is possible is called Huntington disease.

The effect a mutation has on a person's growth, development or health is determined by a number of factors including how it affects the gene product (the protein); which cells in the body carry the mutation; and when the mutation arose in that individual.

TYPES OF MUTATIONS

There are a number of different types of variations in genes that make them faulty (gene mutations) that have been discovered.

a) Spelling changes in the code

Changing the spelling of a word in the message by substituting one letter with another is called a **point mutation** (*Figure 3.1a*).

DNA variations that cause a different amino acid to be included in the protein are called **missense** changes.

DNA variations that cause an early stop message in the protein are called **nonsense** changes.

b) Deletion of a code word

A mutation can also occur when part of the gene is 'deleted' from the genetic code (*Figure 3.1b*). If this occurs, the message will be too short and therefore will not make the correct protein.

c) Insertion of a code word

An insertion mutation occurs when extra DNA is 'inserted' in to the genetic code (*Figure 3.1c*). If this occurs, the message will be too long and therefore will not make the correct gene product or protein.

d) Repeated code words

Another type of gene mutation is called a **trinucleotide repeat** where certain code words are repeated in a sequence more often than usual (*Figure 3.1d*).

	Correct message:	Faulty message:
(a) Point mutation	TAG GCC CAG CAG <u>TCA</u> CTG	TAG GCC CAG CAG <u>TAA</u> CTG
(b) Deletion mutation	TAG GCC CAG <u>CAG TCA</u> CTG	TAG GCC CAG <u>CAG</u> CTG
(c) Insertion mutation	TAG GCC CAG <u>CAG TCA</u> CTG	TAG GCC CAG <u>CAG TCC TCA</u> CTG
(d) Increased repeat mutation	TAG GCC <u>CAG CAG</u> TCA CTG	TAG GCC <u>CAG CAG CAG CAG</u> <u>CAG</u> TCA CTG

Figure 3.1: Types of mutations which lead to a faulty gene message

Many genes contain repeated sequences of the three letter DNA codes as part of their normal message.

The number of code words that are repeated within the message or in the information controlling the message's production is important for the way a gene works.

If the number of repeats increases over a critical level, the gene can become *unstable* and may develop even more repeats of the code words as the gene is copied.

An increase in the number of repeated code words may occur during the production of the egg or sperm.

Some genetic conditions can be caused by different mutations that occur in the same gene in different people.

What this means is that in some people, the condition may be due to a **point mutation**, while in others it may be a **deletion** in the same gene.

FACTORS THAT CAN INFLUENCE HOW A MUTATION AFFECTS THE BODY

Since the chromosomes come in pairs, there are also two copies of each of the genes. The exception to this rule applies to the genes carried on the sex chromosomes called X and Y.

A mutation in a gene will affect the body differently depending on how much it changes the resulting protein, how critical that protein is to the body and how much of that protein is needed in the body.

If a DNA variation occurs in only one of the pair of genes and this causes a health condition, it is called a **dominant mutation**.

If a health condition only occurs when both copies of the gene have a variation that makes them faulty, this is called a **recessive mutation**.

An **autosomal** gene is a gene located on a numbered chromosome and usually affects males and females in the same way.

A **sex-linked** gene is located on the X or Y chromosome and affects males and female differently.

Both recessive and dominant mutations can be found on autosomal or sex-linked chromosomes.

We all have a number of recessive gene mutations which are hidden due to the fact that we have a backup working copy of the gene and therefore the correct gene product is made.