

# About genetics

## An introduction to genetics, genes and the role of DNA

- How we develop in the womb, and how we grow throughout life, is determined by our DNA.
- Genetics is the study of how characteristics are inherited through our DNA.
- Problems in our genetic material can cause medical conditions.

In this factsheet we look at genetics: what it is, how it works, and why it can cause disease.

### What is genetics?

Genetics is the study of genes, and how we inherit characteristics from our parents. This includes our physical characteristics, behavioural characteristics and medical conditions. For example, genetics determines:

- whether we will have blue, green or brown eyes;
- what blood group we will have; or
- whether a cell will be part of a blood vessel wall or a heart muscle cell.

### What are genes?

Genes are individual biological instruction manuals that direct every cell in your body how to grow, how to behave and what function to have in the body. And they do this through the production of proteins. The entire genetic code of an individual (the complete set of instruction manuals) is called the genome.

For instruction manuals to work properly, they have to be spelt correctly and make sense. Sometimes these manuals develop 'printing errors' (called 'variants' or 'mutations') that effect the wording of the instructions. This might mean that the words are changed, change their meaning, or don't make sense. In 'variants' there is a change from the normal, and in 'mutations' the change causes disease. So while some changes have no effect, some can cause diseases to develop. (See more about this in 'Genes: what can go wrong?')

### An analogy

To understand genetics, it can be helpful to use the analogy of a library, where:

- DNA is the individual letters, which make up words. The letters need to be organised correctly to be understood;
- a gene is a sentence which on it's own makes sense;
- a chromosome is a book, made up of thousands of sentences, bound together; and
- your genome is the library of all your books (chromosomes).

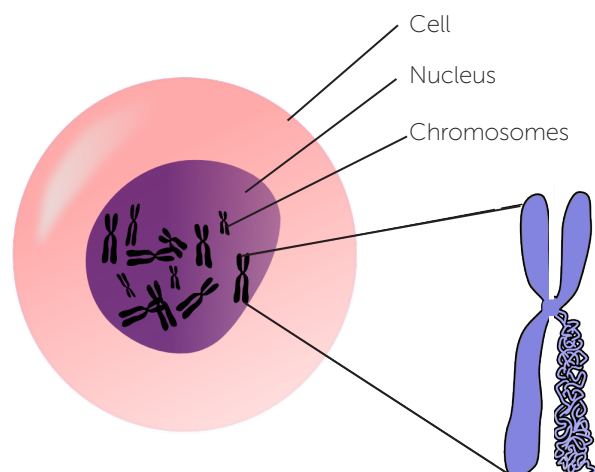
### Inside the cells of the body

Cells in the human body contain an area called the nucleus. The nucleus is the control centre for the cell, and contains all of the cell's genetic material which tells the cell what its role is. Genetic material inside the nucleus is called 'nuclear DNA'.

Inside the nucleus of human cells are 46 structures called chromosomes. Chromosomes are long strands of DNA, which are tightly wrapped into a double-helix shape. 44 of these chromosomes make up 22 matching pairs. These are called 'autosomes', and are numbered 1 to 22, in decreasing size.

The 23rd chromosome pair is the sex chromosomes, that determine the person's gender. They can be one of two types: 'X' and 'Y'. Where there are two 'X' chromosomes the person will be female. Where there is one 'X' and one 'Y' the person will be male.

Most human cells are diploid – that is they have two copies of each chromosome, or 23 *pairs*. However, the human reproductive cells (the female ovum and male sperm) have one copy of each chromosome. When these two reproductive cells come together and join during fertilisation, both give a single copy of each chromosome, which makes up the pair. In this way, half of an individual's genetic make-up (one of each of the 23 pairs of chromosome) comes from the mother (via the ovum) and half from the father (via the sperm).



Human cell

Note: most of the time chromosomes don't have an obvious shape, but are shown here as 'X' for illustration only.



## How do cells know what type of cell to be?

In addition to the genome is the epigenome. The epigenome directs the genome: it tells the genome what to do, when and where. So, the epigenome tells the cell what function to have, which parts of the DNA to use, and what proteins to make, depending on where that cell is in the body. It tells muscle cells to be muscle cells, and skin cells to be skin cells. (Using our analogy above, the epigenome is the author of the book: directing which sentences and paragraphs should be in each chapter.)

## The importance of proteins

Proteins are one of the most important molecules in the human body. They are large and complex structures that make up the organs and tissues of the body, and carry out most of the work in the body. The following are types of proteins and their functions.

- **Antibodies** protect the body from infections such as bacteria and viruses. An example is immunoglobulin, which is part of the body's immune response.
- **Enzymes** speed up chemical reactions in the body's cells (and also have a role in reading DNA). An example is amylase, which is part of the digestive process.
- Some **hormones** are proteins that coordinate activity between cells and organs in the body. An example is insulin, which helps your body to use the sugar in food as energy.
- Proteins which provide **support** and **structure** in the cells. An example is collagen, which gives strength and protection to the skin.
- Proteins which help to **transport** other molecules throughout the body. An example is haemoglobin, which transports oxygen in the red blood cells.

Proteins are made up of chains of hundreds of individual building blocks called amino acids. There are 20 different types of amino acids that make up proteins (such as arginine, glutamine and tryptophan). The arrangement of amino acids determines which protein is made.

## Proteins and DNA

Proteins are vital in order for the body to develop, grow and function. The production of proteins is controlled by DNA.

## DNA: unpacking genes

The chromosomes found in the nucleus of cells are made of a material called deoxyribonucleic acid or 'DNA'. The DNA of each chromosome is made up of two vast strands of nucleotides, which pair up together and twist around each other in a structure called a double-helix. This structure is a way of getting a lot of information tightly packed into a very small space, and also protects it.

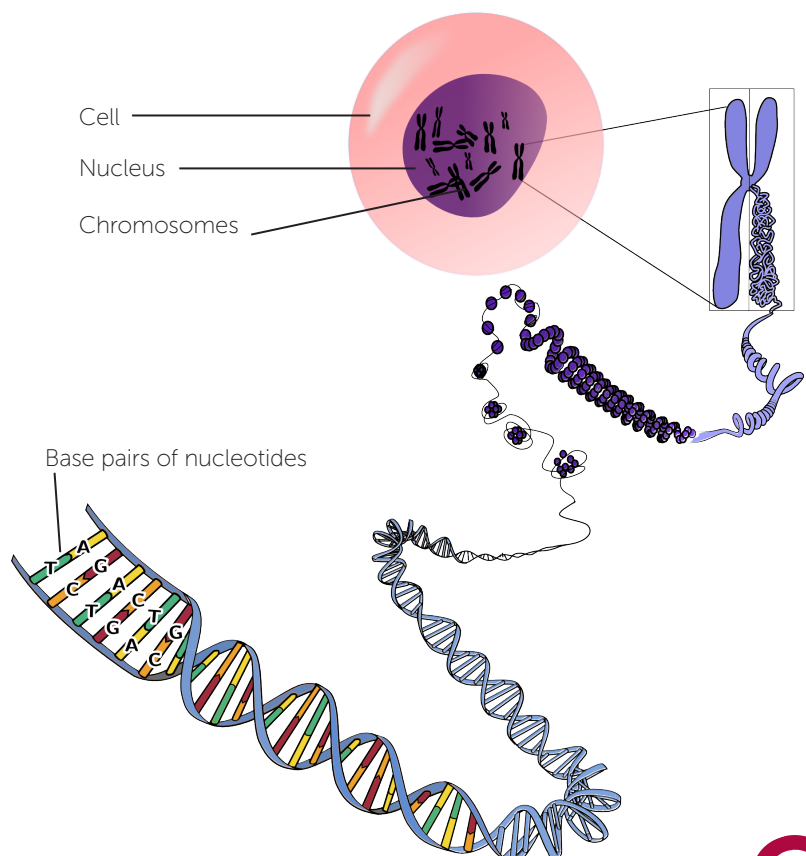
Each strand of DNA is made up of around 20,000 genes. Each gene is made up of a long sequence of nucleotides: individual chemical units which are made of three parts (nitrogen, phosphate and sugar). There are four nucleotides that make up DNA: adenine (or 'A'), guanine (or 'G'), thymine (or 'T') and cytosine (or 'C').

These nucleotides have partners that they always pair with (and are referred to as 'base pairs'): A pairs with T, and C pairs with G. Through these base pairs, the two strands of DNA join together to form the double-helix. Each gene contains 1,000 to 1 million base pairs, and there are around 3 billion base pairs in the human genome.

## How nucleotides make amino acids and proteins

Individual genes contain the instructions needed to make a single protein or a group of proteins. To do this, DNA unwinds from its double-helix structure and the two strands separate. This allows the instructions on one of the strands to be translated into amino acids, in the following way.

Along a single gene, the nucleotides group together into threes (called a 'codon'). Each codon relates to an amino acid, with the specific sequence of nucleotides corresponding with a specific amino acid. Therefore, every amino acid has one or more a specific codons. For example, the amino acid glutamine has the codons CAA and CAG, and the amino acid tryptophan has the single codon TGG. When all the amino acids that are coded for in a gene are arranged together in order, they make up a protein.



## Genetics and inheritance

Genetics is how we inherit characteristics from our parents. As we have seen above, one set of genetic instructions (one of each chromosome) comes from our mother and the other from our father. Together, these sets make up the 23 pairs of chromosomes.

### Dominant and recessive alleles

For each gene in a person's DNA, there are two copies (called 'alleles'): one from the mother and one from the father. So what determines which allele is expressed (used to make the protein): the mother or the fathers?

Alleles are either dominant or recessive.

- In **dominant** alleles, whatever trait that allele codes for will always be expressed. Therefore only one dominant allele is needed in order for the trait to be expressed (regardless of whether the individual has one dominant allele or both alleles are dominant).
- In **recessive** alleles, the allele is only expressed in the *absence* of a dominant allele. Therefore, only individuals in whom both alleles are recessive will express that recessive trait.

### Genotype or phenotype?

'**Genotype**' refers to what is seen in the person's genes (in the example below this would be Bb in the father, and bb in the mother).

'**Phenotype**' refers to how genes are expressed or 'seen' (in the example below the father has brown eyes and the mother has blue eyes).

## Genes: what can go wrong?

Genes can sometimes change in their genetic code. These changes from the 'normal' are sometimes called 'variants', and when they cause disease they are called 'mutations'. As we saw above, genetics is the instruction manual for human cells, and determines how proteins are made in the body. If there is a change in the DNA of a gene, this can affect what amino acid is coded for, and therefore what protein is made. If an abnormal protein is made, this can affect the function of the protein. In 'mutations' this altered function causes disease. Although some mutations are common, most of them are rare.

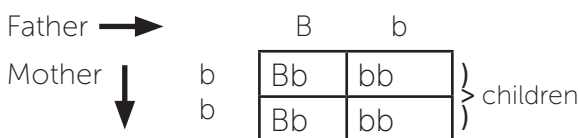
A gene that contains a variant or mutation may be referred to as an 'altered' copy, and the 'normal' gene (not a variant or mutation) is the 'working' copy.

There are many different types of variant or mutation. Here are two examples.

- Deletions are where a single base or part of a gene is missing (or deleted). Using a single base as an example, in the sequence TTC GGA CTC... if the first 'G' is deleted this changes the sequence to TTC GAC TC... Because these groups of three code for particular amino acids, when this sequence is changed, the amino acid encoded for is changed.
- Insertions are where a single base or part of a gene is added (or inserted) into a sequence. Using a single base insertion as an example, in the sequence TTC GGA CTC... if an 'A' is inserted this changes the sequence to TTA CGG ACT C... Because these groups of three code for a particular amino acid, when this sequence is changed, the amino acid encoded for is changed.

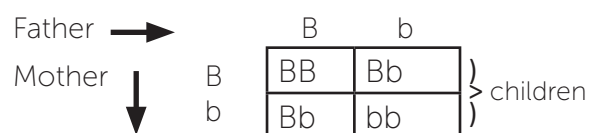
Eye colour: an example of dominant and recessive genes. The allele for brown eyes is dominant (B) and the allele for blue eyes is recessive (b). If someone has at least one 'B' (dominant) allele they will have brown eyes. If someone has two 'b' (recessive) alleles they will have blue eyes.

Example family 1: the father has brown eyes (Bb - one dominant and one recessive allele) and the mother has blue eyes (bb - two recessive alleles). There are four possible combinations for the alleles that the children could inherit.



The children that inherit B from their father will have brown eyes (because they have a dominant allele). The children that inherit b from their father will have blue eyes (because they have a second 'b' from their mother, and so both alleles are recessive). In this example, the children are equally likely to have brown eyes (Bb) as blue eyes (bb).

Example family 2: both the mother and the father have brown eyes, because each has one dominant (B) and one recessive allele (b). There are four possible combinations for the alleles that the children could inherit.



In this example, three of the possible children have at least one B allele (either BB or Bb) and will have brown eyes. The fourth possible child has 'bb' alleles, and so will have blue eyes. In this example, children are three times more likely to have brown eyes than blue eyes.



## When do variants and mutations happen?

- In some people, a variant or mutation happens during fertilisation, while they are developing in the womb or at some point during their life, and this is called '**de novo**' (or 'from new') or acquired. In this case, the variant or mutation has not come from one of their parents.
- In others, the variant or mutation is passed on in one of the chromosomes from one of their parents. In this case, it is '**inherited**'.

This is why 'genetic' does not always mean 'inherited' as some genetic mutations are not inherited from either parent.

## How do mutations cause disease?

Not all mutations cause a problem. 'Silent' mutations do not have any effect on the amino acid or protein (for example if an amino acid has several different codons and the mutation has changed one codon to another, but still codes for the same protein). However, other mutations have a dramatic impact and can be 'pathogenic', and cause diseases. This depends on which gene is affected by the mutation, what type of mutation it is, and the impact this has.

## Why is genetics important in cardiomyopathy?

Cardiomyopathy can have a number of different causes, depending on the type of cardiomyopathy. However, in many cases, it is a genetic condition. So for these people, their cardiomyopathy is caused by a genetic mutation.

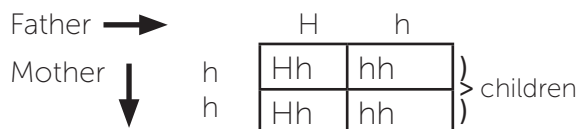
Where cardiomyopathy is genetic, it is often an **autosomal dominant** condition. This means that the mutation is on one of the 22 matching pairs of 'autosomal' chromosomes. It also means that the gene is dominant, so only one copy of the mutated gene is needed in order for the person to have the condition.

Cardiomyopathy can also be a **recessive** condition. (where two mutated genes have to be present to cause the condition) or X-linked (where the mutation is on an 'X' sex chromosome).

Some types of cardiomyopathy can be caused by mutations in **mitochondrial DNA**. Mitochondrial DNA is DNA that is found in a cell's mitochondria. These are small structures within a cells which 'power' the cell: converting food into a usable form of energy.

However, the genetics of cardiomyopathy is complex. One type of cardiomyopathy can be caused by many different gene mutations. And a single gene mutation can be responsible for more than one type of cardiomyopathy.

The following is an illustration of the genetics of cardiomyopathy, using hypertrophic cardiomyopathy (HCM) as an example. HCM is an autosomal dominant condition. We can illustrate this as: H = altered gene (causing HCM) and h = working gene (no HCM). In this example, the father has HCM (Hh) and the mother doesn't (hh).



The children with 'Hh' have the gene for HCM, and the children with 'hh' don't have the gene. Therefore, the children have an equal chance of inheriting and not inheriting the HCM gene.

Although some people will *inherit* the altered copy of the gene for HCM, other people might *develop* the mutation themselves (rather than inheriting it from a parent). In this case, they could pass on the gene to their children.

This is a simplification of how genetics works in cardiomyopathy, and there are many different genetic mutations that can cause cardiomyopathy.

♥ *For more information on the importance of genetics in cardiomyopathy, see our factsheet 'Genetic testing in cardiomyopathy'.*

### Are 'genetics' and 'genomics' the same thing?

Although both words are related to 'genes' they are different things.

- '**Genetics**' is the study of heredity (how characteristics are passed from parent to child).
- '**Genomics**' is the study of genes and their functions.

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