Fact sheet **01**

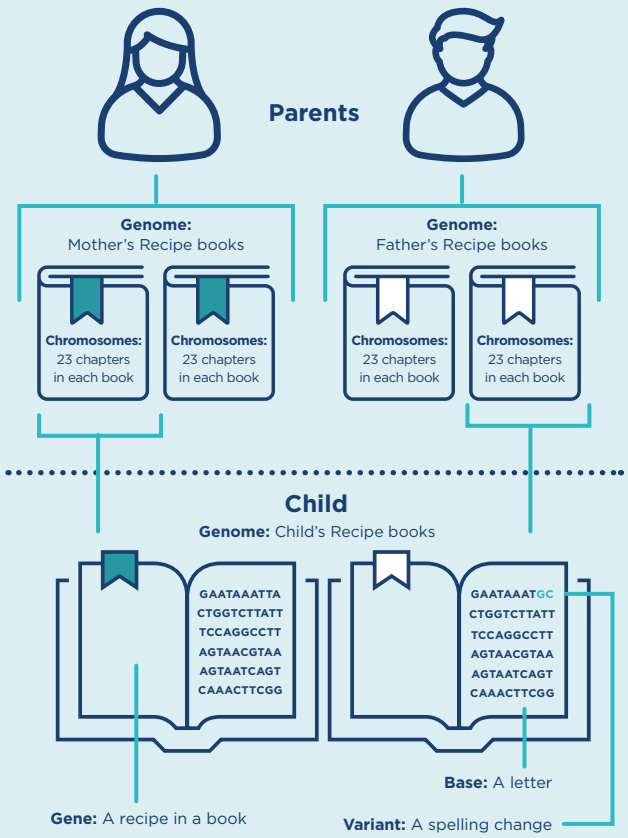
AN INTRODUCTION TO **DNA, RNA, GENES AND CHROMOSOMES**

IN SUMMARY

- **DNA** (**d**eoxyribo**n**ucleic **a**cid) carries the information and **templates** for making and maintaining all living things, including people
- DNA contains long chains of chemicals called **bases**
- These chains coil into 46 **chromosomes**, 23 from each **parent**
- **RNA** (**r**ibo**n**ucleic **a**cid) is similar to DNA; it also contains long chains of **bases** connected by a sugar 'backbone'
- **Genes** are the 1-2% of our genetic code that act as templates for making proteins
- **Proteins** do most of the work in our cells so we can grow and stay healthy
- Changes in our DNA are called **variants**. Variants can also be seen by looking in the RNA.
- Most variants help to make us different from each other or have little to no impact, but others can affect our health and development
- Health conditions that are caused by genetic variants are called **genetic conditions**
- A complete set of DNA is called a **genome**
- Almost all of our **cells** contain usually two copies of our genome.

THE RECIPE BOOK

Figure 1.1:
The human genome is like a recipe book



Genome (recipe books)

A complete set of DNA is called a genome. It is like a recipe book, handed down through generations of a family. The recipes are for making us and keeping us healthy. They also hold information about our families: past, present and future.

We get half our genome from our mother and half from our father. So most of our cells have two mostly similar volumes of the recipe book, one from each parent. They are mostly similar, but have some differences.

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Bases (letters)

The letters in these books are called bases. They are the chemicals adenine (A), thymine (T), guanine (G) and cytosine (C).

Genes (recipes)

- These letters write recipes that make parts of us, such as our eye colour or blood type. These recipes are called genes. Often things about us are the result of many gene recipes, like how you combine cake and icing to make a dessert. Genes make up about 1-2% of our genetic code. The other 98-99% of our DNA isn't directly involved in making proteins (non-coding), but it still has important roles which we continue to learn more about.

Variants (spelling changes)

A change in one or more letters is called a variant. We can inherit a change from our parents, or we can be the first one in our family to have it. We all have lots of these changes. Mostly, they help to make us different from each other or have little to no impact. Some changes can affect our health and development. Health conditions that are caused by genetic variants are called **genetic conditions**.

Chromosomes (chapters)

Many recipes are stored together as chapters of the recipe book. These are called chromosomes. In most of our cells, we have 46 chromosomes, 23 from each of our parents.

MORE ABOUT CELLS, GENES, CHROMOSOMES, DNA & RNA

The nucleus of most of our cells contains a complete set of our DNA (our genome).

Our DNA is tightly coiled around proteins called histones. These histones wind around each other as well, forming into chromosomes. This is how the billions of bases in a human genome fit into the tiny nucleus of a cell.

Figure 1.2:
Diagram of a human cell

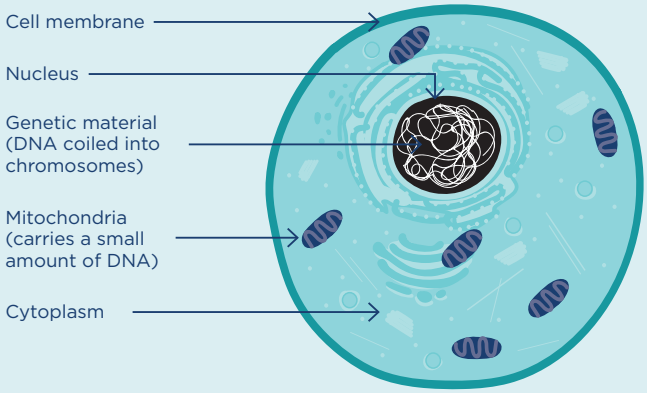
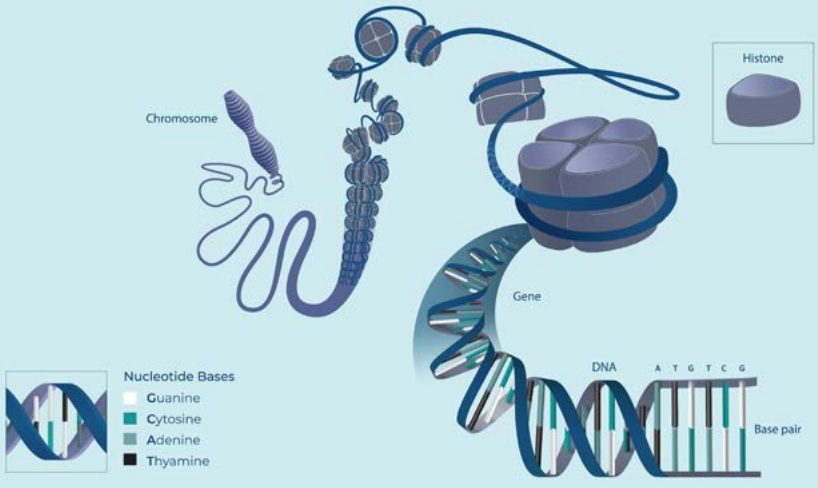


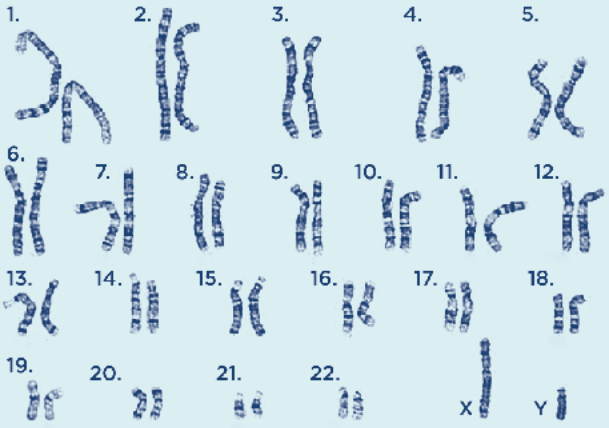
Figure 1.3:
Chromosomes, genes and DNA



Mitochondria, the energy providers of our cells, have their own small set of DNA.

Chromosomes

Figure 1.4:
Chromosome picture (karyotype) from a male (46,XY).



As seen in *Figure 1.4*, we have 46 chromosomes. They are in 23 pairs, half from a father's sperm and half from a mother's egg.

22 of these pairs are called autosomes, labelled in *Figure 1.4* as 1 to 22. The other pair are called allosomes. These are the sex chromosomes: X and Y.

Males have one of each sex chromosome (XY). Females have two X chromosomes (XX). It is only necessary to have one X, so in females one copy is randomly inactivated or 'turned off' in each cell during development of the embryo.

Each chromosome carries thousands of genes plus long sections of non-coding DNA.

Genes

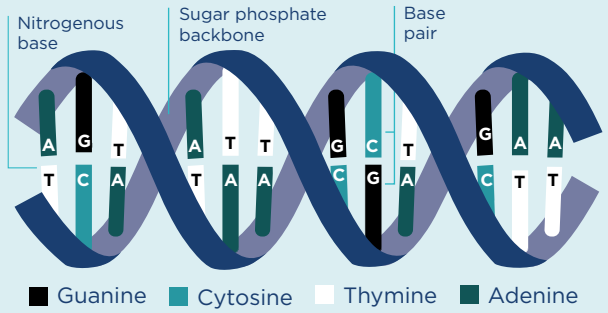
We each have more than 20,000 genes. They are the sections of our DNA that act as templates for building proteins. These proteins do most of the work in cells, so are vital for our development and keeping us healthy day to day.

Not all genes are needed at any given time, in any given cell. So they are turned on (expressed) or off (silenced). Different (epigenetic) mechanisms such as coiling and uncoiling the DNA, or adding chemical markers, can control how genes are turned on and off. Lifestyle, environment and age can all influence these mechanisms.

We have two copies of most genes, because we have two copies of most chromosomes (except the sex chromosomes in males).

DNA

Figure 1.5:
The DNA helix



DNA is made up of very long chains of bases called **a**denine, **t**hymine, **g**uanine and **c**ytosine, referred to as **A**, **T**, **G** and **C**. See *Figure 1.5*.

The bases pair up in a shape like a twisted ladder, known as a double helix. G always pairs with C, and A always pairs with T.

This means that DNA has two chains of bases that run in opposite directions. Markers in the DNA show which direction to read the template to create RNA and eventually proteins.

Figure 1.6:
Examples of variants which lead to a gene message not working properly

	Working message	Non-working message
a. Single nucleotide variant	TAG GCC CAG CAG TCA CTG	TAG GCC CAG CAG TAA CTG
b. Deletion variant	TAG GCC CAG CAG TCA CTG	TAG GCC CAG CAG CTG
c. Insertion variant	TAG GCC CAG CAG TCA CTG	TAG GCC CAG CAG TCC TCA CTG
d. Repeat expansion	TAG GCC CAG CAG TCA CTG	TAG GCC CAG CAG CAG CAG CAG TCA CTG

RNA

RNA, like DNA, is made up of chains of bases. For RNA these are **a**denine, **g**uanine, **c**ytosine and **u**racil (its alphabet is **A**, **C**, **G**, **U**). Unlike DNA, RNA has one chain of bases (called a single strand). RNA is involved in the protein making process, which has three key steps:

1. The first key step in making a protein is called **transcription**.

   During **transcription** a section of DNA that makes up a gene is copied into a matching chemical called 'pre-messenger **r**ibo**n**ucleic **a**cid' or '**pre-mRNA**' for short.

2. In the next step called **splicing**, sections called **exons** are joined together by cutting out the areas in-between (called **introns**) to make **mRNA**. It is a bit like just leaving the ingredients in a recipe by cutting out the introduction and other extra information. This is because not all the information in the pre-mRNA is needed to make a protein.

3. In the last step, called **translation**, a protein making machine called a ribosome binds to the mRNA recipe and attaches amino acids (the ingredients) according to this recipe. The amino acids join together into a long chain that folds into the **protein**.

Variants

Everyone has variants in their DNA. These can be of just one base, or many in a row. As shown in *Figure 1.6*, there are many types.

Variants that are inherited from one or both parents through the reproductive cells (egg and sperm) are called **germline variants**. Because they are present from conception, they may show up in all or most of a person's body.

Those that are acquired throughout our lifetimes are called **somatic variants**. They usually show up in one or some organs or tissue types, rather than being throughout a person's body.

Variants that are not inherited from our parents are called *de novo*. These can happen around the time we are conceived (early development) or occur over our life (somatic).

Most variants are not harmful. Rather, they are what make people different from each other, or have no impact at all (benign).

Some variants do cause or contribute to health conditions. These are called pathogenic.

In genetic or genomic testing, if the effect of a variant is unclear, it is called a variant of uncertain significance (VUS). Our ability to classify variants will keep improving, along with our knowledge of genetic conditions and the genome itself.