

**This fact sheet talks about different ways that a person's genetic information can be looked at. Some changes may mean a person has, or is more likely to have a genetic condition.**



### IN SUMMARY

- Genetic and genomic testing involves studying a person's DNA or the message that the DNA code is sending to the cells of the body
- Testing may be offered during pregnancy, on the developing baby, during childhood or later in life
- Depending on the type of genetic condition being tested for or the type of change (variation), there may be different types of tests.

### CHROMOSOMES, GENES AND DNA

Our bodies are made up of billions of cells. Each cell contains a complete copy of our genetic information or DNA. In all the cells of our body, our genes are found on the chromosomes. We have many thousands of genes that provide information for our body to grow, develop and stay healthy. The genes send messages to the cell to make important chemical products such as proteins.

There are typically 46 chromosomes in each cell that come in 23 pairs. One of each pair is passed on to us from our mother and the other from our father. 22 of these chromosome pairs are numbered. These numbered pairs are known as the autosomes. 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.

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 on the sex chromosomes called X and Y.

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.

Our genes contain less variation. Sections of our DNA that do not code for protein contain much more variation. We do not understand all the functions of these non-protein coding sections of DNA, but we know they can be important for controlling how our genes work.

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

An example of this is eye colour. Everyone has genes that code for 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.

### WHAT IS GENETIC TESTING?

Genetic testing is the study of information in the DNA of a person. There are a number of different types of genetic tests for the different types of variations and also the type of genetic condition in question.

## HOW IS THE TEST DONE?

Genetic testing usually involves taking a sample of body tissue. The type depends on the particular test and may include blood, cells from the lining of the cheek, cells in the roots of a person's hair, amniotic fluid or chorionic villi sampling (CVS) in pregnancy as well as a variety of other body fluids and tissues.

### Looking for pathogenic variants in the genetic code (direct gene testing)

If the sequence of DNA 'letters' in a gene is not able to be read in the correct way, the protein or gene product may not be made in the right way, which can lead to health concerns and may be recognised as a genetic condition.

The first step in working out the cause of a genetic condition is to locate the gene involved. The location or 'address' on a chromosome for a gene linked to genetic condition is not always 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 work out if the sequence of 'letters' (spelling) in the gene. A pathogenic variant is one that makes the gene not work so that it causes a health or developmental concern.

Genetic testing 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 person or other members of their family
- For some common conditions, the results of a genetic test may show that a person has a higher chance of developing a particular condition. This is known as **predictive testing**
- More rarely, a genetic test can work out whether a person **will** develop a condition later in life, based on the presence of a variant. This can be identified long before any symptoms are present and is called **pre-symptomatic genetic testing**.
- **Genomic testing is also known as massive parallel sequencing or next generation sequencing.**

Genomic testing refers to testing that looks for variations in several genes or all of the genes at once. It can even look at all the genes as well as the regions in between them (the **whole genome**), rather than looking at just one or two genes.

Results from genomic testing can be:

- The pathogenic variant(s) causing the condition are found
- No pathogenic variants are found
- Unclear. A variant is found but it is not currently known whether it is harmless, or one that causes a health concern. (This is called a Variant of Uncertain Significance)
- Unexpected and unrelated to the reason for testing (called an Incidental Finding)

Sometimes, because results from genomic testing can be complex, some initial testing is done first.

### Common Types of Genetic and Genomic Testing:

- **Microarray testing:**

Sometimes called chromosome microarray (CMA) testing is a detailed genetic test that can detect extra or missing segments of DNA. A CMA test examines the amount of DNA present and looks for a variation in the number of copies of these segments. Differences in copy numbers of these segments are known as copy number variants. If the test finds a copy number variant, the laboratory will check which genes it contains and if they relate to the suspected condition. CMA testing may be suggested if a person has a pattern of development or health concerns that are suspected to be caused by extra or missing sections of DNA.

- **Single Gene testing:**

Looking at one or two genes known to be linked to a condition.

- **Targeted Panel testing:**

Where a group (a panel) of genes linked to a genetic condition are tested.

- **Whole Exome sequencing (WES):**

The exome is the coding section of DNA and makes up about 1-2% of a person's entire genome. Exome sequencing uses a technique that allows many overlapping small sections of DNA to be sequenced at the same time. The exome is thought to contain most pathogenic variants. Analysing only 1-2% of the genome greatly reduces the amount of information to be filtered (sorted) and resources needed to do the test.

- **Whole Genome sequencing (WGS):**

This is a similar type of test to Whole Exome Sequencing but instead looks at the **whole** of a person's genome. This is all genes as well as the regions in-between. This may identify more types of variants that cause a genetic condition

- **RNA studies:**

RNA stands for ribonucleic acid. RNA is somewhat similar to DNA and plays a key role in turning our genetic information into proteins. Sometimes the way that RNA is made from DNA (and how a gene is expressed) can be informed by DNA testing. Other times, testing the RNA more directly may be needed to work this out better.

### Genetic screening

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Genetic screening is similar to genetic testing but is undertaken for a particular condition in individuals, groups or populations where there is no known family history of the condition. The difference between genetic testing and genetic screening is that the person or people being screened have a lower chance of having a pathogenic variant and the result may be given as a risk figure or a 'high' chance or 'low chance' result.

## WHY CONSIDER A GENETIC OR GENOMIC TEST OR GENETIC SCREENING?

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### a) Newborn screening

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Genetic screening is offered to all newborn babies in Australia and New Zealand by a simple blood test to look for a few rare genetic conditions. The blood sample is taken by a heel-prick before the baby leaves hospital, or for home births, on about day 4, and is sent to a special laboratory.

### b) Genetic carrier testing

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People can also be **genetic carriers** of variations in genes without showing any signs or symptoms of a genetic condition. If, however, both parents are genetic carriers for the same condition, there is a chance that their children may be affected by the condition.

### c) Reproductive genetic carrier screening

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Genetic carrier screening is a genetic test applied to a whole population or to a defined group. Reproductive genetic carrier screening is available for couples who are planning pregnancy or early in pregnancy.

### d) Non-invasive prenatal screening (also known as Non-Invasive Prenatal Testing)

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This is a screening test performed early in pregnancy to work out whether there is an increased chance of the baby having a condition such as Down syndrome. First Trimester Screening is another common type of screening test offered in early pregnancy but this is not a genetic or genomic test because it does not test the genetic material directly.

### e) Diagnostic genetic testing

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Genetic testing can be used to diagnose conditions at all stages of life, from conception to the very end of life. For example, there are ways of taking a sample from a pregnancy (chorionic villus sampling or amniocentesis) or a genetic diagnosis, or from an embryo using IVF techniques (preimplantation genetic diagnosis).

### f) Pre-symptomatic genetic testing

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Direct genetic testing can be used to work out if a person will develop certain inherited conditions later in life. This type of genetic testing is referred to as pre-symptomatic testing. Finding a variant in a person with a family history of a particular condition, but who may not yet show symptoms of that condition, means that that person will certainly develop the condition in later life.

Pre-symptomatic testing is available for a number of conditions including Huntington disease.

### g) Predictive Genetic Testing

Sometimes finding a specific variant implies a person has an increased chance, rather than certainty, that they will develop a particular condition later in life. This type of direct gene testing is called predictive testing.

Predictive testing for some families is available for conditions such as an inherited predisposition to breast cancer.

### LIMITATIONS OF TESTING

Finding that a person has a variation in a gene causing a particular condition does not always tell us how a person is, or will be, affected by that condition. There may be other causes (other genes and/or environmental reasons) that can influence this. This may explain the variability of symptoms between affected members of the one family.

Although the study of DNA has improved, understanding the meaning of variations in the DNA sequences in genes is not always easy; in particular for more extensive tests such as whole exome and whole genome sequencing. The chance of identifying a pathogenic variant can vary for each condition and it is possible that the genetic cause will not be found.

A single gene may have many possible variations – some make the gene not work and cause a condition (pathogenic variants); others have no effect on how the gene works and others are of unknown significance.

For some complex conditions that develop as a result of the interaction between the person's genetic make-up and other environmental or other genetic factors, the testing may have to be done on a family member with the condition to find the family-specific variant in the gene before other healthy family members can be offered predictive testing. Genetic testing in cancer conditions may be an example of this.

### ETHICAL ISSUES

There are advantages and disadvantages to genetic and genomic testing. Testing should only be used after all the benefits, costs and impact have been considered.

Genetic testing can be discussed with a health care professional, and may also involve talking with a specialist genetic team. It is important that the right genetic test is being offered with full consent in the most informed and considered way for a person and their family.