This fact sheet describes a number of ways that a person’s genetic make-up can be looked at to determine whether they have a variation which can mean they or someone else in their family is at increased chance of having a genetic condition.

In summary

- Genetic and Genomic testing involves analysis of a person’s DNA or the message that the DNA code is sending to the cells of the body
- Testing can be carried out on a developing baby (prenatal), during childhood or later in life
- Depending on the type of genetic condition being tested for or the type of variation, different ways of analysing the DNA will be utilised.

DNA AND GENES

Our DNA is made up of sections that code for proteins, our genes, and sections that do not code for proteins. Proteins do the work in our cells and these are very important for normal cell function and our health. Our protein coding DNA, our genes, do not contain much 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 sections can be important for controlling our genes.

People generally have the same number and sequence of genes so that the same messages are sent to the body. However, there can be small variations between individuals in the information contained in 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 two 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, 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. Generally these variants do not have any impact on our health and are called neutral variants or polymorphisms (poly means many; morphisms means forms). Polymorphisms are quite common in the DNA code.

Some gene variations do 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.

WHAT IS GENETIC TESTING?

Genetic testing is the analysis of information in the DNA of an individual. There are a number of different types of genetic tests and the type of genetic test carried out will depend on the type of DNA variation being tested for and also the type of genetic condition in question.

HOW IS THE TESTING DONE?

Genetic testing usually involves taking a sample of body tissue. The type depends on the particular test and may include blood, cells obtained from the lining of the cheek or the cells in the roots of an individual’s hair, amniotic fluid or cells from chorionic villi sampling (CVS) in pregnancy as well as a variety of 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 may not be produced in the right amount, or produced in a form that will not function or is not produced at all. This can lead to health problems 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 letters in the gene is correct (therefore producing the right protein in the appropriate amount) or incorrect and therefore has a variation that makes it faulty or mutation (altering the type or amount of protein produced).

Genetic testing aims to determine whether a person has or does not have a pathogenic variant 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 increased risk 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 later in life, 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.

Genomic testing (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 identified
- No pathogenic variants are identified
- Unclear. A variant is identified but it is not currently known whether this is a harmless variation or one that causes a health concern (called a Variant of Uncertain Significance (VUS))
- Unexpected and unrelated to the reason for testing (called an Incidental Finding).

At present, because results from genomic testing can be complex, usually health professionals and laboratories will first begin with some initial testing.

Common Types of Genetic and Genomic Testing:

- **Microarray testing:**
  Sometimes called comparative genomic hybridisation (CGH), chromosomal microarray (CMA) testing is a detailed genetic test that can detect extra or missing segments of genetic material or DNA. A CMA test examines the amount of DNA present and looks for a variation in the number of copies of the segments. These 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 related to a condition

- **Targeted Panel testing:**
  Where a group (a panel) of related genes are tested, i.e. a panel of genes related to heart disease.

- **Whole Exome sequencing:**
  The exome is the coding section of DNA and makes up about 2% of an individual’s entire genome. Exome sequencing uses a technique that allows multiple strands of DNA to be sequenced simultaneously. The exome is thought to contain the majority of disease-causing mutations. Analysing only 2% of the genome greatly reduces the amount of information to be filtered and the cost of the process.
• Whole Genome sequencing:
  This is a similar type of testing to Whole Exome Sequencing but instead looks at the whole of an individual’s genome. This is all genes as well as the regions in-between.

• Genetic screening
  Genetic screening involves the same processes involved in genetic testing but is undertaken for a particular condition in individuals, groups or populations where there is not a family history of the condition. The difference between genetic testing and genetic screening is the target group for the testing.

WHY CONSIDER A GENETIC (OR GENOMIC) TEST?

a) Newborn screening
  Genetic screening is done on all newborn babies in Australia and New Zealand by a simple blood test to detect 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
  People can also be genetic carriers of variations in genes without showing any signs or symptoms of a genetic condition. However if both parents are genetic carriers of the same mutation, there is a chance that their children may be affected by a genetic condition.

c) Reproductive genetic carrier screening
  Genetic carrier screening is a direct gene test applied to a whole population or to a defined group. Reproductive genetic carrier screening is available (usually at cost) for couples who are planning pregnancy or early in pregnancy.

d) Non-invasive prenatal screening (also known as Non-Invasive Prenatal Testing)
  This is a screening test performed early in pregnancy to determine whether there is a high chance of the baby having one of a small number of conditions (Down Syndrome is one of the conditions). 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) Pre-symptomatic genetic testing
  Direct genetic testing is now being used to determine if a person will develop certain inherited conditions later in life.

  This type of genetic testing is referred to as pre-symptomatic testing where the detection of a mutation in a person with a family history of a particular condition, but who currently has no 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 neurodegenerative diseases such as Huntington disease and some forms of bowel cancer.

f) Predictive Genetic Testing
  Sometimes the detection of a specific mutation implies a person has an increased risk estimate or 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 inherited conditions such as an inherited predisposition to breast cancer.

LIMITATIONS OF TESTING

Finding that a person has a variation in a gene involved in a particular condition does not always relate to how a person is, or will be, affected by that condition. There may be modifying factors (other genes, environmental factors) that can affect the expression of the message from the gene. This may explain the variability of symptoms between affected members of the one family.

Despite the recent advances in DNA analysis, identifying and 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 varies greatly for each condition and it is possible that the genetic cause will not be identified.
A single gene may have many possible variations – some make the gene faulty (called pathogenic variants or mutations); 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, for example in cancer, the testing may have to be done on a family member with the condition to identify the family-specific mutation in the gene (mutation searching) before other healthy family members can be offered predictive testing.

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

Genetic testing will usually be discussed with a specialist genetic team who can provide the most up to date information in order to ensure the test is being offered and undertaken with full consent in the most informed and considered way for the individual and their family.