# GENOMIC TESTING – WHAT YOU NEED TO KNOW

This patient guide has been extracted from the Melbourne Genomics Health Alliance Patient Guide. We kindly acknowledge the hard work and dedication of the Melbourne Genomics Health Alliance in writing this patient guide together and thank them for allowing us to reproduce its content on our website. For more information please visit https://www.melbournegenomics.org.au/

## About this guide

This guide is intended to compliment the genetic counselling patients receive as part of their genomic sequencing test.

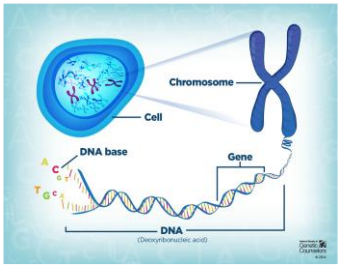
This guide can be used to share information about genomics and your test with family and friends, as you choose.

# Introduction

## About genes

Your body is made up of billions of cells with instructions for how your body should grow and function. These instructions are contained in your DNA – deoxyribonucleic acid – and DNA is packaged into structures called chromosomes.

Your DNA contains stretches of genetic code, which are called genes. Each gene gives an instruction to the body. However, if there is a mistake in one of these genes, it may not work properly.




A genomic sequencing test examines sections of your DNA for changes that may alter the genes and lead to disease.

## About genomic medicine

Genomic medicine is healthcare informed by greater knowledge of our DNA.

A *genetic test* looks at one or a small number of genes at a time.

A *genomic sequencing test* can capture information from many genes at the same time, allowing scientists to analyse all the genes relevant to your condition in the one test.

Reading DNA – genomic sequencing – has huge potential to improve healthcare by helping doctors diagnose illnesses faster and determine what medical care might work best for different individuals. Genomics is advancing rapidly, and there are many and varied ways it can be applied in healthcare.

Your genome is your complete set of DNA, including all of your 23,000 genes. Each gene has a specific function. When a gene contains a change (a variation), it may not work properly and this may affect your health.

Every person has many gene changes throughout their DNA; this is what makes us individual. Most of these gene changes don't cause disease, but some may.

Genomic sequencing allows us to examine your complete genetic information – your genome – to identify gene changes (variants) that may impact health.

# Your genomics team

## Your genetic counsellor

### What is genetic counselling?

Genetic counselling helps individuals, couples and families understand genetic medical conditions, and adapt to the impact of information provided by genetic and genomic testing. Genomic information can have medical, psychological, family and reproductive implications.

Genetic counselling will assist with:

- Helping you make informed choices, taking into account elements such as family goals, attitude to risk, and ethical and religious values.
- Interpreting your family and medical histories to assess the likelihood of an inherited cause and the chance of other family members being affected.
- Helping you better understand your condition if you receive a diagnosis – how it is inherited, whether other medical follow-up is recommended (with input from doctors) and how to access support and/or further research.
- Helping you understand what options may be available if you do not receive a diagnosis; including further testing in future or being linked with a research project.
- Supporting you to adjust to a genetic condition that may be present in your family.

### How can a genetic counsellor support you?

Genetic counsellors do not make decisions for you – their role is to provide information, answer your questions and help you reach decisions which are right for you and your family.

Your genetic counsellor will offer you the opportunity to go over any information provided and can link you with ongoing support.

It is very common for people to have many questions after the genetic counselling session as understanding develops, or symptoms change. Follow-up can be provided in further face-to-face or telephone consultations. A letter summarising your consultation(s) will also usually be provided.

After genetic counselling, you may have to make decisions about:

- whether or not to have genetic testing
- who to tell about the test results
- whether you want medical treatment, if it is available, and what treatment plan to follow
- how you are going to live your life in light of the test results
- how much support you are going to need

## Your genomics team

*Clinicians* – your treating specialist, and any other specialists involved in your care

*Genetic counsellor* – (see above)

*Laboratory scientists* – the experts who extract DNA from your sample

*Bioinformaticians* – statistical specialists who design and monitor the computer programs that analyse your genomic data

*Medical scientists* – the experts who comb through your many genetic variants to identify the one(s) which may be causing your condition

*Multidisciplinary team* – a group of clinicians, medical scientists, genetic counsellors and other related experts who meet regularly to discuss and identify the genetic variants that may be significant for your condition and/or your treatment

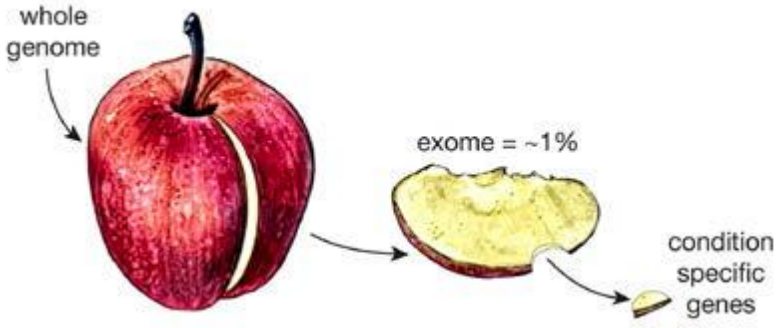
# My genomic sequencing test: How does it work?

## About whole exome sequencing

Your genomic sequencing test is called a ‘whole exome sequencing test’.

We each have about 23,000 genes in our entire genome. Your exome is only about one per cent of your genome – but this is the part most important for health.

A whole exome sequencing test aims to identify changes (variants) in your exome that may help diagnose or treat your medical condition.



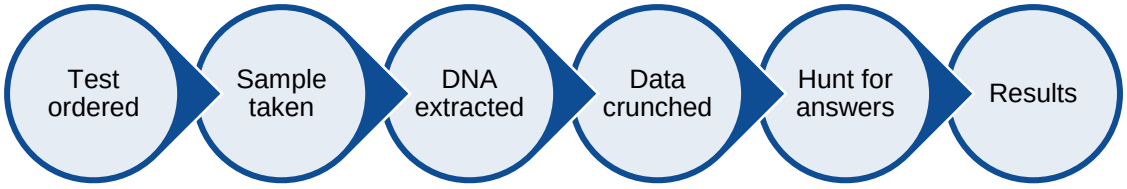

There are different types of variants, for example:

- ‘normal’ variants: these are usually common changes in the DNA that are unlikely to cause a medical condition on their own. (For example, red hair is caused by a variant.)
- variants of unknown significance: these are variants that are not fully understood. They may or may not contribute to a medical condition.
- pathogenic variants: these are variants that can cause a medical condition or increase a person’s chance of developing a medical condition. An example is change in the gene linked to breast cancer, BRCA; sometimes referred to as a mutation.

## Your test, your condition

Genomic sequencing for inherited (genetic) conditions can be helpful to try to find out what’s causing your medical condition, or provide more information that can be used to manage your condition in the best way possible. This test usually uses DNA from a blood sample.

## The process of genomic sequencing



## Ordering a test

Once your doctor decides that a genomic sequencing test may provide useful information for you, they will discuss the pros and cons of this option with you. This discussion will often involve a genetic counsellor.

When you have been fully informed and officially consented to the test by signing consent forms, your doctor will order the genomic sequencing test. The test process is described below and is the same regardless of whether your doctor orders genomic sequencing for you only (a singleton), or for a child and parents as well (a trio).

## Kick-off (Sample)

A DNA sample is needed for your genomic sequencing test. DNA can be taken from several types of body tissue but is usually extracted from a blood sample

The sample is sent to a pathology laboratory where the DNA can be ‘extracted’.

## Off to the laboratory (DNA extraction and sequencing)

DNA is extracted from a blood or tissue sample in the laboratory. The DNA is then turned into data, through a process known as sequencing – usually done in a sequencing machine.

## Data crunching (Bioinformatic analysis)

The sequencing process produces enormous amounts of data that would require hundreds of hours for a scientist to analyse manually.

Computer programs perform the first step, analysing large amounts of raw genomic data by scanning for differences (variants) between your genetic sequence and a reference sequence.

Doctors are most interested in variants in genes associated with your condition (or set of conditions), so usually only variants in these genes are analysed at this stage. This is known as targeted analysis.

Once this bioinformatic analysis is complete, a list of gene variants from your sample is produced. This list of variants is then interpreted (curated).

## Hunting for answers (Variant curation)

There are thousands of variants in your exome. One of the challenges for doctors and scientists is to figure out which variants are harmless and which may be associated with health conditions.

Your list of variants is examined to see if any can explain the medical condition you have and identify the most appropriate treatment. This process is called variant curation.

The first step is to establish whether a variant (or change) in a gene will stop it working properly. This is done by a team of doctors and scientists working together to analyse your DNA in an effort to find the cause of your condition.

## Back to you (Results)

Once the team has reached a conclusion about the variants they’ve found, a report is prepared by the laboratory and sent to the doctor who ordered your test. Your doctor and/or your genetic counsellor will discuss the test results with you.

You may choose to bring a friend or family member for support in such a discussion.

### Understanding your results

The laboratory report includes a section summarising whether the cause for your condition has been identified.

Possible results may include:

- One or more variants that cause your condition have been identified.
- A variant has been found, but it is not known whether it is the cause of your condition.
- No variants are identified as the cause of your condition. You may still have a genetic condition, but the testing may not have been able to identify a variant. Or, you may have a variant in a gene that was not analysed. Alternatively, the gene responsible for your condition has not yet been discovered. In this case, your data could be reanalysed in several years' time in light of new research *(see 'Possibility for reanalysis', page 8)*.

Depending on your results, your doctor may use this information to guide treatment or to inform care for your genetic condition. Your results may also provide information relevant to other family members.

### How long does the test take?

The genomic sequencing process is complex and has many stages. It usually takes four to six months to return a genomic sequencing test.

However, this area of medical science is advancing rapidly. Genomic sequencing will likely become increasingly efficient in coming years, with more of the work done by computers and less by humans.

# Patients' experience of genomics

The Melbourne Genomics Health Alliance first provided genomic sequencing to 315 patients at The Royal Melbourne Hospital and The Royal Children's Hospital, during 2014 and 2015.

They found that when genomic sequencing was provided to patients in the healthcare system, diagnosis rates improved and health dollars were saved. We also found that patients are keen to share their genomic data to help further medical research.

## What we found:

### Patients want genomic sequencing

- More than 90% of those approached agreed to the test
- 96% of patients said they had enough information to make a decision about testing after genetic counselling

### Patients agreed to share their genomic data for research

- 98% of patients agreed to share data for research related to their condition
- 93% agreed to share data for any research.

### Genomic sequencing gives more answers to patients

- Genomic sequencing resulted in six times more diagnoses than standard care: 40% compared to 6%.
- Six times more children were diagnosed: 54% compared to 8%.

### Patients received better tailored medical care

- More than one in five of all patients had an immediate change in medical care, including: stopping unnecessary medications and check-ups; and providing new treatment or check-ups for early detection of known complications

### Sequencing as an early test saves health dollars

- For infants with genetic disorders, providing genomic sequencing early leads to a diagnosis in five times as many infants, at half the cost per diagnosis.

# Issues to consider

## Uncertainty

Genomic sequencing can sometimes provide patients with answers, but it may not provide *all* the answers.

Results are not always clear-cut: for example, the cause of your condition may not be identified through genomic sequencing. And some patients may still experience a sense of uncertainty – including about their future health – even if a genetic cause is identified.

Depending on your life experience, coping skills, family attitudes, cultural and social background, you may view this uncertainty in a positive or negative light.

In a positive response, you may feel or hope that these results will not be significant – and be reassured. You may choose not to pursue any further testing (if available) and prefer to focus on the present rather than the future. This may lead to a reluctance to discuss issues or results further with doctors, genetic counsellors and/or family members.

But uncertainty may also result in negative emotional responses, such as fear or anxiety, and the urge for a more definite outcome. In this situation, a doctor or genetic counsellor will be integral to managing your uncertainty.

Your health professionals can assist by engaging with you to:

- understand and articulate your uncertainties
- encourage you to ask questions
- provide relevant and accurate information
- help you develop health strategies to enhance feelings of ‘safety’ within uncertainty
- refer you to peer support services

## Additional findings

Rarely, one or more variants not directly related to your medical condition may be found by chance. These are sometimes called ‘incidental findings’, ‘additional findings’ or ‘secondary findings’.

An example could be a gene variant associated with an increased risk for a different health condition, or a gene variant which may indicate that you are an unaffected carrier of a genetic condition (so the condition could be inherited by your children).

If your doctor thinks these additional findings may have important consequences for you or your family, they will raise it with you. If medical follow-up is required as a result of an incidental finding, your doctor or genetic counsellor will assist you by making appropriate referrals, if necessary.

Our testing focuses only on at the genes with a known relationship to your current medical condition. This minimises the chance of incidental findings.

## Possibility for reanalysis

The information generated about your genes from exome sequencing will be stored in data files. Your data could be re-analysed – either for the same set of genes that you originally had the test for, or for a different set of genes – without the need to obtain another sample from you.

With global research advances, it is possible that interpretation of your genomic sequencing result may change with time. This is most likely to happen for variants of unknown significance or if no gene changes were found in your original test.

You can ask your doctor to periodically check (for example, every two or three years) if advances in knowledge may have changed the interpretation of your result. On occasion, laboratory experts may contact your doctor if they learn of new information relevant to you.

# Use of your genomic data in medical research

Genomics is a rapidly advancing field. Research access to genomic data will, over time, lead to new treatments and diagnoses.

Secure use of your genomic data for medical research has the potential to improve understanding of 'normal' and disease-causing genomic variants, by comparing variants across thousands of individual genomes. Using your genomic data in medical research may also lead to the discovery of previously unknown genetic causes for disease.

By undergoing the exome sequencing test and signing the consent form, your information may be securely shared with approved researchers in Australia and internationally in a way that does not identify you.

You may also choose for your genomic data to be securely shared in a re-identifiable manner, which means that your identifying data is removed but can be linked back to you if required. As an example, your doctor may share your information with international groups trying to identify variants common to people who all have the same condition. This may involve a re-analysis of your genomic data, with any findings able to be communicated back to you via your doctor.

# Family implications

A genetic diagnosis has the potential to affect not only the individual diagnosed but other family members as well. For instance, other family may be at risk of the same condition and may need to consider options for testing and medical check-ups.

Your genetic counsellor can discuss how to talk to your family about these issues.

Some things to think about:

- Talking to you family about the genetic information may be difficult. This could vary depending on family dynamics.
- How the genetic diagnosis is viewed may differ between family members, as might their level of understanding.
- Family may respond with feelings of grief or loss, both for the affected person and others in the family.

It is important that each family member receives relevant, accurate information appropriate to their needs. This is best provided by health professionals.

Peer support groups and referral to appropriate community and other support services may also be helpful. *(See 'Support and further information', page 8)*

# Insurance

Provided you are having an exome sequencing test to determine the cause of a condition you already have, the test is unlikely to impact on your ability to obtain insurance products.

Insurance may be affected if the test identifies that you are at risk of any other condition. You may wish to speak to your genetic counsellor or doctor about the chances of this happening, depending on the test you are having.

Any genetic or genomic test result must be disclosed when applying for life, disability, trauma or income protection insurance. Companies can use this information to decide whether to offer you insurance, to set your premiums, or to exclude certain conditions from your policy. Any existing policies you have will not be affected.

Your results will not affect private health insurance. Any existing policies you have will not be affected.

We encourage you to do your own research and seek independent advice in relation to disclosing medical information and when applying for different types of insurance.

### More on genomic testing and insurance

Centre for Genetics Education fact sheet

http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FactSheetInsurance

Human Genetics Society of Australia position paper

https://www.hgsa.org.au/documents/item/20

# Support and further information

## Looking after yourself – your wellbeing

The emotional impacts of genomic testing are important to consider.

Each individual patient may have different emotional triggers, responses and coping mechanisms, which can impact decision-making. Looking after yourself during times of stress and anxiety is key to achieving better outcomes and a better journey overall.

Some things that can place you at the centre of your experience, and support your wellbeing:

- understanding factors that may/may not influence your responses, actions and decisions
- awareness of your own notions of what's acceptable/unacceptable to you
- drawing on your strengths, knowledge and experience to guide you and keep you buoyant

Talking to someone trusted, so you can acknowledge and share your experience is a good starting point to supporting your mental health.

*'I know what has worked in the past and how I feel about certain things related to my genetic condition and my health. It doesn't work anymore for me to keep searching for answers and keep testing. The new data doesn't really add anything to my diagnosis at birth. If it adds value to the understanding of which therapeutics work best for me, then I'm into it. If it's just incidental information, then I'd rather the resource be redirected. I talk to my physician a lot about this, and he helps me to make the decisions that sometimes seem difficult.'*

***Louisa Di Pietro, 48**. (Hereditary Haemoglobinopathy and blood-transfusion-dependent)*
*Louisa is a member of the Melbourne Genomics Community Advisory Group.*
*The Melbourne Genomics Health Alliance thanks Louisa for sharing her experience and helping us prepare this section of the guide.*

## Support groups

Health and community support can play an important role in helping people cope with their genomic testing experience.

Support agencies, genetic counsellors and condition-specific support groups are valuable sources of information, and can help with the psychosocial impact of testing – particularly in the case of a new diagnosis or long diagnostic journey.

Connecting with 'other people in the same boat', assistance with navigating the health system and government support, and getting the right information at the right time can improve the experience for those having genomic testing. Seeking support can also benefit overall physical and mental wellbeing.

Patient support groups can provide information around self-advocacy (or advocacy for your family member), to help with decision-making.

The Genetic Support Network of Victoria website maintains an extensive list of patient support groups for different genetic conditions:

https://www.gsnv.org.au/support-groups.aspx

# Useful links

## Genomic sequencing

More information about genomic sequencing can be obtained from your requesting doctor, your genetic counsellor or on the web:

- Melbourne Genomics Health Alliance: www.melbournegenomics.org.au/
- Centre for Genetics Education: http://www.genetics.edu.au/publications-and-resources/facts-sheets/fact-sheet-15-genetic-and-genomic-testing
- Genes in Life – patient-focused information about genetics and disease: http://genesinlife.org
- Cincinnati Children's Hospital: whole exome sequencing https://www.cincinnatichildrens.org/service/d/diagnostic-labs/molecular-genetics/whole-exome-sequencing/families

## Genomics initiatives in Australia and across the world

Victoria: http://www.melbournegenomics.org.au

Australia: https://www.australiangenomics.org.au

Queensland: https://www.qgha.org/

Sydney: https://sgc.garvan.org.au/initiatives

South Australia: https://www.sagenomics.org/

ACT: http://www.anu.edu.au/news/all-news/anu-to-lead-new-era-of-personalised-medicine

New Zealand: https://www.otago.ac.nz/biochemistry/research/themes/otago673820.html

USA: https://allofus.nih.gov

UK: https://www.genomicsengland.co.uk

Canada: https://www.genomecanada.ca/en/why-genomics/genomics-sector/health

Genomicspolicy.org maintains a list of initiatives across the world that are working to bring genomics into healthcare, and discusses the many challenges arising from this: https://www.genomicspolicy.org/