VCGS
Leaders in Genetic Health

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exomes

clinical exome sequencing

Clinical Exomes Brochure 1

What is clinical exome sequencing?

Clinical exome sequencing uses a technology called Next Generation Sequencing (NGS). It is different from traditional genetic testing because it allows a large number of genes (a section of DNA) to be tested at the same time. Sequencing means we can look for gene changes (variants) that may cause genetic conditions.

A clinical exome can be very useful if you have a medical condition which may be caused by one or more gene changes and when it's not clear exactly which gene the change is in. It is most useful when your doctor has some idea of which gene or genes may have a change.

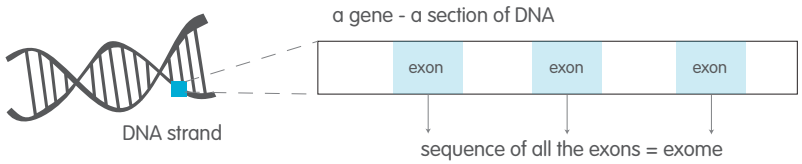
What is a genome & an exome?

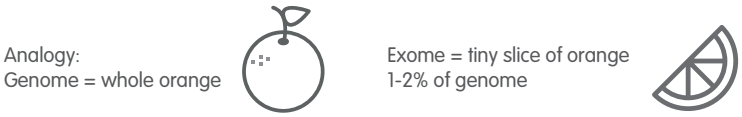
To understand what exomes and genomes are, it is important to understand what genes are first. A gene is a short section of DNA. DNA is made up of four chemical bases represented by the letters A, C, T & G. These bases form a unique sequence and changes (also known as 'variants') to this sequence can cause disease.

Certain parts of a gene, called exons, are the instructions for proteins. Proteins are vital to the structure and function of our bodies and our physical characteristics. The 'exome' is the sequence of all these exons.

While the exome refers to all the protein coding genes, a genome refers to all genes (those that code for protein and those that don't). The exome makes up approximately 1-2% of the genome.

Genetic changes or variants in our exome can cause disease. Exome sequencing is a way to look for genetic changes in genes that may cause disease.





How does exome sequencing work?

Clinical exomes read the sequence of your exome to identify any variants that may be the cause of your health condition.

It is important to note that in most cases the clinical exome will only look at genes that relate to an individual's condition. This is known as targeted analysis.

How is the clinical exome interpreted?

The most complex part of the clinical exome is in the interpretation of results. This is because not all genetic changes (variants) cause genetic conditions.

Some variants are a normal part of what makes everyone different. Variants may be inherited from ancestors, or may be new in an individual (not inherited). Some are known to cause genetic conditions, and for some we don't understand their significance.

Understanding variants:

To find the variants in an individual's exome sequence, special computer programs are used to filter out parts of the sequence that are common to many people in the healthy population. A clinical exome test usually identifies hundreds of variants in any one individual.

A team of experts including doctors, genetic counsellors and laboratory scientists then work together to understand the significance of each variant found and how this might relate to a patient's condition.

How are clinical exome results reported?

Results from a clinical exome are reported based on the type of variant found. Each will have different implications, both for the individual being tested and their family. Your doctor will discuss these implications with you.

Variant type	What this means
Pathogenic	This variant is the likely cause of your condition.
Variant of unknown significance (VUS)	It is not known whether this variation is the cause of your condition.
No variant found	No disease-causing variants were found.
Additional findings	A pathogenic variant outside the analysis requested was found.

How is testing arranged?

Clinical exome sequencing through VCGS is a highly specialised and expensive test. Testing is coordinated through our clinical genetics service. A request for testing is only accepted from specialist doctors after discussion with one of our clinical geneticists or genetic counsellors.

A request form is required from your referring specialist doctor.

This test also requires a completed patient consent form

Blood sample collection from pathology collection service (4ml EDTA blood).

Test results are reported to the referring doctor and can take up to 3 months.

Why is a patient consent form needed?

Although clinical exome sequencing is requested for the purpose of identifying the gene change causing an individual's health condition, the testing can sometimes result in 'additional findings' which provide other information about that individual's health. Genetic tests can also provide information that may be relevant to family members of the individual being tested. The specific patient consent form explains this in more detail.

It is important to understand the possible results of testing, and potential implications for family members, before consenting to clinical exome sequencing. Genetic counselling is provided to individuals before testing to help them be informed before consenting.

Sharing your information:

A large amount of genetic information is analysed by a clinical exome. From time to time this information may be reviewed or shared with other health professionals to help us better understand the significance of any variants found.

In some cases you will be contacted prior to the use of your information and in some cases you will not. The consenting process is required because it is important you understand how your genetic information may be used.

See Clinical Exomes Brochure 2 and the consent form for more information.

How long does testing take?

Given the complex nature of clinical exome testing, results can take up to 3 months. Please ask your doctor or genetic counsellor for an indication of how long your specific test might take.

Contact details

VCGS is a not-for-profit provider of a comprehensive range of clinical and laboratory genetics services. We provide genetic counselling support before and after testing.

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