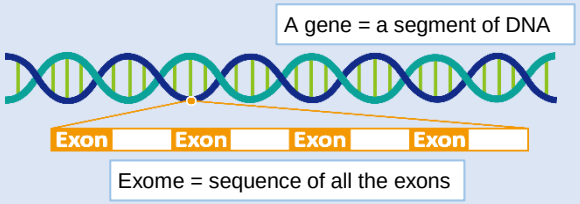
Genomic Sequencing

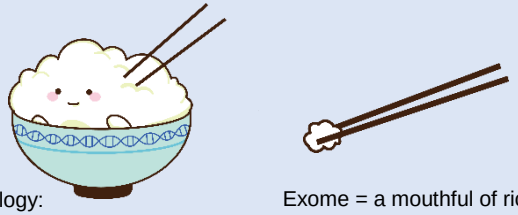
What is genomic sequencing?

Genomic sequencing is a technique using Next Generation Sequencing (NGS) technology to identify any changes or 'variants' in our genetic information that may cause genetic conditions. Compared to traditional Sanger sequencing (Single gene sequencing), NGS technology allows sequencing of large amounts of DNA and is a more effective method of identifying the order of nucleotides in a group of targeted genes, whole exome or whole genome.

What is gene, exome and genome?

Genome is a complete set of all our genetic information, including both the coding and non-coding parts of the DNA. And exome is the specific parts (exons) of DNA that code for proteins and is approximately 1 - 2% of our genome. We all have about 20,000 genes in our genomes. A gene consists of a segment of DNA that codes for a specific protein. When there are genetic changes or variations in a gene, it may not work properly and therefore may affect our health.





Analogy:
Genome = whole bowl of rice

Exome = a mouthful of rice
1-2% of genome

Types of genomic sequencing

A. Gene Panel Sequencing

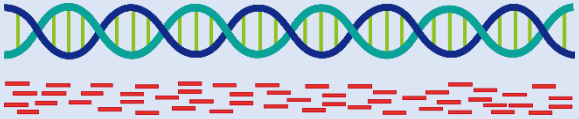
To test a set of genes that are known to cause the particular genetic condition.

B. Whole Exome Sequencing

Sequencing all of the protein-coding regions (exons) of genes and look for any genetic changes in the exome.

C. Whole Genome Sequencing

Sequencing the entire genome including the coding and non-coding regions of all genes.



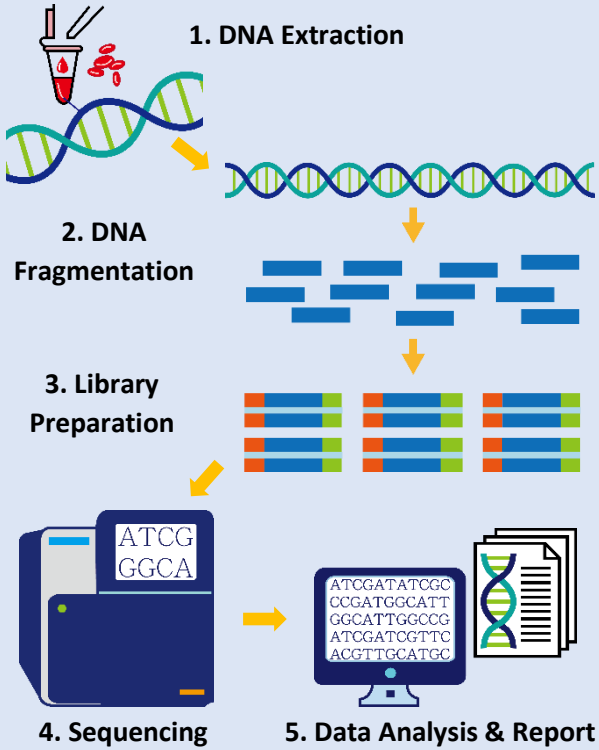
Indications for genomic sequencing

Genomic sequencing technology is a powerful test that can help to find a diagnosis for patients where other tests have failed to find a cause of their health problems. It is commonly used to investigate complex health and developmental problems with a suspected genetic cause and is being used to identify many genetic conditions including rare syndromes, cardiac, neurological, and mitochondrial disorders.

How does genomic sequencing work?

Prior to sequencing, DNA is extracted from specimen sample and is fragmented into smaller pieces. These DNA fragments are then converted into libraries and sequenced into a computer-readable format for analysis. Specialised computer programme is used to compare patient's DNA sequence to a reference sequence and allows laboratory experts to identify variants. Applying gene lists and filters to sequence data may help narrow the field of variants relevant to patient phenotype. It also helps to filter out variants that are common in the healthy population and are unlikely to cause genetic disease. Geneticists look at the order of chemical bases in DNA and can determine if there are any alterations causing specific health condition.

Procedure of genomic sequencing



Interpretation of genomic results

Interpretation of genomic results, which involves input from many health professionals in different specialties, would be the most complicated and time-consuming component in genomic sequencing.

Result	Implications
Disease-causing variant(s) is found	The diagnosis of the disease being investigated is confirmed.
No disease-causing variant is found	The diagnosis of the disease being investigated is not confirmed. It may be due to limitations of the current techniques or other unknown factor(s). Nevertheless, the result does not mean total exclusion of the diagnosis.
Variant(s) of uncertain clinical significance is found	A variant is found. With the latest medical genetic knowledge, it is still unclear whether this variant will result in any disease or is just benign polymorphism. In this circumstance, further genetic studies may be necessary, or genetic counselling and testing for the parent(s) or other family member(s) may be indicated. Despite that, it is still possible that a conclusion cannot be drawn in the end.

Genomic sequencing may possibly reveal incidental findings implicating diagnoses that are unrelated to the original indications of testing, including hereditary cancer syndrome, carrier status of autosomal recessive disorders, late onset neurological disorders, etc. Such results may potentially affect patient and/or family members in terms of insurance, job and academic application, psychological and social issues.

Limitations of genomic sequencing

While NGS is a more efficient way of diagnosing genetic disease, there are still some limitations:

- The clinical significance is currently unknown for many of the identified variants
- Technical limitations like incomplete sequence coverage of testing may cause false negative results

The importance of patient consent

It is crucial to understand the indication and possible outcomes of the test, the potential implications for family members and influences on insurance before proceeding. Genetic counselling is provided to individuals to get you informed before consenting.

Laboratory data sharing

Occasionally, genomic data and associated health information may be reviewed or shared with other health professionals to help us better understand the clinical significance of any variant found. The results and interpretations in the genetic report are based on current technology and knowledge. Future advances may provide further insight and lead to amendment of the genetic results.

For further enquires, you may contact us.

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DEPARTMENT OF CLINICAL GENETICS

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