CLINICIAN PRODUCT SHEET

GENOME.ONE ALL GENE ANALYSIS

Genome.One offers an all gene analysis for patients with suspected genetic conditions, based on either whole genome sequencing (WGS) or whole exome sequencing (WES) technology. The analysis includes all genes with variants that are known to be associated with disease, based on current scientific knowledge.

WGS and WES capture information across the genome for analysis and clinical interpretation. The scope of this analysis and interpretation can then be tailored either to all genes with known disease-associated variants, or a panel of specific genes. For more information on panel analyses, please see our other product sheets available at **www.Genome.One/disease-diagnostics**.

All WGS and WES testing is carried out in our own laboratory, which is accredited by NATA for Medical Testing to ISO 15189 and NPAAC requirements.

Why analyse all genes?

Diagnosing genetic conditions commonly relies on performing a number of single tests in series, often resulting in lengthy and expensive diagnostic odysseys. Analysing the whole genome or whole exome at once has the potential to provide:

- A higher likelihood of diagnosis
- Faster and more cost effective testing
- Easier reanalysis – once sequenced and securely stored, a patient's genome can be reanalysed and reinterpreted to incorporate new discoveries, without having to take another sample or perform additional testing

Genomic sequencing and analysis specifications

	WGS	WES
Price (all gene analysis)	$3,200	$2,200
Turnaround time	8-12 weeks	8-12 weeks
SNPs and indels	✔	✔
Detection of splice sites	✔	✔
Detection of CNVs	✔	✘
Variant detection in non-coding regions	✔	✘
Sample requirements	Whole blood 5mL adults 2mL paediatrics or DNA 100µL at 10-100ng/µL	Whole blood 5mL adults 2mL paediatrics or DNA 100µL at 10-80ng/µL
Analytical sensitivity		
SNPs	>99%	>98.5%
Indels, 1-19 bp	>95%	>89%
CNVs, 49-500 bp	>84%*	Not analysed
CNVs, >500 bp	>98%*	Not analysed
Average coverage	>30x	>75x
Uniformity of coverage (sequencing coverage of protein coding bases)	>97% covered ≥15x	>95% covered ≥20x

*Sensitivity may vary for polycystic kidney disease (PKD) panels

How to arrange a test

Discuss the testing options with the patient and complete the patient consent form. Alternatively, contact us to arrange a pre-test consultation and consent with a Genome.One genetic counsellor. Contact details can be found on the back of this sheet.

Determine whether the costs of the test will be covered by your institution or privately paid for by the patient. Private patients will be sent an invoice by Genome.One for payment.

Complete either our online or paper test request form.

Give a copy of the completed request form to the patient for a whole blood sample collection (5 mL EDTA for adults, 2 mL for paediatric).

You will receive a report detailing the results 8-12 weeks after the specimen reaches Genome.One.

DIAGNOSTIC RATE

Diagnostic yield for WGS and WES varies depending on the condition in question, as well as the sequencing protocol and diagnostic criteria used. WGS will usually have a higher diagnostic rate in many scenarios due to **higher coverage** and **detection of copy number variants (CNVs)**.

In a review of a large number of clinical studies using WES and WGS for diagnosis, the weighted average diagnostic rate for WGS was **49% (SD 15%)**, compared with **28% (SD 11%)** for WES.[1]

This was reflected in a direct comparison in patients with severe intellectual disability, with a diagnostic rate of **42%** for WGS and **27%** for WES.[2]

Bioinformatics

- In 2016, our bioinformatic processes received the award for highest SNP precision (positive predictive value) at the precisionFDA Truth Challenge – a competition designed to test the performance of genome informatics pipelines worldwide.[3]
- Our precision level of 99.98% for detecting SNPs was the best performance of 36 entries from around the world.

Interpretation and reporting

- Variants are curated by an experienced team led by a clinical geneticist, and reported on by a team that includes both clinical scientists and genetic pathologists.
- Reports contain both case summaries, as well as full synoptic variant reports.
- Opt-in approach to determine patient consent for incidental findings.
- For an additional fee, Genome.One offers secondary analyses of the ACMG59 genes (available to all patients 18 years and over) or pharmacogenomics (only available with WGS).

Indications for genomic analysis

Genomic sequencing and analysis of all genes is recommended in patients if:

- Their physical examination and/or family history suggests a genetic condition.
- Their clinical presentation suggests that single gene or panel testing is not likely to give definitive answers.
- They have a broad differential diagnosis – meaning a comprehensive genomic analysis may give a faster and more cost effective diagnosis.
- Other tests haven't resulted in a diagnosis, or the analytical resolution of other tests (e.g. microarray) is not sufficient for diagnosis.

Genetic counselling

The Human Genetics Society of Australasia recommends genetic counselling for all patients considering or undergoing genetic testing. Genetic counselling aims to provide individuals and their families with information and support when there is a suspected genetic condition in the family. Genetic counselling is usually performed pre- and post-genetic testing to help patients understand the implications of genetic information for themselves and their family.

Genome.One offers genetic counselling to individuals undergoing genetic testing with our laboratory at no additional cost. You can refer your patient to our genetic counselling services using the contact details on the back of this sheet.

Alternatively, a list of Australian genetic counselling services can be found here: **www.genetics.edu.au/Genetics-Services/genetic-counselling-services**

Insurance information

Under current Australian law, a person's private health insurance will not be affected by their decision to have genetic testing, or by the result of genetic testing. However, genetic testing can have implications for a person's ability to obtain risk-rated insurance policies, including life insurance, disability insurance and income protection insurance. This could include denial of cover, exclusion from cover or increased premiums.

Patients outside of Australia should obtain advice about the implications of genetic testing for insurance in their home country.

Privacy

Blood or saliva samples are held securely in the Genome.One laboratory in accordance with applicable law and standard laboratory practice.

Patient personal information will be securely stored in paper-based and electronic records in the Genome.One laboratory in accordance with the Genome.One privacy policy and applicable law. Genomic data is held on servers in the United States of America for the purposes of storage and highly specialised data processing and analysis. However, before any genomic data is transmitted to the USA, information identifying the patient is removed and replaced with a secure code. Only staff at Genome.One have the ability to link the code with the patient's personal information.

Information from WGS or WES screening will not be shared with other people without the patient's permission, except where this is required or permitted by law. Information from WGS or WES is important for medical research about the genetic causes of disease. When providing consent, the patient has a choice whether their de-identified genomic information can also be shared with researchers or included in research data banks.

The full Genome.One privacy policy is available at **www.Genome.One/privacy-policy**

Contact us for an example report or for any further information about our WGS or WES analysis.

Contact details

Genome.One

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References

1. Mattick JS *et al.* Whole genome sequencing provides better diagnostic yield and future value than whole exome sequencing. *Med J Aust* 2018 [ePub ahead of print] doi:10.5694/mja17.01176
2. Gilissen C *et al.* Genome sequencing identifies major causes of severe intellectual disability. *Nature* 2014; 511: 344-347.
3. PrecisionFDA Truth Challenge results. Accessed March 2018. Available from: https://precision.fda.gov/challenges/truth/results.

Genome.One mission statement

Genome.One is a pioneering health information company providing genetic answers to health questions, enhancing the lives of patients, families and communities across the world.

As a wholly-owned subsidiary of the Garvan Institute of Medical Research, we're backed by pioneering clinical discovery and translational medicine research excellence. Our laboratory is accredited by NATA for Medical Testing and meets ISO 15189 requirements.

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