Interpreting results

THE GENOMIC INSTITUTE

There are **three possible outcomes** of genomic testing.

Disclosing the result is the responsibility of the requesting clinician/consultant. Ensure there is an agreed plan to disclose the test result with a patient.

What's in a test report?

Genomic test reports vary between laboratories, but all contain the same essential information to facilitate interpretation of results.

The general structure and content of a genetic test report will always include the following:

- Patient demographics
- Sample details
- Clinical phenotype
- Result (in words and/or tabulated with genotype details)
- Variant description and evidence for classification
- Test and analysis methodology
- Recommendations
- Limitations

1 Pathogenic or likely pathogenic variant

A genetic cause *may* have been identified.

Clarify the following:

☐ Does the patient's clinical phenotype match the condition associated with the gene?
- Complete match (explains all features)
- Partial match (explains some but not all features)
- Incidental finding (significant finding with clinical impact but unrelated to clinical presentation)

  E.g. carrier status for autosomal recessive condition

☐ Do the number and location of variants identified in the gene match the mode of inheritance of the condition?

E.g. for autosomal recessive conditions, there must be two pathogenic or likely pathogenic variants on separate copies of the gene.

☐ Are there any management implications for the patient?

☐ Are there any implications for family members?

A referral to Genetic Health Queensland (https://bit.ly/GeneticHealthQLD) is recommended for detailed discussions of the implications of the result for the patient and their family.

2 Variant of uncertain significance (VUS)

This is a variant in a relevant gene, however there is insufficient evidence to fully understand it at this time. The result is ***uninformative***.

A VUS should **NOT** be used for:

✘ confirming a genetic diagnosis
✘ making clinical management decisions
✘ testing unaffected family members
✘ family planning/prenatal testing

Clarify the following:

☐ Does the patient's clinical phenotype match the condition associated with the gene?

☐ Do the number of variants identified in the gene match the mode of inheritance of the condition?

The VUS would be highly suspicious if both of the above are true.

For a highly suspicious VUS:
- Contact the testing laboratory to determine if any of the following will assist in further clarification:
  - Non-genetic investigations to define the clinical phenotype
  - Family segregation studies
  - Functional studies of the variant
- Request a re-review of the VUS with the testing laboratory in 2-3 years, as it may be re-classified as further evidence is obtained.

A referral to Genetic Health Queensland (https://bit.ly/GeneticHealthQLD) is recommended for further assessments, interpretation, and discussion of the results with the patient.

3 No variants

A genetic cause *has not* been identified, but is not excluded.

A negative test result may be explained by:
- Incorrect test type for disease aetiology
- Incorrect or incomplete panel(s) selected, which may result from:
  - Atypical presentation of phenotype
  - Incomplete phenotype due to early presentation
- Technical limitations of the test
- Limited evidence to interpret variants
- Inability to interpret and/or detect variants in non-coding or regulatory regions
- Undiscovered disease aetiology and/or gene
- Non-genetic or complex disease aetiology

Consider further testing (if relevant) or reanalysis of the genomic test data in 2-3 years if there is a strong suspicion of a monogenic condition in the patient.

A referral to Genetic Health Queensland (https://bit.ly/GeneticHealthQLD) is recommended for further assessments of differential diagnoses and alternate genetic testing methods.