Patient Information Leaflet

Cascade Testing

What is cascade testing?

Cascade testing refers to testing offered to family members of an individual diagnosed with a genetic condition, with the goal of identifying and potentially preventing or treating the condition in others at risk. Cascade testing involves testing for the specific genetic change (variant) identified in the affected individual.

Why am I being offered cascade testing?

Testing for a genetic variant previously identified in your affected relative may be offered by your doctor for multiple reasons;

Diagnostic testing – For patients that have clinical signs and symptoms consistent with the familial genetic condition. Testing for the familial genetic variant is requested to confirm a genetic diagnosis.

Predictive testing – For patient who do not have signs or symptoms in keeping with the familial genetic condition, but where there may be variable or later onset of clinical symptoms associated with the condition. Testing for the familial genetic variant is requested to determine if the patient is at risk of developing the familial condition.

Genseq does not standardly test for Variants of Unknown Significance (VUS). However, testing for a familial VUS may be carried out, where there is a high level of evidence supporting pathogenicity, and where further cascade family testing may help re-classify the variant. This is known as segregation testing.

What is involved in a cascade test?

If you decide to have cascade testing, your doctor will collect a blood sample from you and ship it to the Genseq laboratory for analysis. At Genseq, DNA will be extracted from the blood sample and analysed using the Sanger sequencing method. The data generated will be analysed and reported on by Genseq. The tests results will be sent to your doctor who will discuss them with you.

Understanding my cascade test results

Results for diagnostic and predictive cascade tests are reported as “Familial variant was identified” or “Familial variant not identified”. Further interpretation is provided depending on whether the detected variant is classified as pathogenic or likely pathogenic and the reason for cascade testing.

Version 1 (LI-GEN-0033)
July 2025

- **Pathogenic or likely pathogenic familial variant was identified**
  The DNA sample tested positive for the familial pathogenic or likely pathogenic variant. If the test is diagnostic, this confirms, or is consistent with, a genetic diagnosis of the familial condition. Where a predictive test was performed, it means there is a high risk of developing symptoms associated with the familial condition.
- **The familial pathogenic or likely pathogenic variant was not identified**
  This results means that the familial pathogenic or likely pathogenic variant was not identified in the DNA sample tested. For diagnostic cases, a negative result does not exclude the possibility of a genetic cause for the clinical symptoms, as other genetic variants are not tested for. For predictive tests, this results indicates a significantly reduced risk of developing clinical symptoms associated with he familial disorder.

For patient cases where a pathogenic or likely pathogenic variant is detected, Genseq will securely store patient DNA for 5 years to facilitate potential future and/or family based testing.

Test Restrictions

Test results should always be interpreted in conjunction with clinical findings, family history, and other relevant laboratory data. Results are provided based on current knowledge, which may evolve over time.

Technical Limitations

This test only determines the presence or absence only of the specified familial genetic variant and does not include testing for genetic abnormalities in other regions or genes. Where no familial positive control is available, the possibility of a false negative result due to a familial variant under the primer site cannot be completely excluded.