Nystagmus Xpanded Panel

Nystagmus is an involuntary, rapid, and repetitive movement of the eyes most often associated with some degree of visual impairment, and can be congenital or later onset.

Features:

- A comprehensive and dynamic gene list. Currently, the test offers sequencing analysis of approximately 800 nuclear genes, which includes:
  - Genes currently associated with primarily ophthalmic disorders, where clinical features are limited to eye findings including nystagmus
  - Genes currently associated with syndromes exhibiting extra-ocular features, and for which nystagmus is an associated feature
- Utilizes a Trio approach (includes concurrent analysis of the affected proband and both parents) in order to increase the likelihood of identifying a definitive genetic explanation for nystagmus
- TAT: 6 weeks

Why is this Test Useful?

Due to the genetically and phenotypically heterogeneous nature of genetic conditions that include nystagmus as a clinical feature, it can be challenging to determine the underlying cause of nystagmus or predict the disease-causing gene based on clinical features or ancillary testing alone. Furthermore, interpretation of the clinical significance of variants can be difficult in the absence of parental testing to clarify the inheritance of identified variants. This underscores the need for a broad, expansive, flexible, and trio-based molecular test such as the Nystagmus Xpanded panel.

Reporting Strategies:

- Phenotype driven test reports which include the following:
  - Pathogenic or likely pathogenic variants in genes associated with the patient's phenotype
  - Variants of uncertain significance (VUS) in genes that are possibly associated with the patient's phenotype
- Reports will not include a comprehensive list of all observed variants
- Incidental findings will not be reported

Test Sensitivity:

Exome sequencing performed at GeneDx in individuals with nystagmus has demonstrated a diagnostic rate ranging from 26% for singleton (proband only) cases to 38% for trio (typically proband plus parents) cases, with an overall diagnostic rate of **34.6%**. The sensitivity of the Nystagmus Xpanded Panel is expected to be comparable to trio-based exome sequencing since it utilizes a trio approach to test a comprehensive list of genes known to be associated with nystagmus.

Possible Outcomes of Genetic Testing

There are four possible outcomes of genetic testing: positive (pathogenic variant), likely pathogenic variant, variant of uncertain significance (VUS), and negative. Genetic counseling is recommended prior to genetic testing to understand the benefits and limitations of testing.

A positive result indicates that a pathogenic variant (harmful change) was identified in a specific gene and the risk to develop a particular disease is increased.

A likely pathogenic variant result indicates that there is a change, or genetic variant, in a specific gene that is likely pathogenic (harmful). For this type of result, there is significant, but not conclusive, evidence that there is a risk to develop a particular disease.

A variant of uncertain significance (VUS) indicates that the effect of the variant cannot be clearly established. A VUS is a change in a gene that has never been seen before or because of conflicting or incomplete information in the medical literature, its association with disease is unknown.

A negative result means that no reportable changes were identified.

Sample Submission

Genetic testing can be performed on blood, oral rinse, buccal swabs, or extracted DNA samples. GeneDx test kits are available to ordering providers, and include sample collection items (such as mouthwash, collection tubes), the necessary sample submission paperwork, and a self-addressed return shipping label. Buccal Brushes: CANNOT be accepted. Additionally, all test requisition forms are available for download from the GeneDx website: www.genedx.com/forms

Please note that all testing must be performed under the guidance of a healthcare provider. For more information on the sample submission process, please visit our website: www.genedx.com/supplies or email us at: zebras@genedx.com.

Testing must be performed under the guidance of a healthcare provider.

1. Download the Ophthalmology test requisition form from the GeneDx website: www.genedx.com/forms
2. Complete all the forms with required information
3. Ship completed forms along with patient sample to the following address:

   Accessions
   GeneDx
   207 Perry Parkway
   Gaithersburg, MD 20877
4. Accepted sample types include blood, oral rinse, buccal swabs, or extracted DNA.

For more information on the sample submission process, or to place an order for shipping kits, please visit our website: genedx.com/supplies or email us at: zebras@genedx.com

References

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207 Perry Parkway
Gaithersburg, MD 20877
T 1 888 729 1206 (Toll-free), 1 301 519 2100 • **F** 1 201 421 2010
E zebras@genedx.com • www.genedx.com

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an OPKO Health Company