

Retinal dystrophies are a clinically and genetically heterogeneous group of eye disorders, characterized by the degeneration of photoreceptors and retinal pigment epithelium cells.

## Features:

- A comprehensive and dynamic gene list. Currently, the test offers sequencing analysis of approximately 900 nuclear genes, which includes:
  - Genes currently associated with nonsyndromic retinal dystrophies
  - Genes associated with syndromes in which retinal dystrophy 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 retinal dystrophy
- TAT: 6 weeks

## Distinct Test Attributes:

- The ORF15 region of the *RPGR* gene is included. However, this region has inherent sequence properties that yield suboptimal data and pathogenic variants in this region may not be reliably detected.
- Includes analysis of the recurrent c.2991+1655A>G variant in the *CEP290* gene
- Includes analysis of deep intronic variants of *ABCA4* previously reported in the literature in association with Stargardt disease (5196+1216C>A, 5196+1159G>A, 5196+1137G>A, 5196+1136C>A, 5196+1056A>G, 570+1798A>G, 1938-619A>G, 2160+584A>G, 3050+370C>T, 4540-2036C>A, 4539+2064C>T, 4539+2028C>T, 4539+2001G>A, 4539+1729G>T)

## Why is this Test Useful?

Due to the genetically and phenotypically heterogeneous nature of retinal dystrophies, it can be challenging to determine the specific form of retinal dystrophy 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 Retinal Dystrophy 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:

Previous exome sequencing studies evaluating individuals with retinal dystrophy have demonstrated a diagnostic rate of **49-71%**. The clinical sensitivity of the Retinal Dystrophy Xpanded Panel is expected to be comparable to exome sequencing since the test utilizes a trio-based approach to analyze a comprehensive list of genes known to be associated with retinal dystrophy.

## 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](http://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](http://www.genedx.com/supplies) or email us at: [zebras@genedx.com](mailto: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](http://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](http://genedx.com/supplies) or email us at: [zebras@genedx.com](mailto:zebras@genedx.com)

## References

1. Beryozkin et al. (2015) Sci Rep 5 :13187 (PMID: 26306921)
2. Lee et al. (2015) Am. J. Ophthalmol. 160 (2):354-363.e9 (PMID: 25910913)
3. de Castro-Miro et al. (2016) PLoS ONE 11 (12):e0168966 (PMID: 28005958)
4. Haer-Wigman et al. (2017) Eur. J. Hum. Genet. 25 (5):591-599 (PMID: 28224992)
5. Riera et al. (2017) Sci Rep 7 :42078 (PMID: 28181551)
6. Carss et al. (2017) Am. J. Hum. Genet. 100 (1):75-90 (PMID: 28041643)
7. Braun et al. (2013) Human Molecular Genetics 22 (25):5136-45 (PMID: 23918662)
8. Zernant et al. (2014) Hum. Mol. Genet. 23 (25):6797-806 (PMID: 25082829)
9. Bauwens et al. (2015) Hum. Mutat. 36 (1):39-42 (PMID: 25346251)
10. Schulz et al. (2017) Invest. Ophthalmol. Vis. Sci. 58 (1):394-403 (PMID: 28118664)



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](mailto:zebras@genedx.com) • [www.genedx.com](http://www.genedx.com)

