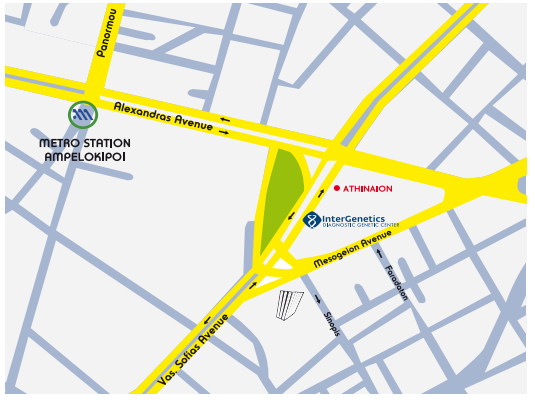
How genomic testing is performed and how long does it take to be completed

The test involves the parallel analysis of the DNA sequence of all the exons of ~200 genes associated with various types of ophthalmogenetic disorders, analyzing genes associated with all known genetic disorders of the eye.

The test is based on the method of Next Generation Sequencing (NGS) and utilizes a special Genome Analyzer instrument together with complex and highly specialized software tools. The test is generally completed within 3-4 months.

Genetic counseling

Proper clinical genetic assessment of each case and genetic counseling, both before and following the test, is essential in order to determine the appropriate strategy for laboratory testing and to interpret correctly the concepts of pathological and normal.



InterGenetics
DIAGNOSTIC GENETIC CENTER

120, Vas. Sofias Av.,
11526 Athens, Greece
T/ (+30) 2107705010 • 2107756588
T/ (+30) 2107705125 • 2104177919
F/ (+30) 2107705011

info@intergenetics.eu
www.intergenetics.eu

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DIAGNOSTIC GENETIC CENTER

GENOMIC TESTING OF OPHTHALMOGENETIC DISORDERS

- ✓ *diagnosis and disease prediction for each ophthalmologenetic disorder are closely associated with the identification of the genetic etiology*
- ✓ *genetic testing was selective and incomplete, often without a conclusive diagnosis*
- ✓ *comprehensive genomic testing of all genes currently known to be associated with numerous ophthalmogenetic disorders, leads in a single step to successful diagnosis and disease management*

Clinical features of the disorders

Genetic diseases of the eye (and/or involvement of the eye) are relatively common, making them the leading cause of blindness in children and adults, and have exhibit considerable clinical and genetic heterogeneity. A number of retinal diseases, such as retinitis pigmentosa, the cone-rod dystriphies, achromatopsia, etc. cause degeneration of the photoreceptor and it is often difficult to distinguish the exact type.

More than 90 forms of retinitis pigmentosa have been described and >60 associated genes have been identified. Correspondingly, Leber Congenital Amaurosis (LCA) is caused by approximately 12 to 15 different genes, is characterized by loss of vision from birth and over time it may manifest with coloboma of the macula and retinopathy.

Most ophthalmic genetic disorders are not yet treatable and/or do not have a therapeutic approach, mainly due to our limited understanding of the pathogenesis.

Ophthalmologists, especially pediatric ophthalmologists, are often the ones who are at the forefront for the evaluation of patients and families with these types of disorders.

The genetic basis of ophthalmogenetic disorders

Currently, numerous genes have been identified in which mutations are associated with one or more ophthalmogenetic disorder.

The broader categories of ophthalmogenetic disorders that are tested include:

1) all types of retinitis pigmentosa,
2) all the different types of cone or cone-rod dystrophies,
3) Leber congenital amaurosis,
4) the macular diseases,
5) retinoblastoma, and generally almost all eye diseases which may have a genetic basis.

The mode of inheritance of ophthalmogenetic disorders varies and includes all possible types: autosomal recessive, autosomal dominant and X-linked.

The ophthalmogenetic disorders have a particular complexity as to the genetic etiology, since mutations in different genes result in similar clinical symptoms and different mutations in a single gene lead to different clinical manifestations. Also, the severity of the disease may vary among patients with the same mutation, due to other modifying genetic or non-genetic factors.

Finally, they have been reported cases with digenic inheritance, requiring mutations in two different genes for expression of the disease.

Why is genomic testing for ophthalmogenetic disorders useful?

Given the nature, seriousness and complexity, genomic testing for ophthalmogenetic disorders is particularly valuable, if not indispensable, and aims for the accurate and efficient identification of the genetic causes for:

1) diagnosis of the specific type of disease,
2) the prediction of disease progression,
3) the prevention of the disease in the the wider family and the possibility of hereditary transmission and
4) properly adjusted treatment options or possible therapy.

Generally, precise diagnosis of an ophthalmogenetic disorder through genetic testing, undoubtedly facilitates the development and introduction of new and personalized treatments.