

Autosomal Dominant Optic Atrophy: *OPA3* Gene Sequencing

Test Code: AF

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Mutations in the *OPA3* gene have been associated with different forms of optic atrophy. Autosomal dominant optic atrophy (ADOA) is characterized by progressive visual loss beginning in childhood, loss of visual acuity, and optic nerve pallor. Mutations in the gene *OPA3* have been associated with ADOA and cataracts (ADOAC) [1]. Type III 3-methylglutaconic aciduria (MGA; Costeff optic atrophy syndrome) is an autosomal recessive disorder characterized by early onset bilateral optic atrophy and later onset ataxia, spasticity, and cognitive decline. A hallmark of disease is increased urinary excretion of 3-methylglutaconic and 3-methylglutaric acid. A founder *OPA3* mutation accounts for the relatively high frequency of Type III MGA in the Iraqi Jewish population [2]. Diagnostic sequencing analysis of the *OPA3* gene coding region is available for patients with optic atrophy and their at risk family members.

For further information call EGL Genetics at 470-378-2200.

For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array KN.

References:

- 1). Reynier, P., P. Amati-Bonneau, C. Verny, A. Olichon, G. Simard, A. Guichet, C. Bonnemains, F. Malecaze, M.C. Malinge, J.B. Pelletier, P. Calvas, H. Dollfus, P. Belenguer, Y. Malthiery, G. Lenaers, and D. Bonneau, *OPA3* gene mutations responsible for autosomal dominant optic atrophy and cataract. *J Med Genet*, 2004. 41(9): p. e110.
- 2). Anikster, Y., R. Kleta, A. Shaag, W.A. Gahl, and O. Elpeleg, Type III 3-methylglutaconic aciduria (optic atrophy plus syndrome, or Costeff optic atrophy syndrome): identification of the *OPA3* gene and its founder mutation in Iraqi Jews. *Am J Hum Genet*, 2001. 69(6): p. 1218-24.

Genes

[OPA3](#)

Indications

- Clinical features associated with *OPA3* gene mutations
- Prenatal testing after a familial mutation has been identified
- Testing for persons at risk for carrying a familial mutation

Methodology

PCR amplification of 2 exons contained in the *OPA3* gene coding region will be performed on patient genomic DNA. Direct sequencing of amplification products is performed in both the forward and reverse directions using automated fluorescence dideoxy sequencing methods. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then classified as mutations, benign variants unrelated to disease or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members.

This assay does not interrogate the promoter region, deep intronic regions or other regulatory elements. Large deletions are not detected by this analysis. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Detection

Analytical Sensitivity: ~99%

Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: Saliva**Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Special Instructions

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

Related Tests

- OPA1 gene sequencing
- [Custom diagnostic mutation analysis \(KM\)](#) is available to family members if mutations are identified by sequencing.
- A deletion/duplication assay is available separately for individuals where mutations are not identified by sequence analysis. Refer to the test requisition or contact the laboratory for more information.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.