Autosomal Dominant Optic Atrophy (Kjer Type): **OPA1** Gene Sequencing

**Condition Description**

Autosomal dominant optic atrophy, Kjer type, is the most common form of hereditary optic neuropathy. The incidence of ADOA is approximately 1 in 50,000 to 1 in 10,000 live births. It is a childhood onset disorder typically characterized by a progressive loss in central vision, color vision deficits (dyschromatopsia), decreased visual acuity, decreased sensitivity of the central retinal field (paracentral scotomas), and asymmetric degeneration of the retinal ganglion cells visible as pallor of the optic disk. The underlying defect is retinal ganglion cell degeneration. The disease phenotype displays both inter- and intra-familial variability with incomplete penetrance. Mutations in the **OPA1** gene, located on chromosome 3q28-q29, cause Kjer type autosomal dominant optic atrophy. **OPA1** consists of 31 exons and encodes a mitochondrial dynamin-related GTPase, a protein thought to be involved in maintaining the structure and function of mitochondria. Approximately 90% of autosomal dominant optic atrophy patients carry a mutation in **OPA1**. For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array KO.

**Genes**

**OPA1**

**Indications**

This test is indicated for patients with a diagnosis of optic atrophy. Sequencing is not appropriate for prenatal samples in which familial mutations have not been identified.

**Methodology**

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

**Detection**

Approximately 90% of autosomal dominant optic atrophy patients carry a mutation in **OPA1**. This assay will detect sequence variants in the coding region and splice junctions. Large deletion and insertion mutations will not be detected by this assay. It is possible that some patients with typical presentation may not carry a mutation detected by this analysis.

**Specimen Requirements**

**Submit only 1 of the following specimen types**

**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 24 hours of collection. Do not refrigerate or 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.

**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.

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
Specimen Collection and Shipping:
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

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

Related Tests
- Leber Hereditary Optic Neuropathy (QC) is a mitochondrial disorder characterized by atrophy of the optic nerve.
- OPA3 gene 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 may be available for couples with confirmed OPA1 mutations.

Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by sequencing. Prenatal testing may be available to couples who are confirmed carriers of OPA1 mutations. Please contact the laboratory genetic counselor to arrange prior to collecting a prenatal specimen.