### 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

**Type: Whole Blood**

- **Specimen Requirements:**
  - In EDTA (purple top) or ACD (yellow top) tube:
    - Infants (2 years): 3-5 ml
    - Older Children & Adults: 5-10 ml

  Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

- **Specimen Requirements:**
  - Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

  Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection 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 is available to family members if OPA1 mutations are identified by sequencing. Please contact the laboratory genetic counselor to arrange prior to collecting a prenatal specimen.