**Condition Description**

The *PAX6* gene (11p13) has been described as a master regulator of eye development and is also reported to influence development of the central nervous system, pancreatic islets, and the pituitary gland. Pathogenic variants in the *PAX6* cause aniridia and non-aniridia eye disorders.

**Aniridia**

Aniridia is complete or partial iris hypoplasia. It is associated with foveal hypoplasia and reduced visual acuity. These features present in early infancy. Additional ocular abnormalities that may occur later in life include glaucoma, cataract, and corneal opacification and vascularization. Pathogenic variants within the *PAX6* gene only cause isolated aniridia without any systemic involvement. Wilms tumor-aniridia-genital anomalies-retardation (WAGR) syndrome is caused by a larger deletion of 11p13 that includes both the *PAX6* and *WT1* genes. Isolated aniridia is inherited in an autosomal dominant manner. Haploinsufficiency of the *PAX6* gene causes aniridia.

Please note that a chromosomal microarray is the recommended test for detecting the WAGR deletion.

**Optic Nerve Malformations**

In rare cases, pathogenic variants in the *PAX6* gene cause non-aniridia phenotypes that include anterior segment anomalies, congenital cataracts, and foveal hypoplasia. These highly variable ocular phenotypes include Peter’s anomaly, ectopic papillae, and autosomal dominant keratitis.

**References:**

- GeneReviews
- OMIM #607108: *PAX6* gene

**Genes**

*PAX6*

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of a *PAX6*-related disorder.
- Carrier testing in adults with a family history of a *PAX6*-related disorder.

**Methodology**

PCR amplification of 9 exons contained in the *PAX6* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are 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, and does not detect large deletions.

**Detection**

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

**Specimen Requirements**

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Store sample at room temperature. 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: 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.

**Related Tests**

- Deletion/duplication analysis of the PAX6 gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Several comprehensive next generation sequencing Eye Disorder Panels are available.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.