Clinical Features
Aniridia is characterized by complete or partial hypoplasia and can result in a range from readily visible, almost complete absence of the iris, through enlargement and irregularity of the pupil mimicking a coloboma, to small slit-like defects in the anterior layer seen only with a slit-lamp (1). Although the phenotype can be variable within a family, individuals usually show little difference between the two eyes.

Molecular Genetics
Aniridia may be caused by heterozygous mutations in PAX6 [OMIM#607108]. PAX6 encodes a transcription factor involved in islet cell differentiation and function and members of families carrying PAX6 mutations also exhibit impaired glucose tolerance and diabetes later in life (2). PAX6 haploinsufficiency through loss of function mutations result in classic aniridia, while PAX6 missense mutations typically produce atypical or variable-phenotype aniridia. PAX6 mutations have also been described in a number of other ocular developmental disorders including Aniridia, Cerebellar Ataxia and Mental retardation [OMIM#206700], Foveal Hypoplasia and Presenile Cataract syndrome [OMIM#136520] and Peters anomaly [OMIM#604229].

Inheritance
While the majority of PAX6 mutations are inherited in a dominant fashion, two cases carrying biallelic mutations in PAX6 have been reported: the first case died at 1 week of life and exhibited severe brain malformations, microcephaly, and anophthalmia, without mention of hyperglycemia. Another surviving case had brain malformations, microcephaly, microphthalmia, and panhypopituitarism, along with neonatal-onset diabetes (3).

Test methods:
Comprehensive sequence coverage of the coding regions and splice junctions of the PAX6 gene is performed. Targets of interests are captured and amplified using Agilent SureSelect System. The constructed genomic DNA library is sequenced using Illumina technology and reads are aligned to the reference sequence. Variants are identified and evaluated using a custom collection of bioinformatic tools and comprehensively interpreted by our team of directors and genetic counselors. All pathogenic or likely pathogenic variants are confirmed by Sanger sequencing. The technical sensitivity of this test is estimated to be >99% for single nucleotide changes and insertions and deletions of less than 20bp. Deletion/duplication analysis is performed by oligonucleotide array-CGH. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

PAX6 sequencing
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1000
CPT codes: 81406
Turn-around time: 4 weeks

PAX6 deletion/duplication analysis
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1000
CPT codes: 81405
Turn-around time: 4 weeks

Results:
Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References: