PAX2 Gene Analysis in Renal-Coloboma Syndrome / Papillorenal Syndrome

Clinical Features:
Renal-coloboma syndrome is principally characterized by ocular and renal abnormalities. The PAX2 gene encodes a transcription factor that is expressed in the developing eye, kidney, ear, ureteric bud, and midbrain/hindbrain. Individuals diagnosed with renal-coloboma syndrome present with highly variable clinical manifestations. The most common abnormalities in patients with renal-coloboma syndrome are bilateral optic nerve colobomas and renal hypoplasia with or without renal failure. Patients may also present with auditory abnormalities, urogenital defects causing vesico-ureteral reflux, and central nervous system malformations. The phenotypes among patients can vary both within and between families, and definitive genotype-phenotype correlations have largely been elusive.[1-5]

Inheritance Pattern/Genetics:
Autosomal dominant

Test Methods:
Analysis of the PAX2 gene is offered in two tiers. These tiers may be ordered as reflexive testing where Tier 2 will only be completed if Tier 1 is negative or may be ordered concurrently so that Tier 1 and Tier 2 will analyzed simultaneously. Tier 1 will consist of sequence analysis of exon 2 of PAX2 gene, where a large majority of pathogenic variants have been identified. Tier 2 analysis will consist of sequence analysis of the remaining exons of the PAX2 gene (exons 1 and 3-12) not included in Tier 1. Targeted array CGH analysis with exon-level resolution (ExonArrayDx) is also available as a separate test to evaluate for a deletion or duplication of one or more exons of the PAX2 gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

Test Sensitivity:
Variants in the PAX2 gene have been identified in approximately 50% of all patients diagnosed with renal-coloboma syndrome / papillorenal syndrome.[1-4] A deletion of the entire PAX2 gene has been reported in one patient.[5]

References:

1. Dureau et al. (2001) Ophthalmology 108(10):1912-16 (PMID: 11581073).
2. Eccles et al. (1999) Clin Genet 56:1-9 (PMID: 10466411).
3. Cunliffe et al. (1998) J Med Genet 35:806-12 (PMID: 9783702).
4. Bower et al. (2012) Human mutation 33 (3):457-66 (PMID: 22213154).
5. Raca et al. (2011) Genetics in Medicine 13(5):437-42 (PMID: 21285886).