PAX2 Gene Analysis in Renal-Coloboma Syndrome / Papillorenal Syndrome

CLINICAL FEATURES

Renal-coloboma syndrome is principally characterized by ocular and renal abnormalities. ThePAX2 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

Autosomal dominant

TEST SENSITIVITY

Variants in the PAX2 gene have been identified in approximately 50% of all patients clinically diagnosed with renal-coloboma syndrome / papillorenal syndrome.[1-4] Variants detectable by sequencing analysis comprise approximately 95%of variants. Gross deletions have occasionally been observed; however, the exact sensitivity of deletion/duplication testing isunknown.[5] The difference between the clinical sensitivity and the lab sensitivity arises from the range of phenotypes possible in this disorder and the resulting difficulty in diagnosis.

TEST METHODS

Using genomic DNA from the submitted specimen, the coding regions and splice junctions of the requested gene are PCR amplified and capillary sequencing is performed. Bi-directional sequence is assembled, aligned to reference gene sequences based on NCBI RefSeq transcript and human genome build GRCh37/UCSC hg19, and analyzed for sequence variants. Concurrent deletion/duplication testing is performed for most, if not all, of the coding exons using exon-level oligo array CGH (ExonArrayDx), and data analysis is performed using gene-specific filtering. Probe sequences and locations are based on human genome build GRCh37/UCSC hg19. Reported clinically significant variants are confirmed by an appropriate method. Sequence and copy number variants are reported according to the Human Genome Variation Society (HGVS) or International System for Human Cytogenetic Nomenclature (ISCN) guidelines, respectively. Reportable variants include pathogenic variants, likely pathogenic variants and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported but are available upon request.

REFERENCES

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