

## Nephronophthisis via *NEK8/NPHP9* Gene Sequencing (Test #657)

**Brief Description of Clinical Features:** Nephronophthisis (NPH) is the most common genetic cause of progressive renal failure in children and young adults. NPH is characterized by polyuria, growth retardation and progressive deterioration of renal function with normal or slightly reduced kidney size (Hildebrandt et al. Nat Genet 17:149-153, 1997; Hildebrandt et al. J Am Soc Nephrol 20:23-35, 2009). Nephronophthisis Type 9 (NPH9) results in juvenile and adolescent nephronophthisis (Otto et al. J Am Soc Nephrol 19:587-592, 2008; Hildebrandt et al. 2009).

**Genetics:** NPH9 is inherited in an autosomal recessive manner. Mutations in the *NEK8* (also called *NPHP9*) gene cause juvenile and adolescent nephronophthisis (Otto et al. 2008). *NEK8* encodes a protein kinase (never in mitosis kinase NEK 8), which is localized to the cilia and to centrosomes and plays a major role in cell-cycle regulation (Otto et al. 2008). Three missense mutations have been reported in *NEK8/NPHP9* (Otto et al. 2008). Nephronophthisis exhibits locus heterogeneity. Nine NPH genes have been identified (*NPHP1*, *INVS/NPHP2*, *NPHP3*, *NPHP4*, *IQCB1/NPHP5*, *CEP260/NPHP6*, *GLIS2/NPHP7*, *RPGRIP1L/NPHP8* and *NEK8/NPHP9*) (Hildebrandt et al. 2009).

**Description of This Particular Test:** This test involves bidirectional sequencing using genomic DNA of all the 15 coding exons (exon 1-15) of the *NEK8/NPHP9* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on each side are sequenced. As required, we will also perform sequencing of any single exon or pair of exons for family members of patients with known mutations and to confirm previous research results (\$190-340 charge).

**Reference Sequences:** Genomic: NC\_000017.10 mRNA: NM\_178170.2 Protein: NP\_835464.1 (CCDS 32597.1)

**Indications for Test:** Candidates for this test are patients with symptoms consistent with juvenile and adolescent NPH and the family members of patients who have known mutations. Conclusive connections between clinical features and individual mutated genes have not yet been made.

**Sensitivity of Test:** Mutations in the *NEK8/NPHP9* gene are estimated to cause less than 1% of NPH cases (Hildebrandt et al. 2009).

**Turnaround Time:** Maximum of 40 calendar days, although many tests are completed in 2-3 weeks.

**Specimen Requirements:** See page 4 of the Requisition Form.

**Prices:** Sequencing of *NEK8/NPHP9* gene \$ 840

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x15	83898 \$ 230	Sequencing x15	83904 \$ 350
Separation x1	83894 \$ 70	Interpretation/Report x2	83912 \$ 120

**Accreditation Info.** CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

**Contact:** Dr. Keith Nykamp, [keith.nykamp@preventiongenetics.com](mailto:keith.nykamp@preventiongenetics.com), [www.preventiongenetics.com](http://www.preventiongenetics.com)