

Nephronophthisis via *GLIS2/NPHP7* Gene Sequencing (Test #656)

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 7 (NPH7) (OMIM 611498) is a form of juvenile nephronophthisis (Attanasio et al. Nat Genet 39: 1018-1024, 2007; Hildebrandt et al. 2009).

Genetics: NPH7 is inherited in an autosomal recessive manner. Mutations in the *GLIS2/NPHP7* gene cause NPH7 (Attanasio et al. 2007). *GLIS2* encodes a Gli-similar protein 2 (GLIS2), which is localized to the primary cilia. GLIS2 is a Kruppel-like zinc finger transcription factor essential for normal renal cell maintenance (Attanasio et al. 2007; Kim et al. Mol Cell Biol 28:2358-2367, 2008). Only a single splicing mutation has been reported in the *GLIS2/NPHP7* gene (Attanasio et al. 2007). 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 6 coding exons (exon 1-6) of the *GLIS2/NPHP7* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on each side are sequenced. As indicated, 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_000016.8 mRNA: NM_032575.2 Protein: NP_115964.2 (CCDS 10511.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with juvenile 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 *GLIS2/NPHP7* gene are estimated to cause less than 1% of the NPH cases (Hildebrandt et al., 2009).

Turn Around 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 the *GLIS2/NPHP7* gene \$ 540

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x7	83898 \$ 140	Sequencing x7	83904 \$ 200
Separation x1	83894 \$ 50	Interpretation/Report x1	83912 \$ 80

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

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