

Nephronophthisis / Senior-Loken Syndrome and Bardet-Biedl Syndrome via *SDCCAG8* Gene Sequencing (Test #659)

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 10 (NPH10) (OMIM 613615) is a form of juvenile nephronophthisis with Leber Congenital Amaurosis known as Senior-Loken syndrome 7 (SLSN7; OMIM 613615) with or without clinical features of Bardet-Biedl Syndrome (Otto et al. Nat genet 42:840-850, 2010). Bardet-Biedl Syndrome (BBS) (OMIM 209900) is a pleiotropic disorder characterized by retinal degeneration, obesity, post-axial polydactyly, cognitive impairment, hypogenitalism and renal and cardiovascular anomalies (Green et al. N Engl J Med 321:1002-1009, 1989; Elbedour et al. Am J Med Genet. 52:164-169, 1994).

Genetics: NPH and BBS are inherited in an autosomal recessive manner. Mutations in the *SDCCAG8* gene cause NPH10/SLSN7 with or without clinical features of Bardet-Biedl Syndrome (Otto et al. 2010). *SDCCAG8* encodes serologically defined colon cancer antigen 8 (SDCCAG8), which is localized to the distal ends of both centrioles and colocalized to the centrosomes throughout the cell cycle in both ciliated and non-ciliated cells (Otto et al. 2010). *SDCCAG8* interacts directly with another ciliopathy protein known as oral-facial-digital syndrome 1 protein (OFD1) (Otto et al. 2010). Missense, nonsense, splicing, small deletion as well as gross deletion mutations have been reported in the *SDCCAG8* gene (Otto et al. 2010). Both NPH and BBS exhibit locus heterogeneity. Ten NPH and at least twelve BBS genes have been identified (Hildebrandt et al. 2009; Tobin and Beales, Genet Med 11:386-402, 2009).

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of the 18 coding exons (exons 1- 18) of the *SDCCAG8* 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 (Test #100, \$190) or pair of exons (Test #200, \$340) for family members of patients with known mutations and to confirm previous research results.

Reference Sequences: Genomic: NC_000001.10 mRNA: NM_006642.3 Protein: NP_006633.1 (CCDS 31075.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with NPH or BBS and family members of patients who have known *SDCCAG8* mutations. Conclusive connections between clinical features and individual mutated *NPH* or *BBS* genes have not yet been made.

Sensitivity of Test: Mutations in the *SDCCAG8* gene are estimated to cause approximately 3.3% of SLSN cases (Otto et al. 2010).

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

Specimen Requirements: See page four of the Requisition Form.

Prices: **Sequencing of *SDCCAG8* gene** **\$ 1040**

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x19	83898 \$320	Sequencing x19	83904 \$470
Separation x1	83894 \$ 60	Interpretation/Report x1	83912 \$120

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

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