

Bardet-Biedl Syndrome via *BBS2* Gene Sequencing (Test #253)

Brief Description of Clinical Features: 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). Bardet-Biedl syndrome 2 (*BBS2*) (OMIM# 606151) is characterized by the cardinal features of BBS (Nishimura et al. Hum. Molec Genet 10:865-874, 2001).

Genetics: *BBS2* is primarily inherited as an autosomal recessive disorder, although complex inheritance has been reported in few families (Katsanis et al. Science 293:2256-2259, 2001). Mutations in the *BBS2* gene cause BBS (Nishimura et al. 2001). *BBS2* encodes BBS2 protein, which is localized to basal bodies of the primary cilia (Nishimura et al. Proc Nat Acad Sci 101:16588-16593, 2004). *BBS2* protein interacts with six other BBS proteins (*BBS1*, *BBS4*, *BBS5*, *BBS7*, *BBS9* and *BBS11*) to form a complex known as BBSome, which has a role in cilia maintenance and function (Nachury et al. Cell 129:1201-1213, 2007). A mix of missense, nonsense, frameshift and splicing mutations has been reported in *BBS2* (Nishimura et al. 2001; Katsanis et al. 2001). BBS exhibits locus heterogeneity; at least 12 BBS genes have been identified (*BBS1*, *BBS2*, *BBS3*, *BBS4*, *BBS5*, *MKKS/BBS6*, *BBS7*, *TTC8/BBS8*, *BBS9*, *BBS10*, *TRIM32/BBS11* and *BBS12*) (Tobin and Beales, Genet Med 11:386-402, 2009). In addition, hypomorphic mutations in two Meckel-Gruber syndrome genes (*MKSI* and *CEP290*) were reported to be associated with BBS, representing *BBS13* and *BBS14* respectively (Leitch et al. Nat Genet 40:443-448, 2008).

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of all the 17 coding exons (exon 1-17) of the *BBS2* 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_000016.9 mRNA: NM_031885.3 Protein: NP_114091.3 (CCDS_32451.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with BBS and the family members of patients who have known *BBS2* mutations. Conclusive connections between clinical features and individual mutated *BBS* genes have not yet been made.

Sensitivity of Test: Mutations in the *BBS2* gene are estimated to cause approximately 8% of BBS cases (Katsanis Hum Mol Genet 13 Spec No. 1:R65-71, 2004).

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 <i>BBS2</i> gene	\$ 890
CPT Codes:		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x16	83898 \$ 260	Sequencing x16 83904 \$ 380
Separation x1	83894 \$ 70	Interpretation/Report x2 83912 \$ 110

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

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