

Bardet-Biedl Syndrome via *BBS5* Gene Sequencing (Test #256)

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 5 (*BBS5*) (OMIM# 603650) is characterized by the cardinal features of BBS (Li et al. Cell 117:541-552, 2004).

Genetics: BBS is primarily inherited as an autosomal recessive disorder, although complex inheritance has been reported in a few BBS families (Katsanis et al. Science 293:2256-2259, 2001). Mutations in the *BBS5* gene cause BBS (Li et al. 2004; Hjortshoj et al. Am J Med Genet 146A:517-520, 2008). *BBS5* encodes BBS5 protein, which is localized to basal bodies of the primary cilia (Li et al. 2004). BBS5 protein interacts with six other BBS proteins (*BBS1*, *BBS2*, *BBS4*, *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, splicing and small deletion mutations has been reported in *BBS5* (Li et al. 2004; Hjortshoj et al. 2008). 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 (*MKS1* 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 12 coding exons (exons 1-12) of the *BBS5* 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_000002.11 mRNA: NM_152384.2 Protein: NP_689597.1 (CCDS 2233.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with BBS and the family members of patients who have known *BBS5* mutations. Conclusive connections between clinical features and individual mutated *BBS* genes have not yet been made.

Sensitivity of Test: Mutations in the *BBS5* gene are estimated to cause approximately 2% of BBS cases (Li et al. 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>BBS5</i> gene	\$ 740	
CPT Codes:			
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x12	83898 \$ 200	Sequencing x12	83904 \$ 310
Separation x1	83894 \$ 60	Interpretation/Report x2	83912 \$ 100

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

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