

Bardet-Biedl Syndrome via *BBS10* Gene Sequencing (Test #262)

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 10 (BBS10) (OMIM# 610148) is characterized by the cardinal features of BBS (Stoetzel et al. Nat Genet 38:521-524, 2006).

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 *BBS10* gene cause BBS (Stoetzel et al. 2006). *BBS10* encodes a CCT/TRiC chaperonin protein (BBS10), which is localized to the basal body of the primary cilium (Marion et al. Proc Nat Acad Sci 106:1820-1825, 2009). BBS10 protein interacts with two other CCT/TRiC chaperonin-like BBS proteins, MKKS/BBS6 and BBS12, to form a chaperonin complex that mediates BBSome complex assembly (Seo et al. PNAS 107:1488-1493, 2010). A mix of missense and small deletion mutations has been reported in *BBS10* (Stoetzel et al. 2006; Laurier et al. Eur J Hum Genet 14:1195-1203, 2006). 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 the 2 coding exons (exons 1 and 2) of the *BBS10* 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_000012.11 mRNA: NM_024685.3 Protein: NP_078961.3 (CCDS 9014.2)

Indications for Test: Candidates for this test are patients with symptoms consistent with BBS and the family members of patients who have known *BBS10* mutations. Conclusive connections between clinical features and individual mutated *BBS* genes have not yet been made.

Sensitivity of Test: Mutations in the *BBS10* gene are estimated to cause approximately 20% of BBS cases (Stoetzel et al. 2006).

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 *BBS10* gene \$ 490

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x6	83898 \$ 120	Sequencing x6	83904 \$ 170
Separation x1	83894 \$ 40	Interpretation/Report x1	83912 \$ 90

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

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