

Bardet-Biedl Syndrome via *BBS12* Gene Sequencing (Test #264)

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 12 (BBS12) (OMIM# 610683) is characterized by the cardinal features of BBS (Stoetzel et al. Am J Hum Genet 80:1-11, 2007).

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 *BBS12* gene cause BBS (Stoetzel et al. 2007). *BBS12* encodes a group II chaperonin protein (BBS12), which is localized to the basal body of the primary cilium (Marion et al. Proc Nat Acad Sci 106:1820-1825, 2009). BBS12 interacts with two other chaperonin-like BBS proteins, MKKS/BBS6 and BBS10, to form a chaperonin complex that mediates BBSome complex assembly (Seo et al. PNAS 107:1488-1493, 2010). A mix of missense, nonsense and small deletion mutations has been reported in *BBS12* (Stoetzel et al. 2007). 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 only coding exon (exon 2) of the *BBS12* gene. The full coding region of this exon plus ~50 bp of flanking non-coding DNA on each side are sequenced. As indicated, we will also perform sequencing of the relevant portion(s) of the exon for family members of patients with known mutations and to confirm previous research results (\$190-340 charge).

Reference Sequences: Genomic: NC_000004.11 mRNA: NM_152618.2 Protein: NP_689831.2 (CCDS 3728.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with BBS and the family members of patients who have known *BBS12* mutations. Conclusive connections between clinical features and individual mutated *BBS* genes have not yet been made.

Sensitivity of Test: Mutations in the *BBS12* gene are estimated to cause approximately 5% of BBS cases (Stoetzel et al. 2007).

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 *BBS12* gene \$ 490

CPT Codes:

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|-------------------------|--------------|--------------------------|--------------|
| 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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