

Bardet-Biedl Syndrome via *TTC8/BBS8* Gene Sequencing (Test #259)

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 8 (BBS8) (OMIM# 608132) is characterized by the cardinal features of BBS (Ansley et al. Nature 425:628-633, 2003).

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 *TTC8/BBS8* gene cause BBS (Ansley et al. 2003; Stoetzel et al. J Hum Genet 51:81-84, 2006). *TTC8/BBS8* encodes a tetratricopeptide repeat protein (TTC8) that contains 8 TPR domains and shows similarity to a prokaryotic domain pilF that is involved in pilus formation, twitching motility, and pilus assembly. TTC8 interacts with another protein involved in centriolar replication during ciliogenesis (PCM1) and is predicted to have a role in spermatids, cilium of the retina, and bronchial epithelial cells (Ansely et al. 2003). A mix of missense, splicing and small deletion mutations has been reported in *BBS8* (Ansely et al. 2003). 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 15 coding exons (exons 1-15) of the *TTC8/BBS8* 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_000014.8 mRNA: NM_144596.2 Protein: NP_653197.2 (CCDS 32137.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with BBS and the family members of patients who have known *TTC8/BBS8* mutations. Conclusive connections between clinical features and individual mutated *BBS* genes have not yet been made.

Sensitivity of Test: Mutations in the *TTC8/BBS8* gene are estimated to cause approximately 2% 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 *TTC8/BBS8* gene \$ 850

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x15	83898 \$ 240	Sequencing x15	83904 \$ 360
Separation x1	83894 \$ 70	Interpretation/Report x1	83912 \$ 110

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

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