

## Bardet-Biedl Syndrome via *ARL6/BBS3* Gene Sequencing (Test #254)

**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 3 (BBS3) (OMIM# 608845) is characterized by the cardinal features of BBS (Chiang et al. Am J Hum Genet 75:475-484, 2004; Fan et al. Nat Genet 36:989-993, 2004).

**Genetics:** BBS3 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 *ARL6/BBS3* gene cause BBS (Chiang et al. 2004; Fan et al. 2004). *ARL6* encodes ADP-ribosylation factor (ARF)-like-6 (ARL6), which is a member of a subgroup of the ARF family proteins that regulate diverse cellular functions, including regulation of intracellular traffic (Pasqualato et al. *EMBO Rep.* 3:1035-1041, 2002). Although, the precise function of the ARL6 protein is unknown, it has been proposed that ARL6 protein may have a role in cilia function and intracellular transport (Chiang et al. 2004). A mix of missense and nonsense mutations has been reported in *ARL6/BBS3* (Chiang et al. 2004; Fan et al. 2004). 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 7 coding exons (exon 4-10) of the *ARL6/BBS3* 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\_000003.11 mRNA: NM\_032146.3 Protein: NP\_115522.1 (CCDS 2928.1)

**Indications for Test:** Candidates for this test are patients with symptoms consistent with BBS and the family members of patients who have known *ARL6/BBS3* mutations. Conclusive connections between clinical features and individual mutated *BBS* genes have not yet been made.

**Sensitivity of Test:** Mutations in the *ARL6/BBS3* gene are estimated to cause approximately 1% 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 *ARL6/BBS3* gene \$ 540

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x7	83898 \$ 140	Sequencing x7	83904 \$ 200
Separation x1	83894 \$ 40	Interpretation/Report x2	83912 \$ 90

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

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