

Bernard-Soulier Syndrome Testing via *GP1BB* Gene Sequencing (Test #434)

Brief Description of Clinical Features: Bernard-Soulier Syndrome (BSS) (OMIM 231200) (also sometimes called Giant Platelet Syndrome) is a bleeding disorder characterized by mild-severe thrombocytopenia with large platelets. Onset is typically in infancy or childhood. Common bleeding problems include purpura, nose bleeds, gingival bleeding and menorrhagia. BSS is caused by defects in the von Willebrand factor receptor on the platelet cell surface. Platelet-type or pseudo von Willebrand's disease and benign Mediterranean macrothrombocytopenia are variants of BSS (Balduini et al. Haematologica 87:860-880, 2002). BSS is sometimes misdiagnosed as immune (idiopathic) thrombocytopenic purpura (ITP) (Kunishima et al. Eur J Haematol 76:348-355, 2006). For more information, see Lopez et al. Blood 91:4397-4418, 1998; Lanza et al. Orphanet J Rare Diseases 1:46, 2006; and www.bernardsoulier.org.

Genetics: BSS is an autosomal recessive disorder, although carriers of a single causative mutation may have large platelets and mild bleeding problems. Occasionally, the carrier symptoms are so strong that families display dominant inheritance (see for example Savoia et al. Blood 97:1330-1335, 2001). The von Willebrand factor receptor has four glycoprotein (GP) subunits: GPIb α , GPIb β , GPIX and GPV encoded respectively by the *GP1BA*, *GP1BB*, *GP9* and *GP5* genes. Causative mutations have been identified to date in all of these genes except *GP5*. About 15 different causative mutations have been reported in *GP1BB* (Lanza 2006 and www.bernardsoulier.org). These mutations are missense, nonsense and frameshift. In addition, the DiGeorge/Velocardiofacial 22q11.2 deletions often include the *GP1BB* gene (see Budarf et al. Hum Mol Genet 4:763-766, 1995; and McDonald-McGinn et al. GeneReviews 2005 www.genetests.org).

Description of This Particular Test: This test involves bidirectional DNA sequencing of the full coding regions of the *GP1BB* gene. About 50 bp of flanking non-coding DNA on either side of each exon are included. We will sequence the gene in relatives of affected children in cases where DNA from the children is unavailable. We will also perform sequencing of any single or pair of amplicons for family members of patients with known mutations and to confirm research results (\$190-340).

Reference Sequences: Genomic: NC_000022.9 mRNA: NM_000407.4 protein: NP_000398.1

Indications for Test: All patients with symptoms of BSS and their family members are candidates for this test.

Sensitivity of Test: Sensitivity of this test is unknown. This test will not detect the deleted allele in patients carrying the DiGeorge/Velocardiofacial 22q11.2 deletion.

Turn Around Time: Maximum of 40 days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Price: Sequencing of complete coding regions of *GP1BB* Gene **\$ 390**

CPT Codes:

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x3	83898	\$ 90	Sequencing x3	83904	\$ 120
Separation	83894	\$ 40	Interpretation/Report	83912	\$ 70

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

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