

Bernard-Soulier Syndrome Testing via *GP1BA* Gene Sequencing (Test #433)

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 symptoms in carriers 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 25 causative mutations have been reported in *GP1BA* (Lanza 2006 and www.bernardsoulier.org). These mutations are approximately 45% missense, 45% frameshift and 10% nonsense. The middle, coding segment of this gene contains 1-4 copies of a near perfect 39 bp repeat (Afshar-Kharghan et al. *Blood* 103:963-965, 2004). One or more copies of this polymorphic repeated sequence are sometimes presented in databases as an intron. Biologically, however, it is virtually certain that there is no intron within the coding portion of this gene.

Description of This Particular Test: This test involves bidirectional DNA sequencing of the full coding region of the *GP1BA* gene. About 50 bp of flanking non-coding DNA on either side 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_000017.9 mRNA: NM_000173.3 protein: NP_000164.3

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.

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 *GP1BA* Gene **\$ 490**

CPT Codes:

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x5	83898	\$ 120	Sequencing x5	83904	\$ 170
Separation	83894	\$ 50	Interpretation/Report	83912	\$ 80

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

Contact for info: Michael Chicka, PhD, michael.chicka@prevention.genetics.com, www.preventiongenetics.com