

## Bernard-Soulier Syndrome Sequential Testing via *GP1BA*, *GP1BB* and *GP9* Gene Sequencing

**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](http://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 $\alpha$ , GPIb $\beta$ , 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*. Lists of causative mutations have been compiled (see in particular Lanza 2006 and [www.bernardsoulier.org](http://www.bernardsoulier.org)). See the individual Test Descriptions for *GP1BA*, *GP1BB* and *GP9* gene sequencing for more detailed information.

**Description of This Particular Test:** This test has two tiers. In Tier 1 the full coding region of the *GP1BA* gene along with ~50 bp of flanking DNA on either side are bidirectionally sequenced. *GP1BA* contains the most known causative mutations. If Tier 1 is negative, we proceed to Tier 2 which involves bidirectional DNA sequencing of the full coding regions of the *GP1BB* and *GP9* genes.

**Reference Sequences:**

<i>GP1BA</i> : Genomic: NC_000017.9	mRNA: NM_000173.3	protein: NP_000164.3
<i>GP1BB</i> : Genomic: NC_000022.9	mRNA: NM_000407.4	protein: NP_000398.1
<i>GP9</i> : Genomic: NC_000003.10	mRNA: NM_000174.2	protein: NP_000165.1

**Indications for Test:** All patients with symptoms of BSS and their family members are candidates for this test. In cases where DNA from an affected child is unavailable, we will sequence the genes in parents or other family members. We will also sequence any single exon or pair of amplicons in family members of patients with known mutations, and to confirm research results (\$190-340 charge).

**Sensitivity of Test:** The 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.

<b>Price: Tier 1: Sequencing of complete coding regions of <i>GP1BA</i> Gene</b>	<b>\$ 490</b>
<b>Tier 2: Sequencing of complete coding regions of <i>GP1BB</i> and <i>GP9</i> Genes</b>	<b>\$ 490</b>
<b>Sequencing of all three genes (Tiers 1 and 2 together)</b>	<b>\$ 890</b>

**CPT Codes:**

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x11	83898	\$ 250	Sequencing x11	83904	\$ 370
Separation	83894	\$ 70	Interpretation/Report	83912	\$ 130

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

**Contact:** Michael Chicka, PhD, [michael.chicka@preventiongenetics.com](mailto:michael.chicka@preventiongenetics.com), [www.preventiongenetics.com](http://www.preventiongenetics.com)