

Thrombocytopenia via *GATA1* Gene Sequencing (Test #431)

Brief Description of Clinical Features: Germline mutations in the *GATA1* gene located on the X chromosome result in variable defects in platelet and sometimes erythrocyte and neutrophil formation (OMIM 300367 and 314050) (Kacena et al. 2007 Gene Reviews; www.genetests.org). Affected boys usually have moderate to severe bruising and bleeding problems, marked thrombocytopenia (10-40/nl), and average to large-sized platelets. Other clinical features may include erythrocytic anemia, globin gene transcription defects, and porphyria. Female carriers may show mild symptoms. Unlike X-linked Wiskott-Aldrich Syndrome, eczema and immunodeficiency are absent. Molecular diagnosis of this disorder is important to distinguish it from the more common immune thrombocytopenia purpura, and to establish optimal treatment. For additional information, see recent reviews by Balduini et al. (Haematologica 87:860-880, 2002), Drachman (Blood 103:390-398, 2004), and Geddis and Kaushansky (Curr Opin Pediatr 16:15-22, 2004). See also the Platelet Disorder Support Association (www.pdsa.org).

Genetics: *GATA1* mutations are inherited in an X-linked recessive fashion. *GATA1* encodes a transcription factor involved in differentiation of erythrocytes and megakaryocytes. Nearly all causative mutations reported to date have been missense mutations involving amino acids 205-218 encoded in exon 4 (see for example Freson et al. Hum Mol Genet 11:147-152, 2002; Kacena et al. 2007). However, an exon 2 splicing mutation was recently reported that led to patients with macrocytic anemia and neutropenia, but with normal platelet counts (Hollanda et al. Nat Genet 38:807-812, 2006). Connections are beginning to be forged between the specific mutation and phenotype (Kacena et al. 2007).

Description of This Particular Test: This test involves PCR amplification and bidirectional sequencing using genomic DNA of all coding exons (exons 2-6) of the *GATA1* gene. Upon specific request, we will sequence only exon 4 containing the great majority of known, causative mutations (\$190 charge).

We will also perform sequencing of any single exon in this gene for family members of patients with known mutations and to confirm research results.

We do *not* perform testing on transformed cells for cancer diagnosis.

Indications for Test: Candidates for this test are male patients with thrombocytopenia and X-linked pattern of inheritance. Female patients with two causative mutations in *GATA1* are conceivable, but should be very rare and should usually have affected fathers.

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 *GATA1* Exons 2-6

\$ 390

CPT Codes:

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x5	83898	\$ 80	Sequencing x5	83904	\$ 130
Separation	83894	\$ 30	Interpretation/Report	83912	\$ 80

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

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