

Congenital Amegakaryocytic Thrombocytopenia Testing via *MPL* Gene Sequencing (Test #437)

Brief Description of Clinical Features: Congenital Amegakaryocytic Thrombocytopenia (CAMT) (OMIM 604498) is characterized by markedly low platelet counts (average of 21/nl) usually detected in the neonatal period. Affected infants are often identified by easy bruising and/or bleeding episodes. Platelets are of normal size and appearance. Many patients progress to pancytopenia over the first few years of life and require bone marrow transplants. Other patients experience a transient rise in platelet counts over the first few years, before a more gradual transition to pancytopenia. For more information, see recent reviews by Balduini et al. (*Haematologica* 87:860-880, 2002), Drachman (*Blood* 103:390-398, 2004) and Geddis (*Semin Hematol* 43:196-203, 2006). See also the Platelet Disorder Support Association (www.pdsa.org).

Genetics: CAMT is an autosomal recessive disorder caused by mutations with the *MPL* gene on chromosome 1p. *MPL* encodes the cell surface receptor for thrombopoietin. Roughly 40 different causative mutations have been reported. Mutations are about equally split between missense and nonsense/frameshift/splicing. Evidence has been presented that patients with two missense mutations often have a less severe form of disease than patients with two nonsense/frameshift/splicing mutations (Germeshausen et al. *Hum Mut* 27:296, 2006).

Autosomal dominant, germline mutations within *MPL* have also been shown to be responsible for thrombocythemia (thrombocytosis) (Ding et al. *Blood* 103:4198-4200, 2004) and, rarely, in myeloproliferative disorders (Pardanani et al. *Blood* 108:3472-3476, 2006).

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of all 12 coding exons of the *MPL* gene. We will also perform sequencing of any single exon or pair of exons in this gene for family members of patients with known mutations and to confirm research results (\$190-340 charge).

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

Indications for Test: Candidates for this test are patients with symptoms consistent with CAMT, and the family members of patients with known mutations.

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 *MPL* Exons 1-12 **\$ 640**

CPT Codes:

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x10	83898	\$ 180	Sequencing x10	83904	\$ 270
Separation	83894	\$ 40	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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