

MPL Gene Analysis in Congenital Amegakaryocytic Thrombocytopenia

This MPL test is intended for diagnosis of congenital amegakaryocytic thrombocytopenia. It also can be used for certain inherited forms of thrombocytosis. It is not for patients with myeloproliferative disease or other acquired adult disorders.

Disorder also known as:

Thrombopoietin Receptor [TPOR] Deficiency

Clinical Features:

Congenital Amegakaryocytic Thrombocytopenia (CAMT) is a rare disorder characterized by isolated thrombocytopenia and megakaryocytopenia in infancy with no associated physical abnormalities. However, the disorder can evolve into aplastic anemia and leukemia later in life.

Genetics:

CAMT is inherited in an autosomal recessive manner. Almost all confirmed cases of CAMT have two MPL mutations detected by sequencing. For example, of 31 published patients with CAMT whose MPL gene was sequenced in early studies¹⁻⁴, 30 had two disease alleles with various loss-of-function mutations including missense, nonsense and frame shift mutations, while 1 patient had no observed mutations.

Test Methods:

Analysis is performed by bi-directional sequencing of the coding regions and splice sites of exons 1-12 of the MPL gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

Test Sensitivity:

Variants in the MPL gene are the only known cause of CAMT. Typical patients with MPL variants have CAMT, no other congenital physical problems, and elevated blood levels of the platelet-stimulating hormone thrombopoietin (TPO). Variants in MPL are not associated with autosomal dominant congenital thrombocytopenia or with the syndrome Thrombocytopenia-Absent Radii. The test method used by GeneDx is considered better than 95% sensitive because it can detect almost all expected types of MPL gene variants.

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References:

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2. Van den Oudenrijn S. et al, 2000, Mutations in the thrombopoietin receptor, Mpl, in children with congenital amegakaryocytic thrombocytopenia, *Brit. J. Haemat.* 110: 441-448
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4. Tonelli et al., Compound heterozygosity for two different amino acid substitutions in the thrombopoietin receptor (c-mpl gene) in congenital amegakaryocytic thrombocytopenia, 2000, *Hum Genet* 107:225-233.