# 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 studies[1-4], 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:**
Using genomic DNA from the submitted specimen, the coding regions and splice junctions of the requested gene are PCR amplified and capillary sequencing is performed. Bi-directional sequence is assembled, aligned to reference gene sequences based on NCBI RefSeq transcript and human genome build GRCh37/UCSC hg19, and analyzed for sequence variants. Concurrent deletion/duplication testing is performed for most, if not all, of the coding exons using exon-level oligo array CGH (ExonArrayDx), and data analysis is performed using gene-specific filtering. Probe sequences and locations are based on human genome build GRCh37/UCSC hg19. Reported clinically significant variants are confirmed by an appropriate method. If present, apparently homozygous sequence variants are confirmed using alternate primer pairs to significantly reduce the possibility of allele drop-out. Sequence and copy number variants are reported according to the Human Genome Variation Society (HGVS) or International System for Human Cytogenetic Nomenclature (ISCN) guidelines, respectively. Reportable variants include pathogenic variants, likely pathogenic variants and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported but are available upon request.

**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:**


1. Ballmaier M. et al, 2001, C-mpl mutations are the cause of congenital amegakaryocytic thrombocytopenia, Blood 97: 139-146
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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.