Thrombocytosis Gene Sequencing Panel

Condition	Gene(s)	Inheritance*
Thrombocythemia Myelofibrosis	*CALR*	AD, germline or somatic
Thrombocythemia Erythrocytosis Polycythemia vera, somatic Myelofibrosis, somatic Leukemia, acute myeloid, somatic	*JAK2*	AD, germline or somatic
Thrombocythemia Congenital Amegakaryocytic Thrombocytopenia	*MPL*	AD, germline or somatic AR
Thrombocythemia	*THPO*	AD, germline or somatic

***Key:** AD= Autosomal dominant; AR= Autosomal Recessive

Description:

Thrombocytosis, also called thrombocythemia, is characterized by increased platelet production. The increased platelet production can lead to an increased risk for thrombosis. The prognosis for essential thrombocythemia is highly variable and is related to the risk of complications that can occur in those with increased platelets. Hematological transformation into secondary myelofibrosis or acute leukemia can occur, especially in the acquired forms.

Thrombocytosis can be due to somatic or germline variants in the genes *CALR, JAK2, MPL,* and *THPO.* The inheritance pattern is typically autosomal dominant. Of note, the *MPL* gene is also associated with an autosomal recessive condition called Congenital Amegakaryocytic Thrombocytopenia, which typically presents in infancy with thrombocytopenia and megakaryocytopenia.

The Thrombocytosis Gene Sequencing panel uses Next-Generation Sequencing (NGS) to detect variants in four genes that are known to be associated with thrombocytosis. We also offer single gene analysis and targeted variant analysis for any gene on the Thrombocytosis Gene Sequencing Panel. Somatic variants will be detected if they are present in over 12.5% of the alleles in the specimen provided for testing.

Indications:

Thrombocytosis Gene Sequencing Panel:

- Confirmation of genetic diagnosis in a patient with a clinical diagnosis of thrombocytosis

Gene Specific Sequencing:

- Confirmation of genetic diagnosis in a patient with thrombocytosis and in whom a specific gene is suspected

Variant Specific Analysis:

- Carrier testing of parents and other relatives for recurrence risk assessment
- Presymptomatic testing of at-risk family members for medical management
- Prenatal diagnosis of an at-risk fetus, after confirmation of variant(s) in the parent(s) and by prior arrangement only

Specimen:

At least 3 mLs whole blood in a lavender top (EDTA) tube or saliva in an Oragene saliva kit. Please call 513-636-4474 for a free saliva collection kit.

Note: For post-transplant patients, we accept pre-transplant samples or post-transplant skin fibroblasts ONLY (blood, saliva, and cytobrushes are not accepted). Culturing of skin fibroblasts is done at an additional charge. **We are unable to accept blood samples collected within two (2) weeks of a transfusion.**

Testing Methodology:

Next Generation Sequencing (NGS) Panels: This panel performed by enrichment of the coding exons, flanking intronic and untranslated regions (5' and 3'), as well as known pathogenic variants (HGMD 2018.1) in the promoter and deep intronic regions of the genes specified using oligonucleotide probe hybridization followed by next-generation sequencing with >50X coverage at every target base. All pathogenic and novel

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Genetics and Genomics Diagnostic Laboratory
CLIA#: 36D0656333
Phone: (513) 636-4474
Fax: (513) 636-4373
Email: LabGeneticCounselors@cchmc.org
www.cincinnatichildrens.org/genetics

variants, as well as variants of unknown (indeterminate) significance, as determined bioinformatically, are confirmed by Sanger target base. All pathogenic and novel variants, as well as variants of unknown (indeterminate) significance, as determined bioinformatically, are confirmed by Sanger sequencing. Regions with <50X will be filled in by Sanger sequencing. A detailed non-coding variant list is available upon request.

Gene Specific Sequencing: PCR-based sequencing of entire coding region, intron/exon boundaries, as well as known pathogenic variants (HGMD 2018.1) in the promoter and deep intronic regions of the specified gene.

Variant Specific Analysis: Sanger sequencing following PCR amplification of the targeted variant(s) of the specified gene.

Test Sensitivity:

Analytical Sensitivity: The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed.

Limitations: Variants in regulatory regions and non-reported variants in untranslated regions may not be detected by this test. Large deletions/duplications involving an entire single exon or multiple exons and other complex genetic rearrangement events will not be identified using NGS methodology. Rare primer site variants may lead to erroneous results. **Note:** Single gene sequencing is available for all genes on the panel. Deletion/Duplication analysis is available for all genes listed for an additional charge.

Turn-Around Time:

- **Thrombocytosis Gene Sequencing Panel:** 28–42 days
- **Single Gene Sequencing:** 28 days

CPT Codes:

- **Thrombocytosis Gene Sequencing Panel:** 81479 x4
- **Single Gene Testing and Targeted Variant Analysis:** call for information
- **Deletion/Duplication Analysis:** call for information

Please call 1-866-450-4198 for current pricing, insurance preauthorization or with any billing questions.

Results:

Results will be reported to the referring physician or health care provider as specified on the requisition form.

Shipping Instructions:

Please enclose **test requisition** with sample. **All information must be completed before sample can be processed.**

Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship to:

Genetics and Genomics Diagnostic Laboratory
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

References:

Kucine, Nicole, et al. "Primary thrombocytosis in children." Haematologica 99.4 (2014): 620-628.

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Mead AJ. et al (2012) Germline JAK2 mutation in a family with hereditary thrombocytosis. N Engl J Med. 2012 Mar 8;366(10):967-9. doi: 10.1056/NEJMc1200349.

Pardanani, Animesh D., et al. "MPL515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients." Blood 108.10 (2006): 3472-3476.

Rotunno, Giada, et al. "Impact of calreticulin mutations on clinical and hematological phenotype and outcome in essential thrombocythemia." Blood 123.10 (2014): 1552-1555.

Smaili, W., et al. "CALR gene mutational profile in myeloproliferative neoplasms with non-mutated JAK2 in Moroccan patients: A case series and germline in-frame deletion." Current research in translational medicine 65.1 (2017): 15-19.

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