PROMETHEUS®
Therapeutics & Diagnostics
For the person in every patient

PROMETHEUS® TPMT Genetics
Cat. #3300

Test Description

PROMETHEUS® TPMT Genetics helps classify patients as one of three genotypes: homozygous normal (wild type), heterozygous or homozygous recessive. Because each patient metabolizes thiopurines differently, the efficacy and toxicity of thiopurines can vary widely from patient to patient. Knowledge of the TPMT genotype may reduce time to response, allow physicians to individualize dosing, identify patients in whom thiopurine therapy should be avoided and help reduce the risk of leukopenia.

- A qualitative evaluation, to determine a patient's genetic ability to produce the thiopurine methyltransferase (TPMT) enzyme
- **Specimen Requirements** – 5.0 ml whole blood in EDTA / Lavender Top Tube
- **Shipping Requirements** - Ambient or cold pack
- **Storage Stability** - 10 days ambient, 30 days refrigerated
- **Turn Around Time** – 2 business days from date of receipt

Test Information:

Catalog Number	Test Name	Assay	Reference Value	Result Identifier*
3300	TPMT Genetics	Genotype	Alleles present are associated with Normal Enzyme Activity	A00004
			TPMT*1/TPMT*1	

* Result identifier provided for use in HL7 applications.

Laboratory Description

- Prometheus is located in San Diego, CA. **Tax ID#** 33-0685754 **NPI#** 1073642641.
- Licensed in several states including New York and California.
- This test was developed and its performance characteristics determined by Prometheus Laboratories Inc. It has not been cleared or approved by the U.S. Food and Drug Administration. Prometheus Laboratories Inc. is a CAP-accredited CLIA laboratory.

CPT Codes (as applied by Prometheus)

- **81401**, TPMT genetics

Literature References

- Lennard, L. et al., The Clinical Pharmacology of 6-Mercaptopurine. *European Journal of Clinical Pharmacology.* Vol.43, 1992, p 329-339.

- Yates, C. et al., Molecular Diagnosis of Thiopurine S-Methyltransferase Deficiency: Genetic Basis for Azathioprine and Mercaptopurine Intolerance. *Annals of Internal Medicine*, Vol. 126, No.8, April 1997, p608-614.

- Relling, M.V., et al., Clinical Pharmacogenetics Implementation Consortium Guidelines for Thiopurine Methyltransferase Genotype and Thiopurine Dosing., *Clin. Pharmacol. Ther.* 89, 387-391 (2011)

Thiopurine Methyltransferase (TPMT) Genotyping, 4 Variants

2012233

Ordering Recommendation

Assess risk, due to genetics, for severe myelosuppression with standard dosing of thiopurine drugs. Appropriate for pre-therapeutic or post-therapeutic assessments. Consider if erythrocyte TPMT activity is abnormal or if such assessment is not possible due to recent heterologous blood transfusion.

Additional Technical Information

ARUP Consult® Disease Topics

- Thiopurine Methyltransferase Testing - TPMT
- Rheumatoid Arthritis - RA
- Inflammatory Bowel Disease - IBD
- Organ Transplantation - Immunosuppressive Drugs

View All...

Mnemonic

TPMT DNA

Methodology

Polymerase Chain Reaction/Fluorescence Monitoring

Performed

Mon, Thu

Reported

5-10 days

New York DOH Approval Status

This test is New York DOH approved.

Submit With Order

Specimen Required

Patient Preparation:

Collect: Lavender (EDTA), pink (K_2EDTA), or yellow (ACD Solution A or B).

Specimen Preparation: Transport 3 mL whole blood. (Min: 1 mL)

Storage/Transport Temperature: Refrigerated.

Unacceptable Conditions: Plasma or serum. Heparinized specimens.

Remarks:

Stability: Ambient: 72 hours; Refrigerated: 2 weeks; Frozen: 1 month.

Reference Interval

By report

Interpretive Data

Background Information for Thiopurine Methyltransferase (*TPMT*) Genotyping, 4 Variants:

Characteristics: Thiopurine therapy is used in the treatment of autoimmune diseases, inflammatory bowel disease and acute lymphoblastic leukemia and is also used to prevent rejection after solid organ transplant. Thiopurine drugs (eg, Azathioprine, 6-mercaptopurine, 6-thioguanine) are antimetabolites and must be metabolized to 6-thioguanine nucleotides (6-TGN) for activity. The inactivation of thiopurine drugs is primarily catalyzed by TPMT. Variants in the *TPMT* gene can lead to low TPMT enzyme activity, resulting in accumulation of cytotoxic metabolites and increased risk for drug-related myelotoxicity with standard doses of thiopurine drugs.

Incidence of TPMT deficiency: In the general population,approximately 0.3 percent of individuals have low TPMT activity and 10 percent have intermediate TPMT activity.

Allele Frequencies:

TPMT *2: African 0.000792, Asian 0.0, Caucasian 0.00190, Mediterranean 0.00408, Mexican 0.00592, Middle Eastern 0.00749

TPMT *3A: African 0.00198, Asian 0.0001118, Caucasian 0.0356, Mediterranean 0.0254, Mexican 0.0533, Middle Eastern 0.0114

TPMT *3B: African 0.0, Asian 0.0, Caucasian 0.000461, Mediterranean 0.00426, Mexican 0.00690, Middle Eastern 0.00562

TPMT *3C: African 0.0495, Asian 0.0157, Caucasian 0.004205, Mediterranean 0.00545, Mexican 0.00888, Middle Eastern 0.00562

Inheritance: Autosomal co-dominant.

Cause: *TPMT* gene variants resulting in enzyme deficiency.

Variants Tested: *TPMT* deficiency alleles: *2 (c.238G>C; p.Ala80Pro), *3A {c.[460G>A;719A>G]; p.[Ala154Thr;Tyr240Cys]), *3B (c.460G>A; p.Ala154Thr), *3C (c.719A>G; p.Tyr240Cys).

No variants detected is predictive of *1 functional alleles and normal TPMT enzyme activity.

(Variants are numbered according to NM_000367 transcript)

Clinical Sensitivity: 95 percent.

Methodology: Polymerase chain reaction(PCR) and fluorescence monitoring.

Analytical Sensitivity and Specificity: 99 percent.

Limitations: Only the targeted *TPMT* variants will be detected by this panel. Because the complex *3A allele contains the variants found in the *3B and *3C alleles, this test cannot distinguish the 3A/Negative genotype (intermediate enzyme activity) from the rare *3B/*3C genotype (no or low enzyme activity). This test does not assess for *TPMT* variants associated with ultra-high enzyme activity. Genotyping will reflect donor status in patients who have received allogenic stem cell or bone marrow transplants. TPMT enzyme activity, drug metabolism and risk for adverse reactions to thiopurines may be affected by additional genetic and non-genetic factors not evaluated by this test. Diagnostic errors can occur due to rare sequence variations. Genotyping does not replace the need for therapeutic drug monitoring and clinical observation.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online at www.aruplab.com.

Statement C: The performance characteristics of this test were validated by ARUP Laboratories. The U.S. Food and Drug Administration (FDA) has not approved or cleared this test; however, FDA approval or clearance is currently not required for clinical use of this test. The results are not intended to be used as the sole means for clinical diagnosis or patient management decisions. ARUP is authorized under Clinical Laboratory Improvement Amendments (CLIA) and by all states to perform high-complexity testing.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

Note

CPT Code(s)

81401

Components

Component Test Code*	Component Chart Name	LOINC
2012238	TPMT Genotype Specimen	31208-2
2012239	TPMT Genotype	41048-0
2012240	TPMT Predicted Phenotype	36922-3

** Component test codes cannot be used to order tests. The information provided here is not sufficient for interface builds; for a complete test mix, please view this test within the Laboratory Test Directory found at www.aruplab.com*

Aliases

- 6-mercaptopurine
- 6-MP
- 6-TG
- 6-thioguanine
- AZA toxicity
- Azathioprine
- S-adenosyl-L-methionine genotype
- Thioguanine
- Thiopurine
- Thiopurine S-methyltransferase genotype
- TPMT genetics
- TPMT mutation