



Thiopurine Methyltransferase (TPMT) Genotyping

TPMT encodes an enzyme that is a negative regulator of thiopurine (e.g., 6-mercaptopurine, azathioprine, thioguanine, etc.) activity. Genetic variants in the TPMT gene can lead to a change in enzymatic activity and the ability to metabolize certain drugs. Pharmacogenetic testing for these variants can identify individuals who may have an increased risk of having adverse drug reactions or failure to respond to standard dosages of drugs metabolized by TPMT¹⁻³.

Alleles Detected

Normal function allele:	*1, *1S
Unknown function allele:	*3D, *24
Probable reduced function allele:	*8
No function alleles:	*2, *3A, *3B, *3C, *4

Phenotype Categories⁴

- Normal Metabolizer:** Presence of two copies of a normal activity allele in the TPMT gene.
Diploypes: *1/*1, *1/*1S, *1S/*1S
- Intermediate Metabolizer:** Presence of one copy of a normal function allele and one copy of a no function allele in the TPMT gene. This is consistent with intermediate activity of TPMT. Such patients **are at risk** for myelosuppression with normal doses of drugs in the thiopurine class.
Diploypes: *1/*2, *1/*3A or *3B/*3C, *1/*3B, *1/*3C, *1/*4, *1S/*2, *1S/*3A, *1S/*3B, *1S/*3C, *1S/*4
- Poor Metabolizer:** Presence of two copies of a no function allele in the TPMT gene. This can be observed as either compound heterozygous or homozygous variant alleles. This is consistent with low or deficient activity of TPMT. These patients **are at high risk** for life-threatening myelosuppression with normal doses of drugs in the thiopurine class.
Diploypes: *2/*2, *2/*3A, *2/*3B, *2/*3C, *2/*4, *3A/*3A, *3A/*3B, *3A/*3C, *3A/*4, *3B/*3B, *3B/*4, *3C/*3C, *3C/*4, *4/*4
- Indeterminate activity - CPIC:** Presence of either one or two copies of an unknown allele in the TPMT gene, including the probable function alleles. At the time of this publication, it is not possible to predict the actual activity of TPMT, and hence the expected phenotype for this patient cannot be determined by genotyping alone.
Diploypes: *1/*3D, *1/*24, *1S/*3D, *1S/*24, *2/*3D, *2/*24, *3A/*3D, *3A/*24, *3B/*3D, *3B/*24, *3C/*3D, *3C/*24, *3D/*3D, *3D/*4, *3D/*24, *4/*24, *1/*8, *1S/*8, *2/*8, *3A/*8, *3B/*8, *3C/*8, *3D/*8, *4/*8, *8/*8, *8/*24, *24/*24

Limitations

The presence of other TPMT variants that are not detected in this assay may influence drug metabolism. Additional variants that are not detected but located proximally to variants interrogated may affect the assay's ability to detect the above listed alleles.

Please consider all relevant patient information (including but not limited to additional medications, gender, weight, etc.) when making any dosing decisions.

Methodology

Real-time polymerase chain reaction with fluorescence detection.

Informed Consent

If required by your state, please obtain informed consent for genetic testing. Please document in the appropriate location on the test request form or order if informed consent has been obtained and filed.

Ordering

Test Name	CNT or NT Panel
CPT Code	81335
Collection	3-5mL peripheral whole blood in EDTA tube Saliva in Oragene Dx, Part # OGD-500
Labeling	Must label with the patient name plus one additional unique identifier, such as date of birth, medical record number, or date of collection
Stability	Samples must be received by RPRD within 7 days of collection. Ambient or refrigerated storage is acceptable
Shipping	Ambient temperature. Ship for RPRD receipt on Monday through Friday only
Rejection	Blood sample may be rejected if frozen, hemolyzed, or clotted

About RPRD Diagnostics

RPRD Diagnostics specializes in providing innovative and end-to-end pharmacogenomics solutions, including diagnostic, analysis and consulting services to clinicians, researchers and drug developers. With decades of combined experience, RPRD's team of experts strives to improve patient lives using pharmacogenomics to enable precision medicine.

References

1. <https://cpicpgx.org/guidelines/>
2. Relling MV, et al, J Natl Cancer Inst. 1999 Dec 1;91(23):2001-8.
3. Lynne Lennard, Br J Clin Pharmacol. 2014 Apr; 77(4): 704–714.
4. <https://www.pharmgkb.org/gene/PA356>

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