



RESULTS REPORT

Scientific Director: Nasioulas Georgios, PhD

SAMPLE INFORMATION

Name :

Date Received :

Medical ID :

Date of Report :

Date of Birth :

Req. Physician :

Material :

Barcode :

TPMT-POLYMORPHISMS

Results

Gene	Genotype	Possible phenotype
TPMT	TPMT*1/ TPMT*1	Normal TPMT activity

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Methodology

Total genomic DNA was extracted from the submitted sample. Analysis for the presence of the **G238C, G460A, and A719G polymorphisms** in the *TPMT* gene was performed using a targeted sequencing approach (KAPA, Roche). Sequencing was performed using the **DNB-SEQ T7 Next-Generation Sequencing (NGS) platform (MGI)**.

Thiopurine drugs, including **mercaptopurine, azathioprine, and thioguanine**, are used in the treatment of various diseases, including as immunosuppressive agents in gastroenterology and dermatology, in the treatment of acute lymphoblastic leukemia, rheumatoid arthritis, following organ transplantation, and in Crohn's disease.

These drugs are metabolized into inactive metabolites by the enzyme **thiopurine S-methyltransferase (TPMT)**. Polymorphisms in the *TPMT* gene are among the major factors responsible for interindividual differences in the efficacy and toxicity of thiopurine drugs. Approximately **10% of individuals have intermediate TPMT activity due to heterozygosity**, while approximately **1 in 300 individuals have TPMT deficiency due to homozygosity**.

Three polymorphisms (**G238C, G460A, and A719G**) have been identified that are associated with reduced TPMT enzyme activity. These polymorphisms define four defective alleles: **TPMT2, TPMT3B, TPMT3C, and TPMT3A**. The **TPMT2, TPMT3B, and TPMT*3C** alleles contain variants at nucleotides 238, 460, and 719, respectively, whereas the **TPMT*3A** allele contains variants at both nucleotides 460 and 719. The normal allele is designated **TPMT*1**.

The frequencies of these alleles vary among different ethnic populations. In Caucasian populations, the reported frequencies of the **TPMT3A, TPMT3C, and TPMT*2** alleles are approximately **3.2–5.7%, 0.2–1.0%, and 0.2–0.7%**, respectively.

Note: Every molecular analysis has an inherent analytical error rate of approximately **0.5–1%**. This may be attributable to rare molecular events and factors associated with sample preparation and analysis.

BIBLIOGRAPHY

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- Coulthard SA, Hall AG. Recent advances in the pharmacogenomics of thiopurine methyltransferase. *Pharmacogenomics J.* 2001;1(4):254-61.
- Tumer TB et al..The low frequency of defective TPMT alleles in Turkish population: a study on pediatric patients with acute lymphoblastic leukemia. *Am J Hematol.* 2007 Oct;82(10):906-10.