

WT1 Mutation Detection by Sequencing

DETECTS WT1 MUTATIONS IN CYTOGENETICALLY NORMAL ACUTE MYELOID LEUKEMIA (AML)

Clinical Background

- Wilms tumor 1 (WT1) is a transcription factor expressed in embryonic kidney cells and hematopoietic stem cells. Mutations in the *WT1* gene in patients with various cancers reveal both a tumor suppressor and an oncogenic function of the protein.¹
- Approximately 10% of patients with cytogenetically normal acute myeloid leukemia (CN-AML) harbor *WT1* mutations. The majority of these mutations cluster in exons 7 and 9 encoding the zinc-finger DNA binding domain and confer a poorer prognosis.^{2,3,4}
- In addition, approximately 25% to 35% of individuals harbor the synonymous single-nucleotide polymorphism (SNP) rs16754 in *WT1* exon 7. The G allele of this SNP has been reported to confer an improved prognosis in the high-risk subset of CN-AML cases with mutated *FLT3* and wild-type *NPM1*.⁵

Indication for Ordering

The principal use for this test is to determine the risk group of newly diagnosed cases of AML with normal cytogenetics.

Interpretation

- Not detected: No mutations were detected.
- Positive: A mutation was detected in exon 7 or 9 of the *WT1* gene.
- rs16754 SNP: The G allele of the rs16754 SNP is present.

Limitations

- Results of this test must always be interpreted in the context of morphologic and other relevant data, and should not be used alone for a diagnosis of malignancy.

- Samples that do not show a *WT1* mutation by this test may still harbor mutations but in too few AML cells, below the detection limit of this test.

Methodology

- Genomic DNA is extracted, and two fragments covering exons 7 and 9 of the *WT1* gene are amplified by polymerase chain reaction. The fragments are sequenced, and the results are compared to the published unmutated sequence.
- This test may not accurately detect mutations if present in fewer than 40% of white blood cells.

References

1. Yang, et al. A tumor suppressor and oncogene: the WT1 story. *Leukemia*. 2007;21(5):868–76.
2. Gaidzik, et al. Prognostic impact of WT1 mutations in cytogenetically normal acute myeloid leukemia: a study of the German-Austrian AML Study Group. *Blood*. 2009;113(19):4505–11.
3. Becker, et al. Mutations of the Wilms tumor 1 gene (WT1) in older patients with primary cytogenetically normal acute myeloid leukemia: a Cancer and Leukemia Group B study. *Blood*. 2010;116(5):788–92.
4. Paschka, et al. Wilms' tumor 1 gene mutations independently predict poor outcome in adults with cytogenetically normal acute myeloid leukemia: a cancer and leukemia group B study. *J Clin Oncol*. 2008;26:284595–602.
5. Damm, et al. Single nucleotide polymorphism in the mutational hotspot of WT1 predicts a favorable outcome in patients with cytogenetically normal acute myeloid leukemia. *J Clin Oncol*. 2010;28(4):578–85.

Test Information

2005766

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For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult[®] at www.arupconsult.com.

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