



Wilms Tumor 1 (WT-1) Gene Methylation as an Epigenetic Biomarker in Acute Myeloid Leukemia

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Abstract

Acute myeloid leukemia (AML) is a highly heterogeneous hematological malignancy characterized by different genetic and epigenetic aberrations. Several epigenetics modifications were observed in the promoter regions of the cellular epigenome, including hypomethylation or hypermethylation of CpG islands during the onset and progression of AML. DNA methylation is an epigenetic modification that regulates gene expression and plays a pivotal role in tumorigenesis, including AML. Wilms tumor 1 (WT-1) is a transcription factor involved in the differentiation and proliferation of AML. The clinical relevance of WT-1 gene expression and its underlying epigenetic alterations has not been fully addressed in AML.

Objective

This work aimed to investigate promoter methylation and mRNA expression of WT-1 gene in AML.

Background

- AML is the second most prevalent type of leukemia diagnosed in adults and children [1].
- Wilms Tumor-1 (WT-1) gene plays a crucial role in regulation of apoptosis, cell survival, promotes cell proliferation, cell growth, metastasis, differentiation, and normal cellular development [2].
- WT-1 gene has dual functioning of acting as tumor suppressor as well oncogenic gene. It encodes a transcription factor that plays a regulatory role in normal and malignant haematopoiesis [3].
- Frequent monitoring of the WT-1 gene expression level during follow-ups in AML patients is useful as a marker for residual blast populations or even to predict the risk of relapse following allogeneic SCT [4].

Materials & Methods

Patients: Bone marrow samples were collected at the time of diagnosis and after completion of induction chemotherapy from 10 newly diagnosed AML patients. Five non-malignant BM samples were recruited as controls.

Methods: Quantitative assessment of WT-1 gene transcripts was performed using real-time PCR. In addition, methylation-specific PCR was done to evaluate the promoter methylation status of the WT-1 gene in AML.

Result

Robust promoter hypermethylation and higher expression of the WT-1 gene were observed in AML patients at time of diagnosis. In contrast, hypomethylation and lower WT-1 gene expression were observed after completion of induction therapy ($p < 0.001$).

Conclusion

This is the first report, to our knowledge, regarding WT-1 gene overexpression hypermethylation signature as a characteristic marker that correlates with leukemic burden in AML among the Indian population. Increased expression and methylation signature of the WT-1 gene can be used as a promising molecular marker for diagnosis, clinical progression of the diseases, or monitoring response to treatment, as well as a target for the development of novel therapeutic approaches.

References

1. Cancer statistics, 2020. CA Cancer J Clin.
2. Acute Myeloid Leukemia-Genetic Alterations and Their Clinical Prognosis. Int J Hematol Oncol Stem Cell Res.
3. Transcription Factors in Cancer: When Alternative Splicing Determines Opposite Cell Fates. Cells.
4. Molecular update on biology of Wilms Tumor 1 gene and its applications in acute myeloid leukemia. Am J Blood Res.