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Study of alternative *Wilms tumor* gene methylation as an epigenetic biomarker in acute myeloid leukemia

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Background: Overexpression of the *Wilms tumor 1 gene* (*WT1*) is implicated in the prognosis of acute myeloid leukemia (AML) with high expression predicting disease progression, as well as being intensively studied as a potential molecular marker for minimal residual disease (MRD) and treatment response. Many different isoforms for *WT1* are generated by alternative transcription initiation, mRNA splicing and alternative translation initiation. Recently, an alternative promoter incorporating a unique first exon, alternative *WT1* transcript (*AWT1*), has been described. The *AWT1* expression and the underlying epigenetic alterations associated with its expression in AML are still unknown.

Objectives: We studied the *AWT1* gene specific methylation changes and its relationship with other clinicopathological features. We also integrated the corresponding gene expression profile to explore the role of methylation in regulating gene expression.

Materials & Methods: Bisulfite PCR followed by pyrosequencing were done to determine the methylation status of *AWT1* gene promotor CPG islands in 50 newly diagnosed AML patients and 50 healthy subjects as a control group. The level of *AWT1* expression was assessed using RQ-PCR.

Results: *AWT1* expression level was significantly higher in the AML patients in comparison to the control group ($P < 0.001$) and it was surprising to find robust hypermethylation of the *AWT1* promoter in AML patients compared to the controls ($P < 0.001$). A statistically significant negative correlation between *AWT1* expression and methylation level was found ($r = 0.67$, $P < 0.001$). At a cutoff value of 45.2% *AWT1* promoter hypermethylation was found to be a highly specific marker for AML (specificity 95% and sensitivity 97.5%)

Conclusion: We described an expression methylation signature of the *AWT1* that are promising markers for diagnosis and MRD assessment in AML.

Biography

Reham Abo Elwafa is a Lecturer of Clinical Pathology, Faculty of Medicine in Alexandria University, Egypt. She has expertise in Research, Teaching and Administration in Hospital and Education Institution. She is expert in Molecular Techniques: PCR (conventional, and real time PCR), microarray, pyrosequencing and NGS in addition to FISH techniques including Prenatal Genetic Diagnosis (PGD) and flow cytometric immunophenotyping of different types of hematologic malignancies. She has several international publications in the field of Molecular Biology, Genetics and Epigenetics.

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