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Target Genes of WT1 in Leukemic Cells

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Introduction
Wilms' tumor is a childhood kidney cancer, in which the gene Wilms' tumor gene 1 (WT1) is involved in about 20% of the cases. The transcription factor WT1 is also recurrently mutated in acute myeloid leukemias (AMLs). Mutations and high expression of WT1 associate with a poor prognosis in AML (1). In mice, overexpression of WT1 contributes to the induction of acute leukemia (2), further emphasizing a role for WT1 in leukemia development. Molecular mechanisms and target genes for WT1 in leukemia are, however, incompletely understood.

Background to the study
High expression of the transcription factor WT1 is found in leukemic blasts from most AML patients (1). To identify putative novel target genes for WT1 in leukemia, we identified partial correlations in gene expression between WT1 and other genes in a large cohort of 3,844 AML patients. We found that QPRT (quinolinate phosphoribosyltransferase), NAB2 (NGFI-A binding protein 2), and FSCN1 (fascin) were genes with high transcriptional correlation to WT1. This finding led us to investigate functional relationships between WT1 and putative target genes.

Conclusion
Overexpression of the oncogene WT1 is common in acute myeloid leukemia (AML). QPRT, NAB2, and possibly FSCN1 have been found to be direct target genes of the transcription factor WT1. QPRT, NAB2 and FSCN1 may be important for the leukemic phenotype.

References

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