Transcriptional upregulation of p21/WAF/Cip1 in myeloid leukemic blasts expressing AML1-ETO.

Abstract:
An inducible model for conditional expression of AML1-ETO in myeloid U-937 cells was generated previously to determine cellular effects of AML1-ETO and to identify target genes. Induction of AML1-ETO expression in U-937 resulted in reduced cell growth, G1 arrest and apoptosis. Microarray analysis showed more genes up-regulated than down-regulated (180 vs. 69). Clustering of AML1-ETO-positive and -negative cell lines was possible based on these differentially expressed genes. p21/WAF/Cip1 (CDKN1A) was up-regulated 4.6-fold upon induction of AML1-ETO which was confirmed in additional experiments. Knock-down of AML1-ETO by siRNA could reduce p21/WAF/Cip1 expression in Kasumi-1 cells. mRNA expression analysis of p21/WAF/Cip1 in a large cohort of acute myeloid leukemia patients demonstrated a significantly higher expression in AML1-ETO-positive leukemia. The increased expression of p21/WAF/Cip1 in primary leukemic blasts suggests that elevated p21/WAF/Cip1 levels may contribute to specific features observed in AML1-ETO positive leukemia.