Genome-wide analysis of histone H3 acetylation patterns in AML identifies PRDX2 as an epigenetically silenced tumor suppressor gene

With the use of ChIP on microarray assays in primary leukemia samples, we report that acute myeloid leukemia (AML) blasts exhibit significant alterations in histone H3 acetylation (H3Ac) levels at > 1000 genomic loci compared with CD34+ progenitor cells. Importantly, core promoter regions tended to have lower H3Ac levels in AML compared with progenitor cells, which suggested that a large number of genes are epigenetically silenced in AML. Intriguingly, we identified peroxiredoxin 2 (PRDX2) as a novel potential tumor suppressor gene in AML. H3Ac was decreased at the PRDX2 gene promoter in AML, which correlated with low mRNA and protein expression. We also observed DNA hypermethylation at the PRDX2 promoter in AML. Low protein expression of the antioxidant PRDX2 gene was clinically associated with poor prognosis in patients with AML. Functionally, PRDX2 acted as inhibitor of myeloid cell growth by reducing levels of reactive oxygen species (ROS) generated in response to cytokines. Forced PRDX2 expression inhibited c-Myc-induced leukemogenesis in vivo on BM transplantation in mice. Taken together, epigenome-wide analyses of H3Ac in AML led to the identification of PRDX2 as an epigenetically silenced growth suppressor, suggesting a possible role of ROS in the malignant phenotype in AML.