題名:Downregulation of c-Myc is critical for valproic acid-induced growth arrest and myeloid differentiation of acute myeloid leukemia

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摘要:Valproic acid (VPA), an agent used for neurological disorders, has been shown to be a novel class of histone deacetylase inhibitor (HDACI), able to induce apoptosis and myeloid differentiation of acute myeloid leukemia (AML). In this study, we examined the underlying mechanisms in VPA-mediated activities in AML cells. VPA not only inhibited the growth of HL-60, U937 and NB4 cells by causing cell-cycle arrest at G(0)/G(1) phase and apoptosis, but also induced morphologic and phenotypic changes. VPA markedly increased p21WAF1, and downregulated c-Myc expression at transcriptional levels. Ectopic expression of wildtype c-Myc and T58A mutant significantly inhibited VPA-mediated growth inhibition. As with results from cell line studies, VPA also downregulated c-Myc levels, and induced apoptosis and myeloid differentiation of primary AML cells, leading to decreased colony-forming ability. Given the role of c-Myc in leukemogenesis, our study suggests that VPA might be a potential therapeutic agent for AML.