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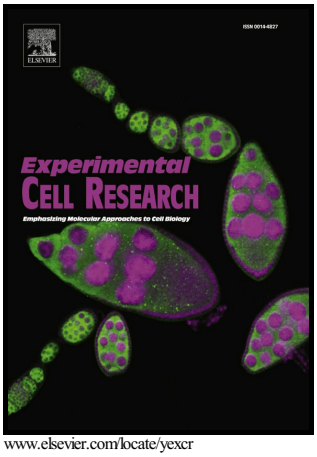

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Abstract

Acute myeloid leukemia (AML) is a highly heterogeneous disease, with biologically and prognostically different subtypes. Although a growing number of distinct AML subsets have been increasingly characterized, patient management has remained disappointingly uniform. The molecular mechanism underlying AML needs to be further investigated. Here we identify IRF9 as a negative regulator of human AML. We show that IRF9 mRNA and protein levels are down-regulated in human AML samples compared with samples from healthy donors. IRF9 knockdown promotes proliferation, colony formation and survival of OCI/AML-2 and OCI/AML-3 cells, whereas IRF9 overexpression obtains oppose results. Mechanism analysis shows that IRF9 binds SIRT1 promoter and represses SIRT1 expression in OCI/AML-2 and OCI/AML-3 cells. In AML samples, the expression of SIRT1 is up-regulated and negatively correlated with IRF9 level. IRF9 also increases the acetylation of p53, a deacetylation substrate of SIRT1, and promotes the expression of p53 target genes. Knockdown of p53 blocks the effects of IRF9 on cell survival and growth in vitro. These findings provide evidence that