Uniwersytet Wrocławski

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Histone acetyltransferase activiyt of p300 is required for transcriptional repression by the promyelocytic leukemia zinc finger protein.

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Streszczenie

Histone acetyltransferase (HAT) activities of proteins such as p300, CBP, and P/CAF play important roles in activation of gene expression. We now show that the HAT activity of p300 can also be required for down-regulation of transcription by a DNA binding repressor protein. Promyelocytic leukemia zinc finger (PLZF), originally identified as a fusion with retinoic acid receptor alpha in rare cases of all-trans-retinoic acid-resistant acute promyelocytic leukemia, is a transcriptional repressor that recruits histone deacetylase-containing corepressor complexes to specific DNA binding sites. PLZF associates with p300 in vivo, and its ability to repress transcription is specifically dependent on HAT activity of p300 and acetylation of lysines in its C-terminal C2-H2 zinc finger motif. An acetylation site mutant of PLZF does not repress transcription and is functionally deficient in a colony suppression assay despite retaining its abilities to interact with corepressor/histone deacetylase complexes. This is due to the fact that acetylation of PLZF activates its ability to bind specific DNA sequences both in vitro and in vivo. Taken together, our results indicate that a histone deacetylase-dependent transcriptional repressor can be positively regulated through acetylation and point to an unexpected role of a coactivator protein in transcriptional repression.

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