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**Epstein-Barr virus nuclear antigen 3C and prothymosin alpha interact with the p300 transcriptional coactivator at the CH1 and CH3/HAT domains and cooperate in regulation of transcription and histone acetylation.**

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The Epstein-Barr virus nuclear antigen 3C (EBNA3C), encoded by Epstein-Barr virus (EBV), is essential for mediating transformation of human B lymphocytes. Previous studies demonstrated that EBNA3C interacts with a small, nonhistone, highly acidic, high-mobility group-like nuclear protein prothymosin alpha (ProT(alpha)) and the transcriptional coactivator p300 in complexes from EBV-infected cells. These complexes were shown to be associated with histone acetyltransferase (HAT) activity in that they were able to acetylate crude histones in vitro. In this report we show that ProT(alpha) interacts with p300 similarly to p53 and other known oncoproteins at the CH1 amino-terminal domain as well as at a second domain downstream of the bromodomain which includes the CH3 region and HAT domain. Similarly, EBNA3C also interacts with p300 at regions which include the CH1 and CH3/HAT domains, suggesting that ProT(alpha) and EBNAC3C may interact in a complex with p300. We also show that ProT(alpha) activates transcription when targeted to promoters by fusion to the GAL4 DNA binding domain and that this activation is enhanced by the addition of an exogenous source of p300 under the control of a heterologous promoter. This overall activity is down-modulated in the presence of EBNA3C. These results further establish the interaction of cellular coactivator p300 with ProT(alpha) and demonstrate that the associated activities resulting from this interaction, which plays a role in acetylation of histones and coactivation, can be regulated by EBNA3C. Furthermore, this study establishes for the first time a transcriptional role for ProT(alpha) in recruitment or stabilization of coactivator p300, as well as other basal transcription factors, at the nucleosomes for regulation of transcription.

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