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Epigenetic control of chromatin-dependent transcription – Lessons from p53, AP-1, Brd4, and HPV.

Cheng-Ming CHIANG
University of Texas Southwestern Medical Center, Dallas, TX, USA

Transcription in higher eukaryotes is controlled by an array of transcription factors, including the general transcription machinery, general cofactors, and gene-specific activators and repressors. The complexity of gene regulation is further conferred by the existence of multiple protein family members recognizing consensus or non-canonical DNA-binding sequences. The chromatin structure in the human genome and posttranslational modification on protein molecules provide an additional level of control in modulating gene activity. In this lecture, I will review these control mechanisms using human papillomavirus (HPV) E6 and E2 proteins as examples to illustrate how DNA tumor virus-encoded transcriptional regulators are able to reprogram cellular activities by targeting p53 tumor suppressor protein and activator protein-1 (AP-1), respectively, via recruitment of distinct coregulators, such as p300 histone acetyltransferase and the chromatin adaptor bromodomain-containing protein 4 (Brd4). The interplay among these viral and cellular proteins and the crosstalk between different posttranslational modifications regulate gene activity in response to various environmental stresses.

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Institut Européen de Chimie et Biologie
2, rue Robert Escarpit - 33607 Pessac, France
Tél. : +33(0)5 40 00 30 38 - Fax. : +33(0)5 40 00 22 15
www.iecb.u-bordeaux.fr