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Commentary

The Regulation of Transcription in Eukaryotic Gene Expression

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DESCRIPTION

The DNA double helix is tightly encircled by nuclear proteins known as histones in the cell nucleus. Chromatin is the name given to the complex made up of DNA and proteins. Gene silencing occurs when DNA is tightly wrapped around histones, preventing it from reaching various chromosomal regulatory proteins. The two forms of chromatin are: Euchromatin, which can participate in transcription and is less condensed; and heterochromatin, which cannot be transcribed and is extremely condensed. The nucleosome, which is made up of 147 base pairs of DNA wrapped around two copies of each of four histone proteins H2A, H2B, H3, and H4 is the fundamental component of chromatin. Between the two subsequent nucleosomes, a small piece of free DNA exists, giving the chromosome the appearance of beads on a string.

Eukaryotic gene expression is controlled by chromatin remodeling, which makes tightly condensed DNA accessible to various regulatory factors like transcription factors and DNA replication components. During the process of forming an active RNA polymerase II transcription pre-initiation complex, the transcriptional machinery of eukaryotes is confronted with a number of difficulties. Transcription factors must first gain access to a DNA template that is folded into chromatin fibers that are compact and 30-400 nM thick. Gene-specific transcriptional activators target promoter regions for the unfolding or remodeling of chromatin structure because nucleosome assembly virtually eliminates the ability of general transcription factors, such as TFIID and the RNA polymerase II holoenzyme, to interact with promoter sequences. The remodeling of chromatin is not a characteristic of transcriptional activators; instead, activators mobilize specialized enzymes to carry out the chromatin remodeling processes necessary for the subsequent assembly of the pre-initiation complex. Additionally, activators are crucial in recruiting the basal transcription machinery, necessitating the orchestration of interactions with a wide variety of targets for effective transcription initiation.

Through interactions with transcriptional activators, there are two types of chromatin remodeling enzymes that can be directed toward promoters. The first class of enzymes, which are related to the 2 MDa yeast SWI/SNF complex, are capable of hydrolyzing approximately 1000 ATP molecules per minute and utilizing the energy generated by ATP hydrolysis to disrupt interactions between histones and DNA. Nuclear Histone Acetyltransferases (HATs), such as yeast Gcn5p, mammalian GCN5/PCAF, and the CBP/p300 proteins, belong to the second group. By acetylating lysine residues in the amino-terminal domains of nucleosomal histones, these enzymes covalently alter chromatin structure. Specifically, we focus on possible mechanisms that could explain the interdependent recruitment of SWI/SNF-like enzymes and HATs that we discuss in this article. These new developments address the roles that these enzymes play in transcription.

The regulation of eukaryotic gene expression has recently been the subject of several novel paradigm shifts. First, transcription from chromatin templates *in vivo* and *in vitro* frequently necessitates a HAT and a SWI/SNF-like ATP-dependent chromatin remodeling enzyme that work together. Second, different chromatin remodeling enzymes' recruitment may depend on each other and be interdependent. Thirdly, the bromodomain and other histone-binding domains have the potential to influence subsequent activator-dependent recruitment events, which in turn can contribute to transcriptional control.

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