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Epigenetic Modification Observed in Yeast Chromatin Remodeler Ino80p

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Abstract : The packaging of DNA into nucleosomes is critical to genomic compaction, yet it can leave gene promoters inaccessible to activator proteins or transcription machinery and thus prevents transcriptional initiation. Both chromatin remodelers and histone acetylases (HATs) are the two main transcription co-activators that can reconfigure chromatin structure for transcriptional activation. Ino80p is the core component of the INO80 remodeling complex. Recently, it was shown that Ino80p dissociates from the yeast INO1 promoter after induction. However, when certain HATs were deleted or mutated, Ino80p accumulated at the promoters during gene activation. This suggests a link between HATs' presence and Ino80p's dissociation. However, it has yet to be demonstrated that Ino80p can be acetylated. To determine if Ino80p can be acetylated, wild-type Saccharomyces cerevisiae cells carrying Ino80p engineered with a double FLAG tag (MATa INO80-FLAG his3Δ200 leu2Δ0 met15Δ0 trp1Δ63 ura3Δ0) were grown to mid log phase, as were non-tagged wild type (WT) (MATa his3Δ200 leu2Δ0 met15Δ0 trp1Δ63 ura3Δ0) and ino80Δ (MATa ino80Δ::TRP1 his3Δ200 leu2Δ0 met15Δ0 trp1Δ63 ura3Δ0) cells as controls. Cells were harvested, and the cell lysates were subjected to immunoprecipitation (IP) with α-FLAG resin to isolate Ino80p. These eluted IP samples were subjected to SDS-PAGE and Western blot analysis. Subsequently, the blots were probed with the α-FLAG and α-acetyl lysine antibodies, respectively. For the blot probed with α-FLAG, one prominent band was shown in the INO80-FLAG cells, but no band was detected in the IP samples from the WT and ino80Δ cells. For the blot probed with the α-acetyl lysine antibody, we detected acetylated Ino80p in the INO80-FLAG strain while no bands were observed in the control strains. As such, our results showed that Ino80p can be acetylated. This acetylation can explain the co-activator's recruitment patterns observed in current gene activation models. In yeast INO1, it has been shown that Ino80p is recruited to the promoter during repression, and then dissociates from the promoter once de-repression begins. Histone acetylases, on the other hand, have the opposite pattern of recruitment, as they have an increased presence at the promoter as INO1 de-repression commences. This Ino80p recruitment pattern significantly changes when HAT mutant strains are studied. It was observed that instead of dissociating, Ino80p accumulates at the promoter in the absence of functional HATs, such as Gcn5p or Esa1p, under de-repressing processes. As such, Ino80p acetylation may be required for its proper dissociation from the promoters. The remodelers' dissociation mechanism may also have a wide range of implications with respect to transcriptional initiation, elongation, or even repression as it allows for increased spatial access to the promoter for the various transcription factors and regulators that need to bind in that region. Our findings here suggest a previously uncharacterized interaction between Ino80p and other co-activators recruited to promoters. As such, further analysis of Ino80p acetylation not only will provide insight into the role of epigenetic modifications in transcriptional activation, but also gives insight into the interactions occurring between co-activators at gene promoters during gene regulation.

Keywords : acetylation, chromatin remodeler, epigenetic modification, Ino80p
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