Histone H2B Ubiquitination in Transcription Regulation

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Post-translational modifications of histones play a central role in regulating transcription. Monoubiquitinated histone H2B-K120 (humans; K123 in yeast) is a hallmark of actively transcribed genes that plays multiple roles in activating transcription, while monoubiquitinated H2A-K119 is a hallmark of transcriptionally silent chromatin. Histone H2B-K120 (in humans; K123 in yeast) is dynamically ubiquitinated and deubiquitinated during transcription. Our structural studies provideinsights in the mechanism by which histone H2B is specifically ubiquitinated in yeast by the E3 ligase, Bre1, and deubiquitinated by the SAGA deubiquitinating module. The ubiquitin modification itself plays multiple roles in activating transcription, including stimulating methylation of histone H3K79 by DOT1L and of histone H3K4 by the yeast COMPASS complex and human MLL1. Our structural studies of these enzymes has shed light on the molecular basis of cross-talk between histone ubiquitination and methylation. We will also present work addressing the role of H2B-K120 ubiquitin in gating access to the nucleosome acidic patch, which is a hotspot for interactions with many chromatin-modifying enzymes.