

Histone H2B ubiquitination in transcription regulation

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Post-translational modifications of histones play a central role in regulating all cellular processes requiring access to DNA. Cross-talk between histone modifications, in which one histone modification regulates deposition of a second, provides an additional layer of regulation and specificity. Monoubiquitinated histone H2B-K120 (in humans; K123 in yeast) is a hallmark of actively transcribed genes that is required for methylation of histone H3K79 and H3K4, two other marks of active regions of transcription. H3K79 is methylated by Dot1L in humans and H3K4 is methylated by the COMPASS complex in yeast. To determine the molecular basis of cross-talk between histone ubiquitination and methylation, we determined cryo-EM structures of human Dot1L and yeast COMPASS bound to H2B-ubiquitinated nucleosomes. In addition to revealing the mechanism of ubiquitin recognition and enzyme stimulation, our studies have revealed surprising plasticity in the histone core of the nucleosome that has implications for interactions with other histone-modifying enzymes.