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Substrate Recognition of Histone H2B by DUBm ELIZABETH HENDERSON, Hunter College, CHRISTOPHER BERNDSEN, CYNTHIA WOLBERGER, The Johns Hopkins University School of Medicine — The SAGA complex is a transcriptional coactivator that regulates gene expression in eukaryotes via histone acetylation and deubiquitination, which are crucial for transcription. Our lab is investigating the SAGA-dependent deubiquitination of histone H2B. The deubiquitinating module (DUBm) of SAGA is comprised of a ubiquitin-specific protease, Ubp8, and three other proteins. It is known that Ubp8 cleaves ubiquitin from histone H2B, however, the specific way in which the enzyme binds to the substrate remains elusive. In order to unravel this mechanism, we attempted to determine the crystal structure of the substrate binding complex. We obtained this substrate by exploiting the techniques of intein chemistry to artificially ubiquitinate a histone H2B peptide, which we then co-crystallized with DUBm. Additionally, we synthesized Ub-K63R-linked chains and Ub-K48-linked chains and co-crystallized them with DUBm.

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