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Acetylation of LYS-16 of H4 Histone Tail May Sequester the Tail and Inhibit its Interactions with Neighboring Nucleosomes DAVIT POTOYAN, GAREGIN PAPOIAN, University of Maryland — Histone tails are highly flexible N terminal protrusions of histone proteins, which help to fold DNA into dense superstructures known as chromatin. On a molecular scale histone tails are poly-electrolites with high degree of conformational disorder, allowing them to function as bio-molecular "switches," regulating various genetic regulatory processes via diverse types of covalent modifications. Because of being intrinsically disordered, the structural and dynamical aspects of histone tails are still poorly understood. Using multiple explicit solvent and coarse-grained MD simulations we have investigated the impact of the acetylation of LYS-16 residue on the conformational and DNA-binding propensities of H4 histone tail. The potential of mean force computed as a function of distance between a model DNA and histone tail center of mass showed a dramatic enhancement of binding affinity upon mono-acetylation of the H4 tail. The estimated binding free energy gain for the wild type is 2kT, while for the acetylated it reaches 4-5 kT. Additionally our structural analysis shows that acetylation is driving the chain into collapsed states, which get enriched in secondary structural elements upon binding to the DNA. We suggest a non-electrostatic mechanism that explains the enhanced binding affinity of the acetylated H4 tail. At last our findings lead us to propose a hypothesis that can potentially account for the celebrated chromatin "fiber loosening effects" observed in many experiments.

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