

A Computational Study of the Interactions Between the Histone Acetyltransferase, Gcn5, and a Histone Tail

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Post-translational modifications (PTMs) can have a profound effect on protein structure and function. One such PTM involves the acetylation of free lysine residues. An essential acetylation reaction involves the transfer of the acetyl group from acetyl CoA to a histone (a protein involved in DNA binding). This transfer neutralizes the positively charged lysine, which allows for the DNA to be exposed for transcription. The histone acetyltransferase our study focuses on is Gcn5. The first step in the reaction is the deprotonation of a lysine on the histone tail by a glutamate in Gcn5. This glutamate is ~ 15 Å away from the transferring acetyl group. Thus, after deprotonation, the Gcn5/histone/acetylCoA complex must reorganize and the lysine must swing back towards the active site. We use molecular dynamics (MD) simulations to probe the interactions between the histone and Gcn5 before and after lysine deprotonation to understand which contacts must be broken before the final acetylation step can occur.