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## **Investigating the Impact of Histone Post-Translational Modifications on Nucleosome Structure and Accessibility: Insights from Molecular Dynamics Studies**

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Substance use disorders are persistent conditions marked by compulsive drug use and intense cravings, despite adverse effects. Recent research highlights epigenetic alterations in chromatin structure as crucial contributors to altered gene expression in response to drug abuse. Key mechanisms include DNA methylation, histone modifications, and non-coding RNAs. Despite evidence implicating physical forces in epigenetic processes, the precise mechanisms by which these forces regulate chromosomal modifications in drug addiction and their potential heritability remain unclear.

This study focuses on histone post-translational modifications (PTMs), which influence nucleosome structure and accessibility, playing critical roles in gene expression, DNA repair, and cellular processes like mitosis and differentiation. Employing all-atom molecular dynamics (MD) simulations, we illustrate that histone PTMs in the nucleosome DNA entry/exit region can induce a more open DNA conformation compared to the canonical nucleosome. Our simulations offer atomic-level insights into how subtle modifications prompt dynamic changes in nucleosome structure, facilitating DNA exposure for gene expression.