Inhibition of Histone Binding by Supramolecular Hosts

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H. F. Allen, K. D. Daze, T. Shimbo, A. Lai, C. A. Musselman, J. K. Sims, P. A. Wade, F. Hof and T. G. Kutateladze, *Biochem. J.*, **2014**, *459*, 505.

Abstract:

In this seminar, I will introduce about the supramolecular host-guest chemistry and its possibility for analyzing biological functions.

Supramolecules can include small molecules or parts of big compounds with reversible noncovalent linkages, such as ionic bonding, hydrogen bonding or van der Waals interaction. These molecular assemblies are similar as protein-protein or protein-substrate interactions and that means to be able to apply supramolecular chemistry to the artificial regulation of biofunctions. In this paper, the authors find that calixarene-based supramolecular hosts disrupt binding of the CHD4 (chromodomain helicase DNA-binding protein 4) -PHD2 (plant homeodomain 2) finger to H3K9me3, but do not affect the interaction of this protein with the H3K9me0 (unmodified histone H3) tail. A similar inhibitory effect, observed for the association of chromodomain of HP1γ (heterochromatin protein 1γ) with H3K9me3, points to a general mechanism of methyl-lysine caging by calixarenes and suggests a high potential for these compounds in biochemical applications. Monitoring this disruption using immunofluorescence analysis revealed that the supramolecular agents induce changes in chromatin organization that are consistent with their binding to and disruption of H3K9me3 sites. These results suggest that the aromatic macrocyclic hosts can be used as a powerful tool for characterizing methylation-driven epigenetic mechanisms.

References:

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