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# Deciphering Interactions of Heterochromatin Protein 1 (HP1) with Chromatin and DNA in Phase Separation Environment

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As key chromatin-associated effectors, HP1 proteins carry nonredundant biological roles whose underlying mechanisms remain incompletely defined. Previous evidence indicates that LLPS by HP1 proteins and their nucleosome interactions are central to chromatin regulation. In this work, we characterize LLPS of HP1$\alpha$ (HP1$\alpha$) using NMR spectroscopy, confocal imaging, and identify the phosphorylated N-terminal extension (NTE) together with the hinge region as major molecular determinants of condensate formation. We further examine how pHP1$\alpha$ engages telomeric nucleosome arrays versus a more open Widom 601 nucleosome array under phase-separating conditions. These data support a model in which pHP1$\alpha$–nucleosome association arises from pHP1$\alpha$ self-assembly mediated by intermolecular contacts between the NTE and hinge, coupled with specific recognition of the H3K9me3 N-terminal histone tail by the chromodomain (CD). Finally, we show that DNA can modulate pHP1$\alpha$ LLPS by competing with the NTE for binding to the hinge region. Collectively, our results provide atomic-level insight into the features that drive pHP1$\alpha$ self-association and its interactions with DNA and nucleosomes.