Cooperation between the C-terminal domains of nucleoplasmin is key to stabilize and transfer the histone octamer to DNA

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Histone chaperones are key components of the machinery that regulates chromatin dynamics. We have previously shown that the distal face of nucleoplasmin (NP), the first histone chaperone described, is the protein region involved in substrate binding, and that the complexes formed between NP and the distinct core histones differ in stoichiometry and overall architecture. One NP pentamer binds five H2A-H2B dimers, with each C-terminal domain interacting with one dimer. In contrast, a more complex structure is obtained in the case of H3-H4 and the histone octamer, in which two NP pentamers face each other through their distal face, encaging the basic ligand. In this work, we characterize the NP/octamer complex and present its cryoEM structure. We also demonstrate that post-translational NP modifications contribute to stabilize the NP/histone octamer complexes and that several C-terminal domains must cooperate to form stable complexes with H3-H4 and histone octamers, in contrast with what is observed with H2A-H2B dimers. Finally we show that, in vitro, NP is capable of transferring the histone octamer to DNA, assembling nucleosomes. This activity could have biological relevance in processes in which the histone octamer must be rapidly removed from or deposited into the DNA, such as DNA replication in the first steps of embryo development and transcription in highly active genes.