

Centromeric protein M18BP1 is a condensin II loading factor

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Condensin II is a multi-subunit protein complex that, together with Condensin I, Cohesin, Top2A and Kif4A, is responsible for the correct compaction and organization of the genome during cell division in humans. Condensin II belongs to the SMC family of proteins that use the energy from ATP in a process named loop extrusion, to generate loops of DNA that compact the disordered genome into chromosomes. Importantly, since Condensin II is always in the nucleus throughout the cell cycle, its activity must be tightly regulated to only start chromosome compaction during mitosis. Previous studies have demonstrated how the activity of Condensin II is negatively regulated by the MCPH1 protein, that prevents premature chromosome condensation in interphase.

In our work we used cryo-EM, biochemistry and cell biology approaches to unveil the role of the centromeric protein M18BP1 as a novel regulator of Condensin II. M18BP1 directly binds Condensin II to recruit it to chromatin during G2-M phase. Binding is mediated by a conserved region of M18BP1, which contains a CDK1 phosphorylation site and a “central motif” of the NcapG2 subunit of Condensin II, previously found to be essential for MCPH1 binding. We found that while CDK1 phosphorylation of MCPH1 reduces its affinity for Condensin II, CDK1 phosphorylation of M18BP1 increases its affinity for Condensin II, suggesting a mechanism where phosphorylation mediates a switch between MCPH1 to M18BP1 binding, activating Condensin II at the start of mitosis.

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