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Lysine acetylation of nuclear Pif1 alters its enzymatic function

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Petite integration frequency 1 (Pif1) is a 5'-3' helicase that is implicated in the maintenance of the fidelity of nuclear and mitochondrial DNA. The protein's preference for unwinding RNA-DNA hybrids makes it a key player during various DNA transactions in the cell such as DNA replication, repair, and telomere maintenance, where such substrates are abundant. We recently discovered Pif1 was post-translationally modified by lysine acetylation both in mammalian and *Saccharomyces cerevisiae* cells. The current focus of our work is to define the role of lysine acetylation in modulating the enzymatic properties of the Pif1. Genetic knockouts of the dynamic modifiers of lysine acetylation have implicated specific lysine acetyltransferases and deacetylases in the dynamic modification of Pif1. Using purified recombinant yeast acetyltransferases to in vitro acetylate full-length recombinant Pif1 protein, we tested the alterations in the enzymatic activities of acetylated Pif1 protein compared to the unmodified form. From the electromobility gel shift assays (EMSA) and biolayer interferometry (BLITZ) analysis, we found that the acetylated form of Pif1 had higher binding affinity compared to the unmodified form. Directly correlating to increased substrate binding, the acetylated form of Pif1 also showed significantly higher helicase and ATPase activity. Additionally, using mass spectrometry, we have mapped out the sites of lysine acetylation of both in vivo and in vitro acetylated Pif1. We are currently in the process of understanding specific cellular triggers of Pif1 acetylation and also the impact of lysine acetylation of Pif1 on genetic stability.

Biography

Onyekachi Ononye is a graduate student in Dr Balakrishnan's laboratory at Indiana University-Purdue University Indianapolis. Her research focus explores the role of lysine acetylation in modulating DNA replication proteins on the lagging strand. Using a plethora of biochemistry techniques, Onyekachi is working towards defining one of the regulatory pathways required for high fidelity processing of DNA.

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