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Journal club

ORCHESTRATING TRANSCRIPTION WITH THE POL II CTD

A hallmark of eukaryotic RNA polymerase II (Pol II) is the unusual carboxy-terminal domain (CTD) of its largest subunit, RPB1. The Pol II CTD contains tandem repeats of a heptapeptide with a consensus YSPTSPS sequence.

Elegant biochemical and genetic studies carried out in the past 30 years have revealed that the Pol II CTD becomes extensively phosphorylated as Pol II elongates transcripts and, furthermore, that the phosphorylated CTD functions as a scaffold that recruits to elongating Pol II a host of enzymes and proteins involved in several co-transcriptional events. These factors are required for diverse processes such as the regulated release of Pol II from promoter-proximal pausing; pre-mRNA capping, methylation, splicing and polyadenylation; and co-transcriptional chromatin modification.

> “Pol II CTD phosphorylation is associated with the transition from transcription initiation to elongation”

Although the pivotal role of the CTD in mRNA synthesis and maturation is well appreciated today, many of the critical experiments that led to our current understanding of CTD function are less so. At the time of its discovery in the mid-1980s, the Pol II CTD attracted considerable attention and provoked rampant speculation about its function.

It was in the midst of this frenzy that a series of papers from Dahmus and co-workers first linked CTD phosphorylation to transcript elongation. Bartholomew *et al.*, and Cadena and Dahmus showed using chemical crosslinking that the CTD of transcribing Pol II is highly phosphorylated. Chesnut *et al.*, and Laybourn and Dahmus went on to show that Pol II bearing an unphosphorylated CTD is recruited to initiation complexes at core promoter sequences, where it can then be rapidly phosphorylated.

These papers and others firmly established that Pol II CTD phosphorylation is associated with the transition from transcription initiation to elongation and laid the foundation for all future studies addressing mechanisms by which the CTD orchestrates co-transcriptional processes.

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