News and Views: Focusing on the tail

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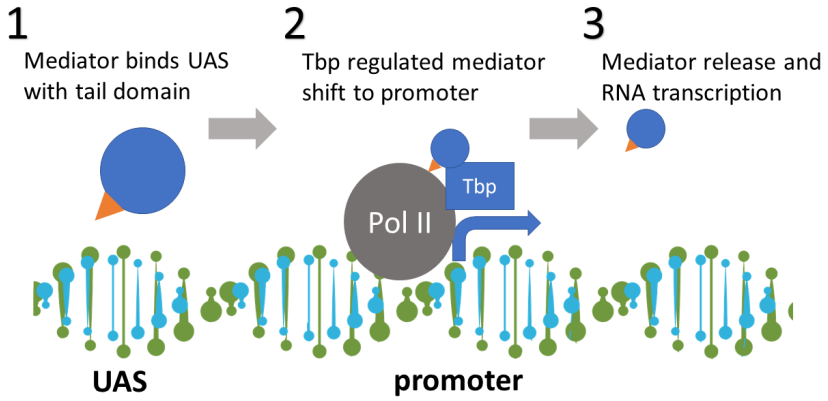
Abstract

In a 2018 paper published in eLife, Dr. Morse and colleagues shed light on the different roles for individual tail subunits of mediator in transcription, explaining an additional layer of complexity in gene expression regulation.

Keywords: Mediator, Transcription, Genetics



Findings

Mediator is a protein complex central to transcriptional regulation across many different organisms. Mediator is known to be a key regulator in response to changes in metabolism and the environment(Youn, Xiaoli, Pessin, & Yang, 2016).

In a 2018 eLife paper (Knoll, Zhu, Sarkar, Landsman, & Morse, 2018), Morse and colleagues employ genetic and biochemical assays to study the interaction between different subunits of mediator and other proteins present at the sites from which gene expression occur. To accomplish this, they use the innovative approach of performing Chromatin Immunoprecipitation with sequencing (ChIP-seq) of mediator subunits in combination with an inducible system for protein exclusion from the nucleus. This approach has the advantage of allowing for necessary (lethal on knockout) genes, such as mediator (Yin & Wang, 2014), to have their function studied in a classical genetics centric approach.

Using this system, they find that the different components of mediator, mainly the head and tail, have differential association with the upstream region of genes. Specifically, they found that the association of the head and tail are dependent and independent of interactions with the other pre-initiation complex proteins, Taf1 and Tbp, respectively.

Going further, Morse and colleagues then go on to study the mechanism of mediator shifting from the upstream activator sequence (UAS) to the promoter. In brief, mediator initially localizes to the UAS of genes, but is then known to shift to the promoter region of genes. This shift is important, as it is after this point that mediator is kicked off the promoter, allowing for transcription to proceed. Interestingly, Morse and colleagues study the regulation of this process by pre-initiation complex proteins. Using the same system of nuclear exclusion, they find that the exclusion of Tbp from the nucleus prevents the shift of mediator from the UAS to the promoter via ChIP-seq. This result indicates that Tbp is important for the staging of the gene regions bound by mediator, and may act as a larger coordinator of the steps leading to gene expression.

In sum, this new research from Morse and colleagues expands our understanding of the sequence of events leading to transcription. Importantly, this research establishes a new level of resolution of our understanding of the roles of mediator at the UAS, and the dependence of those roles on the functioning of other proteins, such as Tbp. Going forward, this research advances a new understanding of mediator, differentiating the function of the head and tail subunits.

References

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