

Structural Insights into Transcription Preinitiation Complex Assembly on Chromatin

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We would like to present our recent finding on the +1 nucleosome-bound PIC-Mediator structures [1]. Our previous studies reveal assembly of transcription preinitiation complex (PIC) on TATA box and TATA-less promoters [2] and Mediator facilitates PIC assembly and phosphorylation of Pol II C-terminal domain for transcription activation [3]. These structures were obtained on naked promoters. We therefore investigated how PIC-Mediator complex is assembled in the context of chromatin.

The +1 nucleosome is well positioned about 40 base pairs downstream of the transcription start site (TSS) and is commonly known as a barrier of transcription. Our structural and biochemical studies show that PIC-Mediator prefers binding to T40N nucleosome located 40 base pairs downstream of TSS and contacts T50N but not the T70N nucleosome. The nucleosome facilitates the organization of PIC-Mediator on the promoter by binding TFIID and Mediator subunits and may contribute to transcription initiation. PIC-Mediator exhibits multiple nucleosome-binding patterns, supporting a structural role of the +1 nucleosome in the coordination of PIC-Mediator assembly. Our study reveals the molecular mechanism of PIC-Mediator organization on chromatin and underscores the significance of the +1 nucleosome in regulating transcription initiation

References:

[1] Chen X, Wang X, Liu W, Ren Y, Qu X, Li J, Yin X and Xu Y. Structures of +1 nucleosome-bound PIC-Mediator complex. *Science*. 378:62-68 (2022).

[2] Chen X, Qi Y, Wu Z, Wang X, Li J, Zhao D, Hou H, Li Y, Yu Z, Liu W, Wang M, Ren Y, Li Z, Yang H and Xu Y. Structural insights into preinitiation complex assembly on core promoters. *Science*. 372:eaba8490 (2021)

[3] Chen X, Yin X, Li J, Wu Z, Qi Y, Wang X, Liu W and Xu Y. Structures of the human Mediator and Mediator-bound preinitiation complex. *Science*. 372:eabg0635 (2021)