S60-5 Studies on molecular switch function of Mediator complexes during transcription regulation

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In eukaryotes, the switch between transcriptional activation and repression is thought to be regulated by the Mediator complex consisting of 30 subunits. But its precise mechanisms await to be elucidated. Recently, it became clear that there were two CDK subunits possessing kinase activities for RNA polymerase II (Pol II) in this complex fraction. We, therefore, examined the role of two CDKs, CDK8 and CDK11 (also called CDK8-L), for the purpose to elucidate how Pol II is activated for transcription activation. And the findings were as follows: i) each CDK formed a distinct Mediator complex but possessed the same set of subunits except each CDK subunit. ii) both CDKs localized in the nucleus but more than half of them located differently from the other CDK.

To study the functional roles at transcription activation in the cell, the expression of each CDK was knocked down by siRNA and the effects on transcription activation were examined and it was observed in the end that transcription was repressed upon CDK8-knockdown and, on the other hand, transcription activation was further augmented upon CDK11-knockdown. These results suggest that CDK8-formed Mediator complexes play roles at transcription activation and CDK11-formed Mediator complexes play roles at repression. Though it is important for Pol II activation to form a complex of general transcription factors and Pol II, it is predicted that Mediator is highly involved in this activation. We will discuss about this point together with our recent results that one of the interaction target of Mediator is the general transcription factor TFIIE.