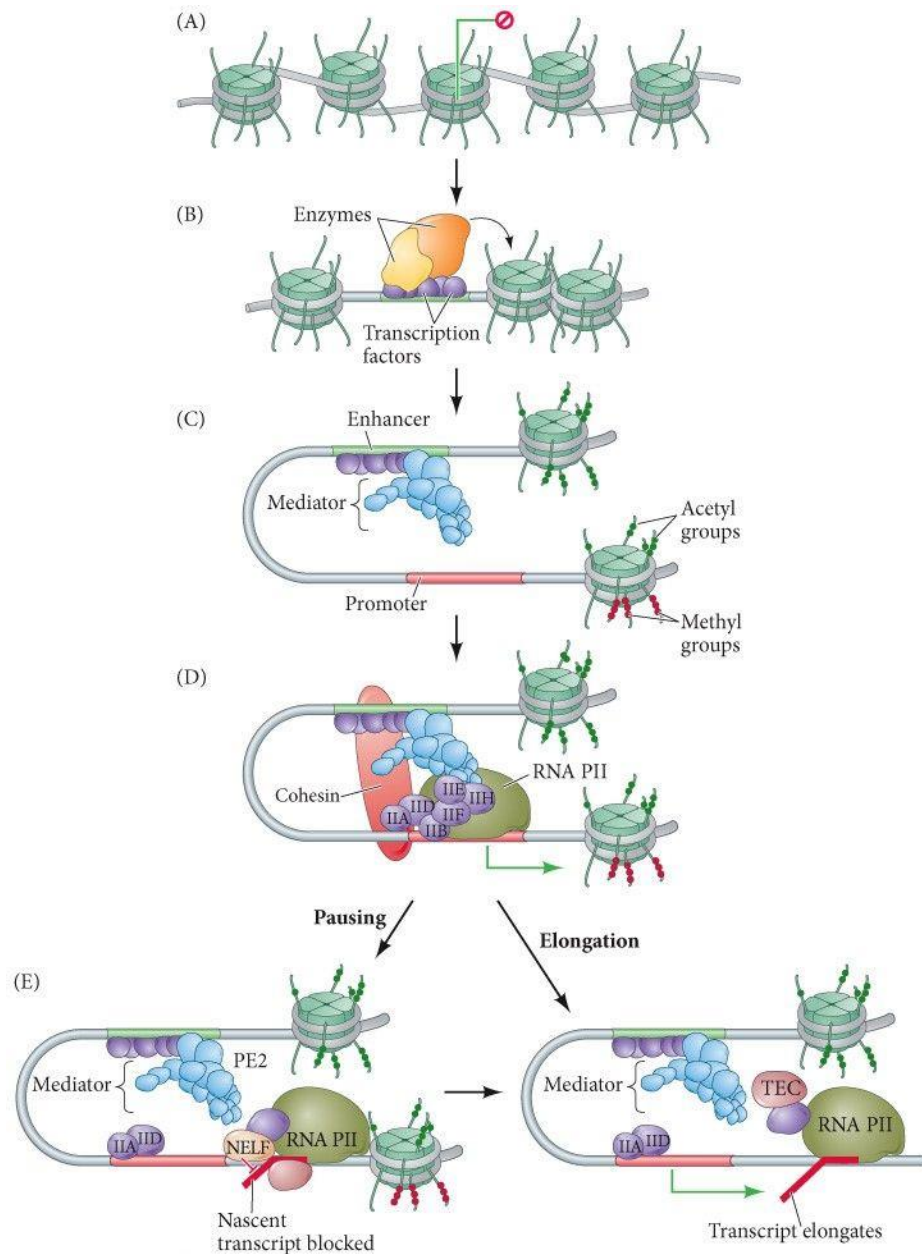


The Mediator Complex: Linking Enhancer and Promoter

In many genes, a bridge between enhancer and promoter is made by a large, multimeric complex called the mediator, whose nearly 30 protein subunits connect RNA polymerase II to enhancer regions that relay developmental signals (Malik and Roeder 2010). This bridge forms the pre-initiation complex at the promoter. Therefore, the Mediator helps create a chromatin loop, bringing the enhancer to the promoter. This chromatin loop is stabilized by the protein cohesin, which wraps around portions of this loop like a ring upon association with the Mediator after the Mediator is bound by transcription factors (Figure 1).

Although the Mediator may help bring the RNA polymerase II to the promoter, for transcription to take place the connection between the Mediator and the RNA polymerase II has to be broken, and RNA polymerase II must be released from the promoter. The release of RNA polymerase II is accomplished by a transcription elongation complex (TEC), which is made up of several transcription factors and enzymes (e.g., Ikaros, NuRD, and P-TEFb; Bottardi et al. 2015). This release coincides with the capping of the transcript, phosphorylation of the polymerase, and elongation of the transcript. In some instances, however, the RNA polymerase II either does not dissociate from the Mediator, or it dissociates but only transcribes a short stretch of nucleotides before it pauses. In the latter case, a transcription elongation suppressor (such as NELF) functions to prevent the TEC from associating with the polymerase, and the RNA polymerase II is paused, held in readiness for a new developmental signal.



After Malik and Roeder 2010; Ohlsson 2010

Figure 1 The role of the Mediator complex in forming the transcription pre-initiation complex. (A) Relatively open chromatin is composed of DNA coiled around nucleosomes. (B) Transcription factors (TFs) bind to the enhancer and to nucleosome-modifying enzymes that remove nucleosomes from the area, including the enhancer and promoter. (C) The transcription factors also bind a large protein complex called the Mediator. (D) The Mediator is able to recruit and stabilize RNA polymerase II (RNA PII) and its cofactors (TFs IIA, IIB, etc.) at the promoter site. These factors bound with RNA polymerase II are called the pre-initiation complex. The chromatin looping is further stabilized by cohesin. (E) After RNA polymerase II leaves the promoter, there are generally two outcomes. One outcome (right) is that RNA polymerase II can associate with the transcription elongation complex (TEC) to elongate the pre-mRNA while the Mediator continues to recruit new RNA polymerase II proteins to the complex. Alternatively (left), RNA polymerase II can be instructed to stop elongation by a repressive transcription factor (NELF) that prevents the assembly of the TEC. When given a second developmental signal, NELF can be removed and transcription elongation continued. (After Malik and Roeder 2010; Ohlsson 2010.)

All the material on this website is protected by copyright. It may not be reproduced in any form without permission from the copyright holder.

© 2023 Oxford University Press |

ⁱ Ikaros is a type of zinc-finger transcription factor that binds the histone deacetylase NuRD, which recruits P-TEFb (Positive transcription elongation factor b) to form a complex that breaks transcriptional pausing and promotes pre-mRNA elongation (Bottardi et al. 2015). Interestingly, the repertoire of bound factors can be gene specific. For example, progenitor blood cells expressing high levels of Ikaros differentiate into various types of white blood cells, whereas those expressing low levels differentiate mostly into red blood cells (Frances et al. 2011).