Threonine and tyrosine phosphorylation of the C-terminal domain of RNA Polymerase II regulate specific phases of the transcription cycle

Department of Molecular Epigenetics

Threonine and tyrosine phosphorylation increase RNA Polymerase II capacity for complex gene regulation

The carboxy-terminal domain (CTD) of RNA polymerase II (RNAPII) in mammals undergoes extensive posttranslational modifications, which are essential for transcriptional initiation, elongation, and termination.
Here, we show that threonine and tyrosine residues of the CTD of RNAPII are phosphorylated by Polo-like kinase and c-Abl kinase, respectively.
Both phosphorylations of CTD play critical roles for the process of RNA elongation and termination and orchestrate the binding and dissociation of cellular factors from CTD.

1. Hintermair, C.*, Heidemann, M.*, Koch, F.*, Descostes, N., Gut, M., Gut, I., Fenouil, R., Ferrier, P., Flatley, A., Kremmer, E., Chapman, R.D., Andrau, J.C. §, and Eick, D. § (2012) Threonine-4 of RNA polymerase II CTD is targeted of polo-like-kinase 3 and required for transcriptional elongation.
EMBO J, **31**, 2784-2797

2. Mayer, A.*, Heidemann, M.*, Lidschreiber, M., Schreieck, A., Sun, M., Hintermair, C., Kremmer, E., Eick, D. §, Cramer, P. § (2012) CTD tyrosine phosphorylation impairs termination factor recruitment to transcribing RNA polymerase II.
Science, 336,1723-1725.

(* equal contribution, § corresponding authors)

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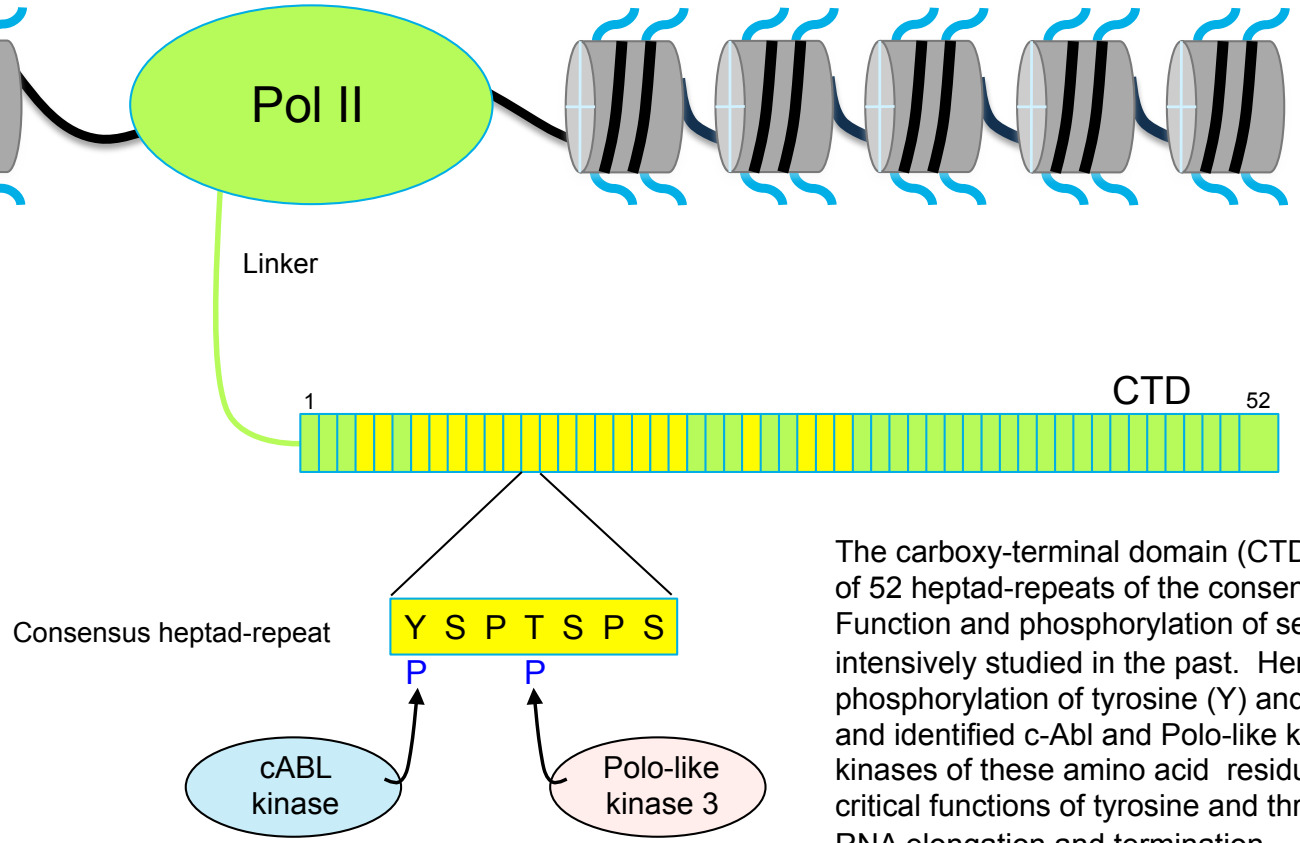

The carboxy-terminal domain (CTD) of RNA polymerase II consists of 52 heptad-repeats of the consensus repeat (green: variants). Function and phosphorylation of serine (S) residues has been intensively studied in the past. Here we described the phosphorylation of tyrosine (Y) and threonine (T) in CTD and identified c-Abl and Polo-like kinase 3 as the relevant kinases of these amino acid residues. Genetic analyses revealed critical functions of tyrosine and threonine residues in CTD for RNA elongation and termination.