Supplementary information S1 (box) | RNA Polymerase II post-translational modifications

RNA Polymerase II (Pol II) can be extensively post-translationally modified, mainly at its carboxy-terminal domain (CTD), which consists of several dozen repeats of a highly conserved heptapeptide (reviewed in REF. 1). Specific modifications of the CTD define different states of Pol II throughout the transcription process[2]. They are involved in regulating Pol II transitions between the initiation, elongation and termination states, and in coupling of various co-transcriptional processes, such as mRNA capping or splicing, with specific phases of transcription[3].

The most studied modifications involved in transcription are phosphorylation of Ser2, Ser5 and Ser7. Phosphorylated Ser5 (Ser5P) and Ser7P are associated with initiating Pol II, whereas Ser2P is a mark of actively elongating Pol II after pause-release. The phosphorylation of these residues is catalysed by specific kinases whose activity can be regulated, thereby controlling Pol II progression and transcription. Ser5P and Ser7P are deposited by cyclin-dependent kinase 7 (CDK7), which is a subunit of the general transcription factor TFIIH (transcription factor IIH), and in yeast this is stimulated by the Mediator complex[4]. Ser2P is deposited by CDK9, which is a subunit of positive transcription elongation factor b (P-TEFb), and which also phosphorylates negative elongation factor (NELF) and DRB sensitivity inducing factor (DSIF), thereby allowing Pol II to overcome pausing and enter productive elongation[5]. P-TEFb can be recruited to core promoters by the transcription cofactor bromodomain-containing protein 4 (BRD4)[6,7], which is employed by many enhancers and is involved in regulating specific subset of genes[8-10]. Interestingly, BRD4 itself has kinase activity and can phosphorylate Ser2 *in vitro*[11], but it is not clear how this contributes to activation of transcription by Pol II at core promoters *in vivo*.

Additional modifications of the Pol II CTD involved in transcription include Lys acetylation by p300 downstream of transcription start sites, which has a role in the induction of growth-factor response genes[12].

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