Rpb1-CTD phosphorylation is differentially modulated by Rpb4/7

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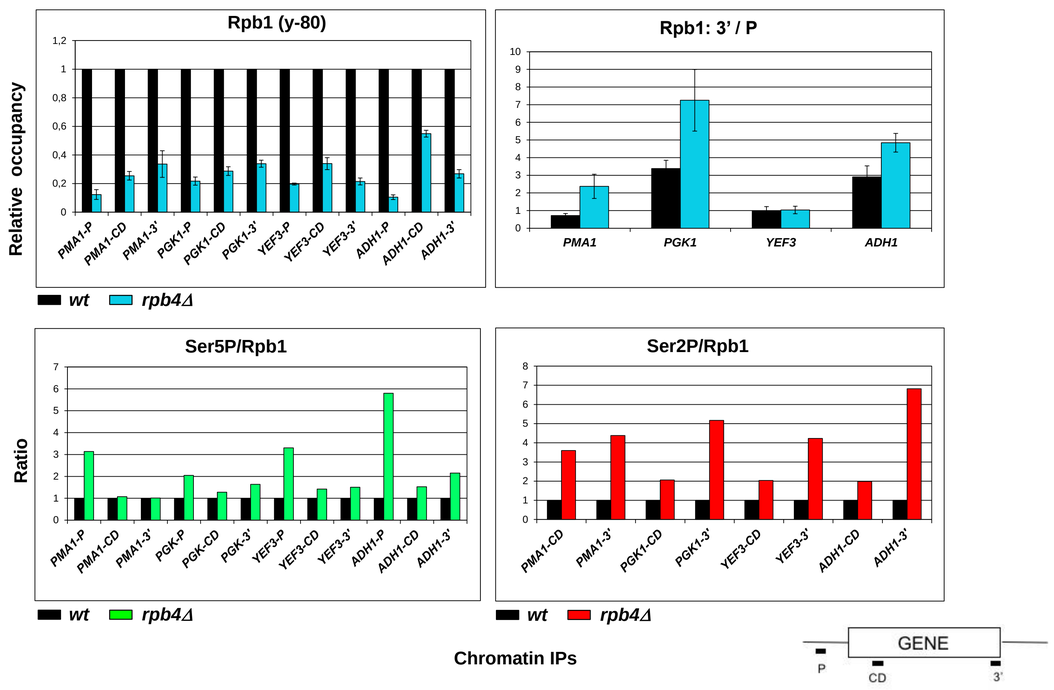
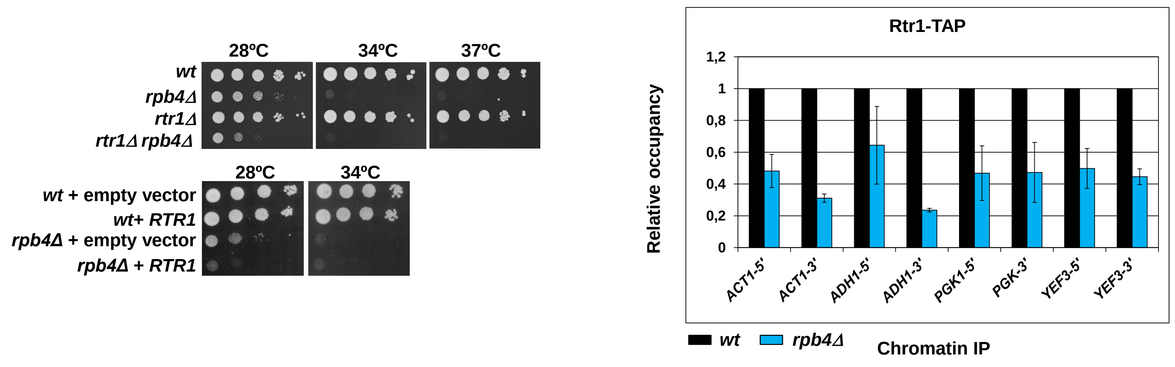
The Rpb4 and Rpb7 subunits of eukaryotic RNA polymerase II (RNAPII) participate in a variety of processes from transcription, DNA repair, mRNA export and decay, to translation regulation and stress response. In addition, we have recently shown that the Rpb4/7 heterodimer in *S. cerevisiae* plays a key role in controlling phosphorylation of the carboxy terminal domain (CTD) of the Rpb1 subunit of RNAPII. Deletion of *RPB4,* and mutations that disrupt the integrity of Rpb4/7 or its recruitment to the RNAPII complex, increased phosphorylation of Ser2, Ser5, Ser7. We showed that Rpb4 is important for Ssu72 and Fcp1 phosphatases association, recruitment and/or accessibility to the CTD, and that this correlates strongly with Ser5P and Ser2P levels, respectively [1]

Here we show that, in addition, *rpb4Δ* cells display increased Thr4P and Tyr1P. Our data suggest that Fcp1 is the Thr4P phosphatase in yeast, as in vertebrate [2]. Moreover, we present evidences that Rpb4 may be also linked to the function of the CTD phosphatase Rtr1, which has been involved in Ser5P and Tyr1P dephosporylation [3]. On the other hand, Rpb4 also influences the recruitment of the CTD-Ser2 kinase Ctk1 during transcription elongation. We proposed a model where Rpb1-CTD phosphorylation levels are differentially modulated by Rpb4/7. Thus, increased Ser2P phoshorylation levels in the *rpb4Δ* mutants are due to altered Fcp1 and Ctk1 functions, while increased Ser5 phosphorylation is the result of changes in Ssu72. Our data and others, and the close localization of Rpb4/7 to the CTD [1,4,5,6], suggest that Rpb4/7 might modulate the access of the CTD modifying enzymes to their substrate during the whole transcription cycle.

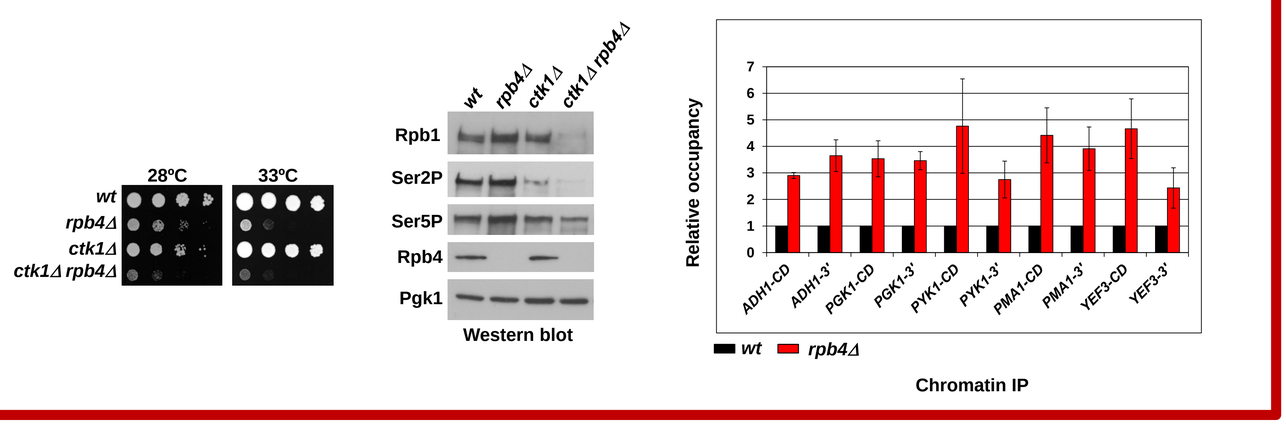
A functional Rpb4/7 heterodimer is required to maintain proper Rpb1-CTD Ser5P and Ser2P levels



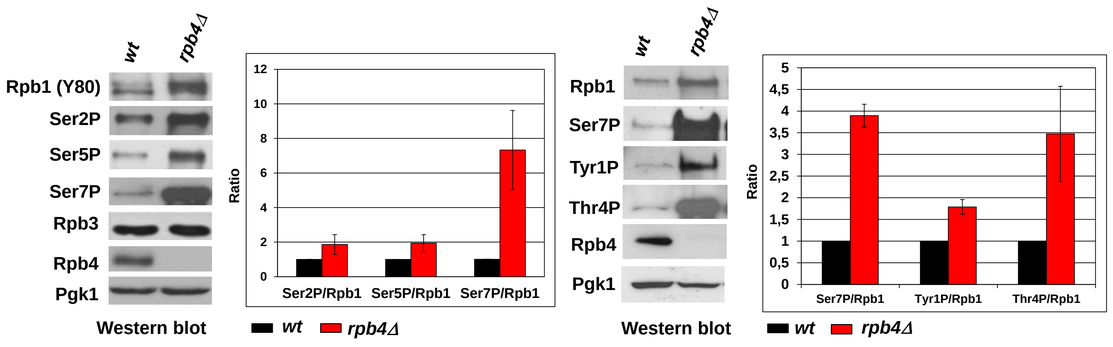
Rpb4 may be also linked to the function of the CTD phosphatase Rtr1



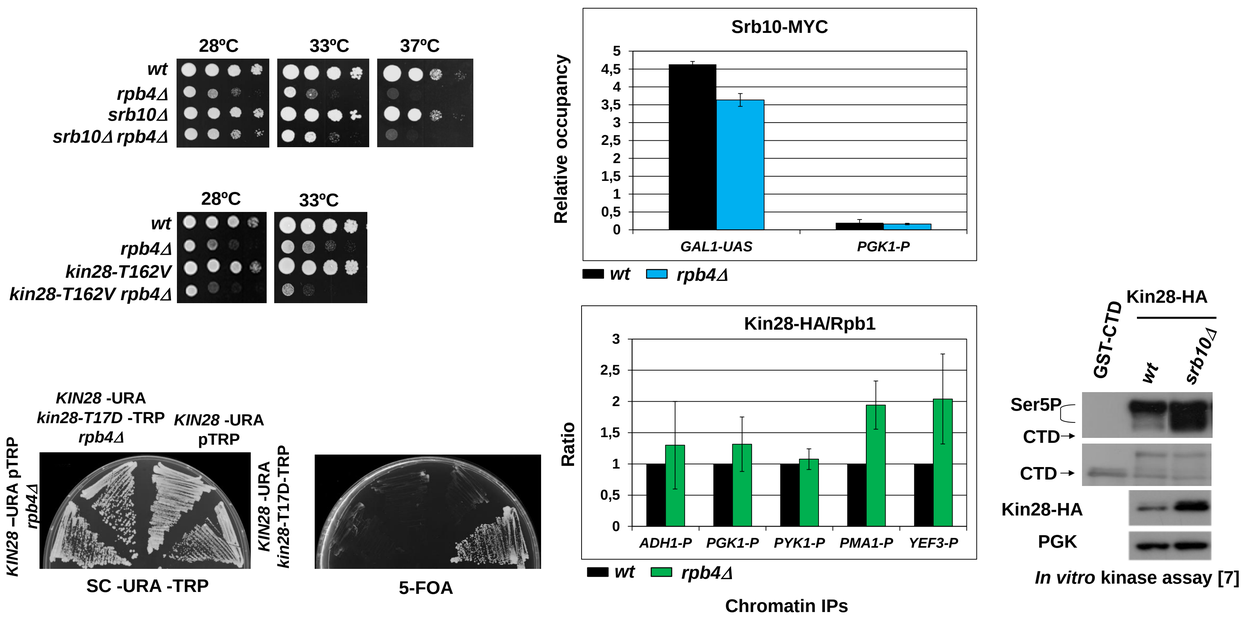
Rpb4 influences the recruitment of the CTD-Ser2 kinase Ctk1 during transcription elongation…



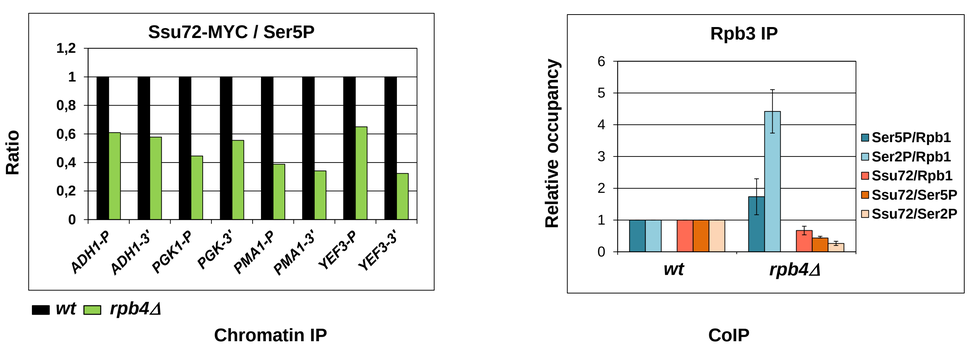
rpb4Δ cells also display increased Ser7P, Thr4P and Tyr1P levels



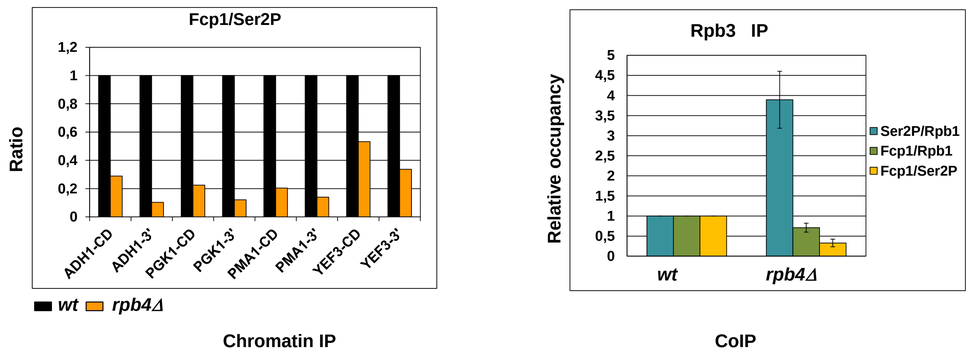
…and affects differentially to the PIC kinases, Srb10 and Kin28



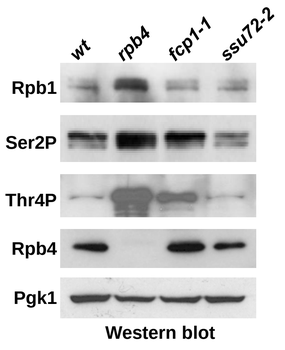
Ssu72 association to chromatin and RNAPII is facilitated by Rpb4/7



Proper Fcp1 association to chromatin and to RNAPII is dependent on Rpb4/7,

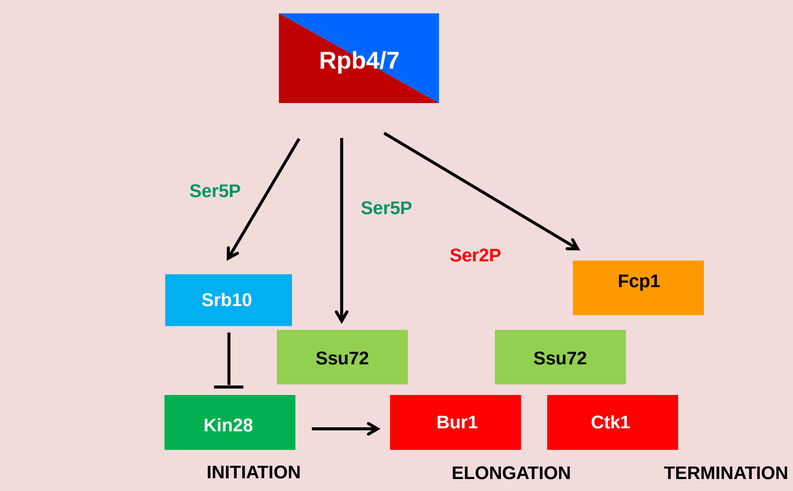


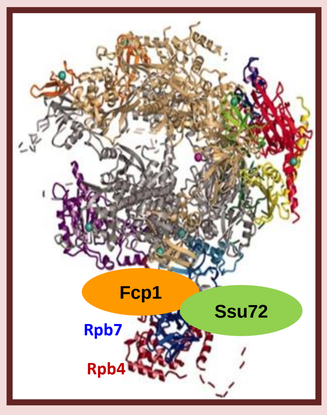
and Fcp1 phosphatase activity is require for Rpb1-CTDThr4P dephosphorylation



Our model:

Rpb1-CTD phosphorylation levels are differentially modulated by Rpb4/7





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AKNOWLEDGMENTS

Francisco Navarro. Universidad de Jaén. Spain
Carlos Fernández Tornero . CIB. Madrid. Spain

This work was funded by the MINECO (BFU2013-48374-P)