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Transcription in the nucleus and mRNA decay in the cytoplasm are coupled processes

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Maintaining appropriate mRNAs levels is vital for any living cell. mRNA synthesis in the nucleus by RNA polymerase II core enzyme [Pol II] and mRNA decay by cytoplasmic machineries determine these levels. Yet, little is known about possible cross-talk between these processes. The yeast Rpb4/7 is a nucleo-cytoplasmic shuttling heterodimer that interacts with Pol II and with mRNAs and is required for mRNA decay in the cytoplasm. Here we show that interaction of Rpb4/7 with mRNAs and eventual decay of these mRNAs in the cytoplasm depends on association of Rpb4/7 with Pol II in the nucleus. We propose that, following its interaction with Pol II, Rpb4/7 functions in transcription, interacts with the transcript cotranscriptionally and travels with it to the cytoplasm to stimulate mRNA decay. Hence, by recruiting Rpb4/7, Pol II governs not only transcription but also mRNA decay.

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mRNA levels are determined by two distinct processes: transcription, catalyzed by RNA polymerase II [Pol II], and mRNA decay. Transcription occurs in the nucleus whereas the major mRNA decay pathways operate in the cytoplasm. As synthesis and decay processes contribute equally to maintaining mRNA levels, it is quite likely that organisms have evolved a mechanism to coordinate events in the two compartments. To date, little is known about any relationships between these processes.

In yeast, the major mRNA decay pathways occur in the cytoplasm, triggered by shortening of the mRNA poly[A] tail. One pathway culminates in exonuclease digestion of the mRNA from 5’ to 3’ by Xmrlp. The second pathway culminates in exonucleolytic degradation of the mRNA from 3’ to 5’ [for recent reviews, see Coller and Parker 2004; Amrani et al. 2006; Garneau et al. 2007].

Structural studies indicate that the Pol II complex, comprising Rpb1p to Rpb12p, consists of two discrete parts [Armache et al. 2003; Bushnell and Kornberg 2003]. The core comprises 10 subunits and includes the catalytic active site. The other part comprises two subunits, Rpb4p and Rpb7p, which form a heterodimer, designated Rpb4/7, that can bind RNA (for review, see Choder 2004). The interface between the two substructures is small and consists of several residues in Rpb7p, termed the “Rpb7p tip”, and a small pocket in the core formed by five protein regions: three small regions from Rpb1p, one region from Rpb2p, and one region from Rpb6p [Armache et al. 2003; Bushnell and Kornberg 2003]. As Rpb4/7 is present in excess over Pol II complexes [Rosenheck and Choder 1998; Choder 2004], it is possible that Pol II–free Rpb4/7 interacts independently with transcripts either in the nucleus or in the cytoplasm. Alternatively, Rpb4/7 may bind RNA only during transcription in association with Pol II.

Recently, Rpb4p and Rpb7p were found to shuttle between the nucleus and the cytoplasm by a transcription-dependent pathway [S elitrennik et al. 2006] and to play roles in the decay of mature mRNAs in the cytoplasm [Lotan et al. 2005, 2007]. Importantly, genetic analyses indicate that the roles of Rpb7p in the two major mRNA decay pathways are distinct from its role in transcription [Lotan et al. 2007]. Although it is conceivable that the nuclear and the cytoplasmic functions of Rpb4p and Rpb7p are mechanistically unrelated, an intriguing alternative is that their two functions are coupled, and thus Pol II influences both mRNA synthesis and decay. Here we provide evidence for the second alternative.

Results and Discussion

Pol II mutant that poorly recruits Rpb4/7

To determine whether Pol II controls mRNA decay by recruiting Rpb4/7, we took advantage of a Pol II core that comprises Rpb6Q100Rp. This mutant core binds Rpb4/7 poorly, as the Rpb6Q100R mutation alters one of the very few residues in the core pocket responsible for direct contact with the tip of Rpb7p [Bushnell and Kornberg 2003; Tan et al. 2003; Armache et al. 2005]. Consistently, tandem affinity purification (TAP)-tagged Rpb4p pulls down wild-type Pol II efficiently, whereas its capacity to pull down Rpb6Q100Rp-containing Pol II is compromised [Supplemental Fig. S1A]. Note that the poor immunoprecipitation is observed despite wild-type level of Rpb4p in the mutant cells [Supplemental Fig. S1; see also Supplemental Fig. S4].

rpb6Q100R cells are defective in executing mRNA decay

To determine if rpb6Q100R cells are defective in mRNA decay, we blocked transcription using two approaches. In the first one, we monitored decay of natural mRNAs, exploiting the heat-shock response whereby the transcription of most genes is blocked rapidly in response to heat. Following transcription arrest, we monitored the decay of mRNAs that had existed in the cytoplasm prior to the temperature shiftup [Lotan et al. 2005, 2007, and references therein]. Because the Rpb4/7–Pol II interaction is essential for transcription at high temperatures, transcription is arrested more robustly in response to
temperature increases in rpb6Q100R cells than in wild-type cells [Rosenheck and Choder 1998; Tan et al. 2003; Choder 2004]. Using this approach, we observed that rpb6Q100R cells are defective in the decay of various natural mRNAs [Fig. 1A,B]. Notably, RPL25 pre-mRNA disappears rapidly in both strains [Fig. 1A, "Unspliced RPL25"], consistent with rapid transcription arrest that occurs in both strains upon temperature shiftup.

To gain mechanistic understanding of this difference in mRNA decay kinetics, we compared deadenylation in wild-type and rpb6Q100R cells using the PAGE-Northern technique [Sachs and Davis 1989]. Deadenylation rates are slower in rpb6Q100R cells [Fig. 1C; Supplemental Fig. S3]. Moreover, the fully deadenylated mRNAs are degraded abnormally slowly in the rpb6 mutant. Indeed, whereas 78% of deadenylated RNA was degraded in 10 min in wild-type cells, only 64% of deadenylated RNA was degraded in a much longer time (25 min) in the mutant cells [Fig. 1C]. Notably, defective deadenylation and slow decay of deadenylated RNAs are characteristic phenotypes of mutations in RPB4 and RPB7 [Lotan et al. 2005, 2007].

Using a second approach to block transcription, we next examined decay features of the synthetic Tet-Off-MFA2pG transcript [Hilleren and Parker 2003] after blocking its transcription by doxycycline, a drug that has no significant effect on overall proliferation rate [Gari et al. 1997]. As shown in Figure 1D, MFA2pG mRNA decays more slowly in rpb6Q100R cells [T1/2 = 25 min] than it does in wild-type cells [T1/2 = 12 min]. This occurs at 30°C. Thus, we found that degradation of both synthetic and natural transcripts, under either optimal or stress conditions, is slower in rpb6Q100R cells than it is in wild-type cells. A degradation intermediate of MFA2pG mRNA, designated "Frag.," in Figure 1D, accumulates in the cytoplasm due to a poly(G) tract that blocks 5'-to-3' exonuclease activity of Xrn1p [Vreken and Raue 1992; Decker and Parker 1993]. This fragment is degraded ultimately by the 3'-to-5' pathway [Jacobs Anderson and Parker 1998]; therefore, its accumulation is often due to defects in this pathway. Previously, we showed that Rpb7p stimulates both deadenylation and 3'-to-5' degradation [Lotan et al. 2007]. Consequently, rpb7 mutants accumulate 2.9-fold more MFA2pG fragment than wild-type cells do [Lotan et al. 2007]. As shown in Figure 1D, the rpb6Q100R mutation also leads to abnormally high accumulation of "Frag." We suspect that accumulation of this fragment is due to the poor capacity of rpb6Q100R cells to execute Rpb7p-mediated 3'-to-5' decay [see below]. Summarily, although rpb6Q100R cells carry wild-type RPB4 and RPB7, this mutant strain exhibits several defective features of mRNA decay similar to those reported as characteristic of strains carrying certain RPB7 ts alleles [Lotan et al. 2007] or lacking RPB4 [Lotan et al. 2005]. Based on all these data, we hypothesize that poor association of Rpb4/7 with Rpb6Q100R-containing Pol II results in defective mRNA decay in the cytoplasm. We took various approaches to validate this premise as outlined below.

Figure 1. rpb6Q100R cells exhibit defective mRNA decay. [A] Cells growing optimally at 30°C were shifted rapidly to 42°C to block transcription naturally (Lotan et al. 2005, 2007). Decay kinetics were determined by Northern analysis, using probes indicated on the left (see the Materials and Methods). T1/2 were determined as in B. The ratio between the T1/2 of a given mRNA in the wild-type and its T1/2 in the wild-type [WT] [Fig. 1C] are indicated on the right. [B] Half-lives [T1/2] were determined by plotting mRNA levels as a function of time post-transcription block. A graphic illustration of RPL29 mRNA decay kinetics is shown as an example. To obtain this graph, the intensity of each band, determined by PhosphorImager technology, was normalized to that of SCR1 (a Pol III transcript). The normalized band intensity at time 0 [before transcription arrest] was defined as 100% and the intensities at the other time points were calculated relative to time 0. Results were plotted as a function of time. The graph represents an average of three independent assays. Error bars indicate the standard deviation from the mean values. Half-lives were obtained from these graphs and are depicted on the right. Variations in the calculated half-lives were <15%. [C] Transcription was blocked as in A. RNA samples analyzed by the PAGE-Northern technique [Sachs and Davis 1989], using the probes indicated on the right. The positions of fully adenylated RNA [An] and deadenylated RNA [A0] are shown on the left. Lane "A(n)" shows the position of fully deadenylated RNA [see Lotan et al. 2007]. The asterisk (*) indicates the time point when deadenylation is estimated to be complete. The proportional decrease in radioactivity between this time point and the following time point was used to estimate the degradation rate of the mRNA. Quantitative estimation of the decay kinetics is shown in Supplemental Figure S3. [D] rpb6Q100R cells degrade MFA2pG mRNA abnormally slowly and accumulate abnormally high decay intermediate of MFA2pG mRNA. Wild-type and rpb6Q100R cells expressing Tet-Off-MFA2pG were grown at 30°C to mid-logarithmic phase before transcription was blocked by adding doxycycline (2 µg/mL) [Hilleren and Parker 2003]. Following drug addition, cultures continued to be shaken at 30°C and samples were taken at the indicated time points. RNA samples analyzed by the PAGE-Northern technique [Sachs and Davis 1989], hybridized with an MFA2pG-specific probe [see the Materials and Methods]. The position of MFA2pG full-length mRNA [FL] is indicated on the left. "Frag." indicates a degradation intermediate that accumulates due to a poly(G) tract that blocks 5'-to-3' exonuclease activity by Xrn1p [Vreken and Raue 1992; Decker and Parker 1993]. The ratios between this fragment and MFA2pG, the full-length one, at time points (at steady state) were determined by PhosphorImager technology (normalized to SCR1 RNA) and are indicated at the bottom as percentages. Half-lives were calculated as in B; in wild type it was 12 min and in the mutant, 25 min. The positions of the size marker bands are shown on the right. [E] rpb6Q100R cells are hypersensitive to deletion of XRN1. Strain indicated on the left, carrying pRPB4/TJR3A2/p (overexpressing Rpb4/7) were spotted, in 10-fold dilutions, on 5-FOA-containing plate (the drug kills cells expressing URA3). In parallel, cells were spotted on a synthetic medium lacking uracil that selects for cells carrying the plasmid [designated SC-uracil]. Plates were incubated for 3 d at 30°C.
Overexpression of RPB4/7 in rpb6G100R cells increases association between Rpb4/7 and Pol II, suppresses the cells sensitivity to high temperature, and corrects their transcriptional defect

As shown in Supplemental Figure S4B, overexpressing RPB4 or RPB7 alone has little or no effect on cell proliferation at high temperatures. We used a high-copy plasmid [pRPB4/7/2µ] that expresses both genes while maintaining the relative level of RPB4 mRNA and RPB7 mRNA in both the RPB6 wild-type (Lotan et al. 2007) and rpb6G100R strains (Supplemental Fig. S4A). Introduction of pRPB4/7/2µ suppresses partially the temperature sensitivity of rpb6G100R cells (Supplemental Fig. S4B), encouraging us to examine the mechanistic consequences of this overexpression. First, we observed that overexpression of RPB4/7 increases the association between the mutant Pol II and Rpb4/7 (Supplemental Fig. S1B). We then reasoned that if defective transcription and mRNA decay by the rpb6G100R strain are indeed due to weakened Rpb4/7–Pol II interactions, then overexpression of RPB4/7 should correct both the transcription and the decay defects of rpb6G100R cells. As shown in Supplemental Figure S2, high-copy Rpb4/7 restores the transcriptional defect of the mutant cells during heat shock, suggesting that the mutation in Rpb6p affects transcription only through binding Rpb4/7.

rpb6G100R cells exhibit hypersensitivity to deletion of XRN1 that can be suppressed by overexpressing RPB4/7

As discussed above, excessive accumulation of the MFA2pG mRNA degradation intermediate in rpb6G100R cells [Fig. 1D] suggests that these cells are defective in 3’-to-5’ decay [Vreken and Raue 1992; Decker and Parker 1993]. We took advantage of the observation that strains lacking both the 5’-to-3’ and 3’-to-5’ decay pathways are inviable [Johnson and Kolodner 1995; Jacobs Anderson and Parker 1998; van Hoof et al. 2000]. If our interpretation that the fragment accumulates because of defective 3’-to-5’ decay is correct, then the rpb6G100R allele should be synthetically lethal, or synthetically sick, with deletion of XRN1. Moreover, deletion of XRN1 should not be lethal in mutant cells that overexpress RPB4/7 if such an overexpression indeed suppresses the 3’-to-5’ decay defect. We therefore deleted XRN1 from rpb6G100R cells that also carry pRPB4/7/2µ. Creation of rpb6G100R xrn1A cells overproducing Rpb4/7 [Fig. 1E, right panel] indicates that these cells have the capacity to execute mRNA degradation using the 3’-to-5’ pathway. However, removal of the high-copy RPB4/7 plasmid by 5-FOA uncovers the predicted synthetic sickness phenotype of rpb6G100R xrn1A cells, as their proliferation slows or stops [Fig. 1E, left panel]. In contrast, cells lacking XRN1 but carrying wild-type RPB6 proliferate well irrespective of whether or not they bear pRPB4/7/2µ. These results support our conjecture that rpb6G100R cells are defective in executing the 3’-to-5’ pathway, much like cells carrying some mutations in RPB7 [Lotan et al. 2007]. More importantly, this mRNA decay defect is not a direct effect of the mutation in RPB6 per se, as RPB4/7 overexpression can suppress this defect [Fig. 1E, right panel].

Overexpression of RPB4/7 in rpb6G100R cells suppresses partially the defect in mRNA decay

Next we examined directly the effect of overexpressing Rpb4/7 on mRNA decay. Rpb4/7 overexpression in wild-type cells does not cause detectable changes in mRNA decay or in deadenylation kinetics (Fig. 2A; Supplemental Fig. S5, lanes 1–10). These results suggest that the heterodimer is not a limiting factor in the wild-type decay process. In contrast, Rpb4/7 overexpression in rpb6G100R cells suppresses partially their defect in deadenylation [Supplemental Fig. S5, lanes 11–20] and in overall mRNA decay (Fig. 2B). This partial suppression conferred by exogenous Rpb4/7 argues against a direct and Rpb4/7-independent role for Rpb6p in mRNA decay. Together with the genetic data [Fig. 1E], these results indicate that the defective capacity of rpb6G100R cells to degrade mRNAs and their dependence on XRN1 are related to the poor interaction of Rpb6G100R p with Rpb4/7.

The capacity of Rpb4/7 to associate with mRNAs is smaller in rpb6G100R cells than it is in wild-type cells

Rpb7p was shown to interact with the emerging transcript during in vitro transcription [Ujvari and Luse 2006] and in vivo [Lotan et al. 2005], using at least one of its two RNA-binding domains [Todone et al. 2001; Meka et al. 2003, 2005; Choder 2004]. In order to determine if...
Using the oligo(dT) primer, vested and electrophoresed in 2% gel followed by Southern analysis determined by Southern analysis. PCR was carried out by the real-time PCR fragment and to visually demonstrate the quantification of reverse transcriptase (RT). cDNA levels were determined by qPCR (see the Materials and Methods). The level of each cDNA produced from the IP material was normalized to that produced from the input RNA, diluted 1:1500-fold. Each bar represents average of three experiments; each one was done in triplicate. Error bars indicate the standard deviation. (A) Relative cDNA levels obtained using the random primers. Each bar represents the ratio of cDNA level of RPS22B mRNA (normalized to that of the input) divided by that of SCR1 cDNA (normalized to that of the input). (B) Levels of PCR-amplified RPS22B cDNA, obtained using oligo(dT), determined by Southern analysis. PCR was carried out by the real-time PCR. At late-exponential phase (cycle 31), the sample harvested and electrophoresed in 2% gel followed by Southern analysis using RPS22B probe. (C,D) Levels of the indicated cDNAs obtained using the oligo(dT) primer.

Recruitment of Rpb4/7 to Pol II is required for its association with mRNAs in vivo, we immunoprecipitated TAP-tagged Rpb4p from wild-type or rpb6Q100R cells, or from cells lacking the tag as a control, and examined how much RNA was coimmunoprecipitated with it, using reverse transcription [RT] followed by qPCR. We first used a random hexamer as the primer in the RT reaction, which allowed us to synthesize cDNA using both Pol II and Pol III transcripts as the templates. This permitted us to normalize RPS22B signal with that of SCR1. As shown in Figure 3A, RPS22B mRNA is coimmunoprecipitated together with Rpb4p more efficiently in wild-type cells than it is in rpb6Q100R cells. To obtain cDNA from mature poly[A] mRNAs, we used oligo(dT) as the primer. Also in this case, more mRNAs are associated with Rpb4p-TAP in wild-type cells than they do in rpb6Q100R cells [Fig. 3C,D]. To verify production of correct PCR fragment and to visually demonstrate the quantitative results, the PCR product of one experiment was analyzed by Southern blot hybridization technique [Fig. 3B]. Taken together, the results in Figure 3A-D argue against the possibility that Rpb4/7 interacts with mRNA independently of Pol II, as the levels of Rpb4/7 are identical in both strains (see Supplemental Figs. S1, S4A). Instead, the results are in accord with "conditional interaction" between Rpb4/7 and mRNAs, whereby the interaction occurs in the context of Pol II.

Like rpb6Q100R strain, rpb1C67S, C70S strain is defective in mRNA decay as well.

Finally, we took a last approach to corroborate that the poor interaction of Rpb6Q100R p with Rpb4/7 determines the defective mRNA decay phenotype of rpb6Q100R cells. We reasoned that if the inability of rpb6Q100R cells to degrade efficiently mRNAs is indeed due to the poor interaction between Rpb4/7 and Pol II, then mutations in another Pol II subunit that also binds Rpb4/7 and affects its recruitment to Pol II should result in a similar phenotype. Thus, we investigated the mRNA decay phenotype of a strain carrying C67S and C70S substitutions in Rpb1p, which (like the mutation in Rpb6p) have been reported to compromise recruitment of Rpb4/7 to Pol II [Donaldson and Friesen 2000]. As controls, we examined mRNA decay phenotype in cells carrying mutations in Rpb1p outside the pocket region in Pol II that interacts with Rpb7p tip [Donaldson and Friesen 2000; Armache et al. 2003, 2005; Bushnell and Kornberg 2003]. Like rpb4Δ cells [Lotan et al. 2005], rpb7 mutant cells [Lotan et al. 2007], and rpb6Q100R cells [e.g., Fig. 1], rpb1C67S, C70S cells are defective in both deadenylation and subsequent mRNA degradation [Fig. 4A,B]. However, high-copy Rpb4/7 cannot correct the defective phenotypes of rpb1C67S, C70S cells as it does in rpb6Q100R cells [data not shown]. Perhaps, these specific mutations in Rpb1p compromise more severely the capacity of Pol II pocket to recruit Rpb4/7 than the Q100R substitution in Rpb6p does. In contrast with rpb1C67S, C70S cells, the control mutant cells exhibit normal, or nearly normal, mRNAs decay kinetics [Fig. 4A]. The control mutants are defective in transcription, in vitro [Donaldson and Friesen 2000] and in vivo, as determined by the poor transcriptional induction of HSP104 in response to HS [Fig. 4A] or by the low steady-state levels of YEF3 (33% compared with wild type) and TEF4 (42%) mRNAs. Thus, poor transcription per se is not responsible for poor mRNA decay.

Taken together, the results of both genetic and bio-

Figure 3. Efficient association of Rpb4/7 with mRNAs is dependent on Rpb6p. Equal amounts of cell extracts from wild-type or from rpb6Q100R cells carrying or lacking TAP-tagged Rpb4, as indicated, were subjected to RNA immunoprecipitation (RIP) as detailed in the Materials and Methods. Prior to the RIP procedure, 5% of each extract was removed to determine the levels of the indicated mRNAs in the input material. cDNA was synthesized using either random hexamer (A) or oligo(dT) (B–D) as the primer, in the presence (+) or absence (−) of reverse transcriptase (RT). cDNA levels were determined by qPCR (see the Materials and Methods). The level of each cDNA produced from the IP material was normalized to that produced from the input RNA, diluted 1:1500-fold. Each bar represents average of three experiments; each one was done in triplicate. Error bars indicate the standard deviation. (A) Relative cDNA levels obtained using the random primers. Each bar represents the ratio of cDNA level of RPS22B mRNA (normalized to that of the input) divided by that of SCR1 cDNA (normalized to that of the input). (B) Levels of PCR-amplified RPS22B cDNA, obtained using oligo(dT), determined by Southern analysis. PCR was carried out by the real-time PCR. At late-exponential phase (cycle 31), the sample harvested and electrophoresed in 2% gel followed by Southern analysis using RPS22B probe. (C,D) Levels of the indicated cDNAs obtained using the oligo(dT) primer.

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Taken together, the results of both genetic and bio-

Figure 4. Cells carrying rpb1C67S, C70S, but not another ts allele of RPB1, exhibit defective mRNA decay. (A) Decay kinetics in various mutant cells carrying transcriptionally defective RPB1 allele. Decay kinetics was determined as in Figure 1A. Strains, indicated on top of the autoradiograms are described in Donaldson and Friesen (2000). Half-lives were determined as in Figure 1C. The ratios between the T1/2 values in the mutant cells and those in the wild-type cells (T1/2 ratio) are indicated on the right. (B) rpb1C67S, C70S cells exhibit defective mRNA deadenylation and subsequent decay. Deadenylation kinetics was determined by PAGE-Northern as in Figure 1C. Half-lives were determined using Northern blot hybridization [not shown], as in A. Stability of the deadenylated RPL29 RNA was estimated as described in Figure 1C.
poor interaction of Rpb6 Q100R p with Rpb4/7. We con-
to-5

bodies is apparent mainly during starvation). Rpb4/7 also plays a

2007), where mRNA degradation is executed (association with P

The Rpb4/7

7 complex interaction with the mRNP (Lotan et al. 2005).

Lsm1

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-3

2007). The role of Rpb4/7 in the 5

–to-3

pathway involves its inter-

Svejstrup 2006), with modifications as described in the Supplemental Ma-

RNA immunoprecipitation (RIP) followed by qRT

C. Half-lives

non-HS genes was blocked by shifting cells rapidly to 42

°

, we used doxycycline (2 µg/mL). The transcription of natural

MFA2pG

plasmid. This work was supported by the Israel Science Foun-

Yeast strains and plasmids

Yeast strains and plasmids are described in the Supplemental Material.

Determining mRNA levels and mRNA degradation profile

Two methods were used to inactivate transcription. In case of Tet-Off-

MFA2pG, we used doxycycline (2 µg/mL). The transcription of natural

Non-HS genes was blocked by shifting cells rapidly to 42°C. Half-lives

were determined as described previously (Lotan et al. 2005). For details

see the Supplemental Material.

Materials and methods

Yeasts strains and plasmids

Yeast strains and plasmids are described in the Supplemental Material.

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MFA2pG plasmid. This work was supported by the Israel Science Foundation founded by the Israel Academy of Sciences and Humanities, by the Rappaport Foundation, and by a grant from Paamei Tikva (Israel).

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Pol II controls transcription via a shuttling factor, Rpb4/7, which serves as a mediator

Involvement of a given factor in two machineries does not necessarily signify that they are mechanistically

linked. It is possible that, during evolution, Rpb4/7 has acquired more than one unrelated function. However, the data presented here contradict the “null” hypothesis that the dual functions of Rpb4/7 are unrelated. Our results demonstrate that the cytoplasmic roles of Rpb4/7 in mRNA decay can be executed only if Rpb4/7 is first assembled correctly with the Pol II core. Hence, Rpb4/7 roles in transcription and in mRNA decay are connected.

Rpb4p and Rpb7p bind mRNAs and function in their decay as a heterodimer. Whereas Rpb7p can function in the decay of many mRNAs independently of Rpb4p (Lotan et al. 2007), deletion of or mutation in RPB4 affects class-specific mRNAs (Lotan et al. 2005). We propose that only Rpb4p can recruit a class-specific factor that modulates the decay of this class of mRNAs, explaining rpb4A phenotype.

A model proposed based on this work and previous publications is depicted in Figure 5. This study provides an example for “conditional interaction” between two interacting partners that occurs only within specific molecular context. Such kind of interaction might be the basis for other cases of coupling between two processes.

Summarily, conditional interaction between Rpb4/7 and mRNAs allows Pol II to impact not only transcription but also the fate of its products after they left the nucleus. This is the first indication that Pol II can affect mRNA decay in the cytoplasm and the first evidence for a direct mechanistic coupling between transcription in the nucleus and the two major mRNA decay processes in the cytoplasm.
Pol II impacts mRNA decay


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