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RNA DECAY

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> the promoters of *SWI5* and *CLB2* might recruit factors co-transcriptionally to accompany transcripts into the cytoplasm

The stability of mRNA is often assumed to be dictated by a transcript's sequence features. Two new studies highlight that mRNA stability can be influenced by a memory of the promoter from which expression of the transcript was driven.

Spurred on by their previous discovery that components of the transcription apparatus mediate cytoplasmic mRNA degradation, Bregman *et al.* tested the effect of different promoters on mRNA stability by using reporter constructs to express the usually unstable *RPL30* transcript in *Saccharomyces cerevisiae*. After chemically blocking transcription, the kinetics of mRNA degradation were monitored using northern blotting. When the *RPL30* upstream activating sequence (UAS) was exchanged for the UAS of the *ACT1* gene, the stability of the same *RPL30* transcript was increased to a level that was similar to that of the endogenous *ACT1* transcript, indicating that the promoter sequence was a key determinant of stability.

To identify which sequences were mediating the effect, the authors dissected the UASs to make new constructs. They found that Rap1-binding sites (RapBSs) in the *RPL30* UAS were necessary for *RPL30* transcript instability and were sufficient to confer transcript instability when engineered into the *ACT1* UAS. Depletion of Rap1 caused transcripts to stabilize, particularly those from constructs with RapBSs in the UAS. Therefore, promoter-induced mRNA degradation may involve Rap1 binding to RapBSs and a co-transcriptional 'imprinting' of that transcript for cytoplasmic degradation, although mechanistic details are unclear.

In a related study, Trcek *et al.* developed an RNA-fluorescence *in situ* hybridization (RNA-FISH) technique to study mRNA stability at single-molecule resolution in unperturbed *S. cerevisiae*. They studied two transcripts, *SWI5* and *CLB2,* for which transcription and degradation are closely regulated during the cell cycle. Exchanging the 5′ and 3′ untranslated regions (UTRs) of the *SWI5* transcript with UTRs from constitutively expressed *ACT1* did not perturb the M phase-specific degradation of *SWI5*. Instead, only promoter swapping with *ACT1* converted unstable, cell-cycle-regulated *SWI5* and *CLB2* transcripts into stable, constitutively expressed transcripts and vice versa.

The authors reasoned that the promoters of *SWI5* and *CLB2* might recruit factors co-transcriptionally to accompany transcripts into the cytoplasm to regulate M phase-specific transcript degradation. Protein-interaction databases identified Dbf2 as a candidate for a role in this process, based on it being at the intersection of relevant pathways. Indeed, Dbf2 was bound to *SWI5* and *CLB2* mRNAs *in vivo*, and depletion of Dbf2 destabilized these mRNAs and delayed M phase progression. This indicates that Dbf2 accompanies and protects specific transcripts until appropriate cell cycle-regulated degradation signals are received.

It will be interesting to uncover precisely how the promoter-initiated events lead to the selective induction or prevention of cytoplasmic mRNA degradation. Finally, because other yeast promoters share sequences with *RPL30*, *SWI5* and *CLB2*, it will be intriguing to decipher how widespread and varied promoter-regulated mRNA stability is throughout yeast and metazoan genomes.

Darren J. Burgess, Assistant Editor,
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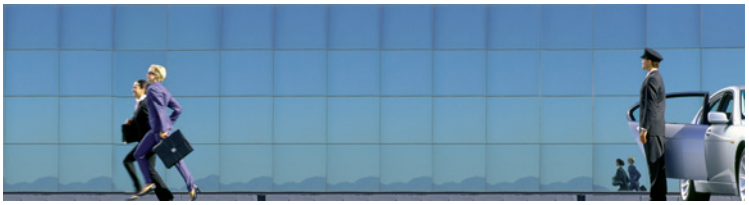

IMAGE 100

ORIGINAL RESEARCH PAPERS Bregman, A. *et al.* Promoter elements regulate cytoplasmic mRNA decay. *Cell* **147**, 1473–1483 (2011) | Trcek, T. *et al.* Single-molecule mRNA decay measurements reveal promoter-regulated mRNA stability in yeast. *Cell* **147**, 1484–1497 (2011)
FURTHER READING Belasco, J. G. All things must pass: contrasts and commonalities in eukaryotic and bacterial mRNA decay. *Nature Rev. Mol. Cell Biol.* **11**, 467–478 (2010)