The mRNA decay factor Pat1 mediates a global control of poly(A) tail length that is suppressed by a ribosome mutation

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Résumé

Eukaryotic mRNAs are key actors of gene expression; thus, their levels need to be finely tuned. Post-transcriptionally, levels of mRNAs are governed by their turnover in the cytoplasm. Critical steps of mRNA decay encompass deadenylation, decapping, and exonucleolytic mRNA body digestion, that constitutes the 5' -> 3' pathway.

The conserved decapping regulator Pat1 appears to impinge on all those processes. Despite evidence that Pat1 is a conserved and central actor of the 5' -> 3' mRNA decay pathway, some studies have reported that only a fraction of the transcriptome is impacted by its deletion. Moreover, Pat1 was described both as a translational repressor of oligoadenylated mRNAs and as a global translation initiation enhancer. Altogether, published data fail to provide definitive clues about the role of Pat1 in cellular mRNA control.

To elucidate Pat1's function, we performed multi-omic and genetic analyses of a pat1 mutant in the yeast Saccharomyces cerevisiae. Transcriptome and proteome analyses revealed that the expression of only a subset of genes is affected by Pat1's inactivation. In contrast, a FLEP-seq analysis, allowing the sizing of the poly(A)-tail of each transcript in the cells by Nanopore sequencing, revealed that the absence of Pat1 impacts the length of the poly(A)-tail at the transcriptome level. Unexpectedly, we have observed that the growth defects caused by Pat1's inactivation are partially suppressed by a mutation in a ribosomal protein. This suppressor mutation also partly rescued the abnormal poly(A)-tail length of pat1 cells. Moreover, we observed that polysome profiles are altered in the absence of Pat1 and further modulated by the suppressor.

Altogether, our analyses are consistent with the model where the activation of decapping, that becomes rate-limiting, is the primary defect in the absence of Pat1. Our study supports the conclusion that Pat1 is a general mRNA decay factor even if its absence results in transcript-specific changes in mRNA levels. Altered mRNA decay in Pat1 deficient cells, and consequent translational impairments, can both be partly rescued by altered ribosomes.

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Mots-Clés: mRNA decay, decapping, ribosome, translation, yeast