Abstract

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Mechanism of polyadenylation and its regulation by signaling pathways and phosphorylation

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Abstract

Star-PAP is a non-canonical poly(A) polymerase that selects mRNA targets for polyadenylation. Yet, genome-wide direct Star-PAP targets or the mechanism of specific mRNA recognition is still vague. Here, we employ HITS-CLIP to map the cellular Star-PAP binding landscape and the mechanism of global Star-PAP mRNA association. We show a transcriptome-wide association of Star-PAP that is diminished on Star-PAP depletion. Consistent with its role in the 3'-UTR processing, we observed a high association of Star-PAP at the 3'-UTR region. Strikingly, there is an enrichment of Star-PAP at the coding region exons (CDS) in 42% of target mRNAs. We demonstrate that Star-PAP binding de-stabilises these mRNAs indicating a new role of Star-PAP in mRNA metabolism. Comparison with earlier microarray data reveals that while UTR-associated transcripts are down-regulated, CDS-associated mRNAs are largely up-regulated on Star-PAP depletion. Strikingly, the knockdown of a Star-PAP coregulator RBM10 resulted in a global loss of Star-PAP association on target mRNAs. Consistently, RBM10 depletion compromises 3'-end processing of a set of Star-PAP target mRNAs, while regulating stability/turnover of a different set of mRNAs. Our results establish a global profile of Star-PAP mRNA association and a novel role of Star-PAP in the mRNA metabolism that requires RBM10-mRNA association in the cell.

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Biography

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