Review of: "Determinants of the temperature adaptation of mRNA degradation"

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The codon optimality is a major determinant of mRNA stability, mRNA degradation is strongly affected by translation, codons recognized by abundant tRNAs stabilize mRNAs, whereas codons recognized by scarce tRNAs destabilize mRNAs. Recent studies revealed a physical link between the Ccr4-Not complex and the ribosome provides mechanistic insight into the coupling of decoding efficiency with mRNA stability. However, little is known whether and how the mRNA degradation and translation are subject to temperature compensation, or sensitization.

This study aims to codon dependence of temperature adaptation in RNA degradation, and the authors reported that Upf1 is an extrinsic determinant of temperature adaptation of mRNA turnover. The authors developed the multiplexed gene control (MGC) to measure mRNA turnover with minimal methodological interference even under different environmental or stressful conditions including heat-stress conditions. The authors argue that other methods such as transcriptional inhibition and the cell wall digestion in the runoff experiments induce perturbations that may explain why the genetic run-on and the metabolic labeling study datasets do not correlate even under standard conditions.
With this method, the authors propose the existence of a neutral half-life above which mRNAs are stabilized by translation but below which they are destabilized. The authors investigated the temperature dependence of mRNA turnover. They analyzed of translation-dependence of mRNA degradation with no-AUG mRNAs and compared the molecular and kinetic properties of no-AUG mRNAs to their AUG counterparts to eliminate translation with minimal disruption of cell physiology. Interestingly, few specific codons are associated with the temperature compensation in mRNA degradation. The degradation of mRNAs enriched in Asn and Ser can be fully or partially temperature compensated but that of mRNAs enriched in Tyr codon sensitize in response to temperature. Ser-rich proteins are overrepresented in cell membrane-related components, they propose that the enrichment of mRNAs in these codons may promote temperature adaptation in specific cellular processes.

Upf1p is a central factor in NMD, and targets both nonsense and normal mRNAs to P-bodies, without promoting the degradation of normal mRNA. Similarly, Upf1 promotes the formation of aggresomes, which accumulate misfolded proteins during heat stress. The most interesting result in this study is that Upf1 mutant cells have increased heat sensitivity. Interestingly, the Upf1 has a stronger effect on mRNA turnover at both low (20˚C) and high (42˚C) temperatures than at 30˚C. Upf1 promotes the stability of no-AUG mRNAs after heat shock, indicating that Upf1 provides a mechanism for temperature compensation by acting directly on the mRNAs. The molecular mechanisms underlying

these observations are largely unknown and need more investigation. Upf1 recognizes highly structured mRNAs in mammalian cells, typically in the noncoding regions. These indicate that do not even require translational termination and provide a clue to uncover the nonclassical function of Upf1 beyond the quality control for aberrant mRNA.