Department of Biochemistry and Molecular Biophysics Seminar

Wednesday, April 22 at 4:00 p.m. in Ackert 120

Coffee and cookies at 3:45 p.m. in Chalmers 168

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eIF3g binding to GUCG boxes located in mRNA coding regions enhances translation of mild heat shock response genes

Translation initiation is the rate-limiting step of protein biosynthesis and an important target for the control of gene expression. Unregulated translation initiation is an important phenotype of malignantly transformed cells. The main player of our projects is translation initiation multifactor complex (MFC), a ~1 MDa complex made of eukaryotic initiation factors (eIF) 1, 2, 3, 5 and the initiator Met-tRNA. We dissect MFC functions by genetics using mutations in translation factors and their regulators. eIF3 is a multi-subunit complex that promotes ribosome recruitment and mRNA selection. Here, we show that its eIF3g subunit, along with the binding partner eIF3i, mediates transcript-specific translation under mild heat stress through direct RNA binding. First, SELEX experiments identified a short GUCG-centered motif preferentially recognized by eIF3g, suggesting a sequence-specific binding preference. Next, ribosome profiling of yeast eIF3i mutant revealed that mRNAs containing GUCG motifs in their 5' coding regions exhibit elevated ribosome occupancy in a manner dependent on eIF3g/eIF3i module. A subset of SELEX-identified motifs, collectively termed the GUCG box, was found enriched in the 5'-terminal coding region of the regulated mRNAs. Reporter assays confirmed that these 5'-terminal coding regions are sufficient to drive heat-induced translation. Mutational analyses and biolayer interferometry demonstrated that disruption of the GUCG motif impairs eIF3g binding and diminishes translational induction. Moreover, GUCG motifs are periodically distributed across coding sequences and enriched near start codons, consistent with their role in stabilizing initiating ribosomes. Overall, this study establishes the GUCG box as a *bona fide* eIF3g-binding motif and validates its functional importance *in vivo*. These findings provide new insight into how eIF3 mediates stress-adaptive translation through sequence-specific RNA recognition.