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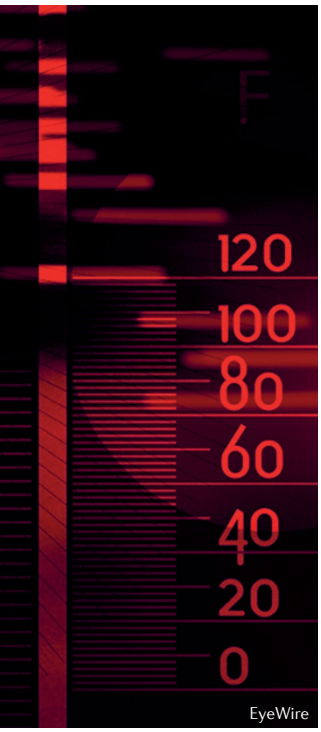
GENE REGULATION

RNAs feel the heat



Stable and transient RNA structures have various scaffolding and regulatory roles in post-transcriptional gene expression, although only a subset of these RNA motifs have been identified and characterized. A new study has mapped and analysed yeast RNA structure transcriptome-wide across a range of temperatures, finding key roles for temperature-sensitive RNA motifs.

Wan *et al*. extracted *Saccharomyces cerevisiae* RNA and subjected it to different temperatures (namely, 23, 30, 37, 55 and 75 °C) while treating with RNase V1, which selectively cleaves dsRNA (folded RNA). The cleavage events facilitated the subsequent cloning and high-throughput sequencing of these regions, allowing the authors to produce a single-nucleotide-resolution transcriptomic map of the melting temperatures at which dsRNA secondary structure unfolds into ssRNA. These temperature profiles were consistent with spectroscopically determined melting temperatures of 12 selected RNAs and were superior to computational estimates of melting temperatures.

The authors then mined the data for biologically relevant features. They found that non-coding RNAs (ncRNAs) were characterized by higher melting temperatures than for mRNAs, which is consistent with stable, structural roles for various ncRNAs, such as ribosomal RNAs.

For mRNAs, the lowest melting temperatures were found in the 5′ untranslated region (UTR) and at the translation start site, probably reflecting the need for ribosomal access during translation initiation. By contrast, peaks of higher melting temperatures were found flanking the translation stop site, although the reason for this remains unclear. Interestingly, stable secondary structure motifs that remained folded at 75 °C were commonly found in 3′ UTRs. Some of these are known intracellular trafficking motifs, indicating that similar functions may exist among the other, currently uncharacterized, motifs.

Wan *et al.* then showed that the set of transcripts that have an unfolding event between 30 °C and 37 °C substantially overlap with transcripts that are known to be degraded during the heat-shock response in yeast, suggesting a role for these transcripts in sensing heat stress. The heat-shock-induced degradations were blocked in yeast that were deficient for exosome function, thus implicating this exonuclease complex in the reading and degradation of unfolded transcripts.

It will be interesting to see how extensively RNA folding transitions serve as stress sensors and gene expression regulators in various organisms.

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ORIGINAL RESEARCH PAPER Wan, Y. *et al.* Genome-wide measurement of RNA folding energies. *Mol. Cell* 13 Sep 2012 (doi:10.1016/j.molcel.2012.08.008)