GENE REGULATION

A multilayered take on gene expression

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URLs

By making quantitative, global measurements at different stages along the road to protein production, a recent study has provided new insights into how gene regulatory mechanisms in eukaryotic cells are coordinated at multiple levels.

Lackner and colleagues used genome-wide assays for levels of gene-expression intermediates in *Schizosaccharomyces pombe* yeast cells under a set of standardized conditions. For large numbers of mRNAs, transcriptional efficiency was determined by looking at RNA polymerase II occupancy, and

steady-state transcript levels were assessed by microarray analysis. The authors also looked at the distribution of poly(A) tail lengths and mRNA half-lives to assess the effects of these features on gene expression. At the level of translation, the association of ribosomes with mRNAs was investigated by fractionating polysomes and hybridizing the mRNAs in each fraction to a microarray, which also enabled estimates of translational efficiency to be made.

To reveal global relationships between regulation at different levels, the different sets of data were compared with each other and with information on ORF length, start-codon context and protein levels. By doing so, the authors uncovered some intriguing features of the gene regulatory programme in *S. pombe*. For example, it turns out that shorter and more abundant mRNAs are translated more efficiently, suggesting that translation is coordinated with both mRNA length and abundance. However, this coordination seems to reflect two distinct mechanisms, as mRNA levels and lengths themselves show no correlation with each other.

The reasons for the link between mRNA length and translational

efficiency are unclear. However, transcriptional efficiency and mRNA stability were both found to be coordinated with translation, suggesting that they both contribute to the link between mRNA levels and translational efficiency. Again, distinct mechanisms of coordination seem to be at play, as the efficiency of transcription was not correlated with transcript half-life. The authors also uncovered other links — for example, between poly(A) tail length and transcriptional efficiency — which are unexpected and will require further investigation to unravel.

Altogether, the global comparisons made in this study reveal a complex, coordinated network of controls on eukaryotic gene expression. The authors have made their data freely available (see the link below), as a basis for further systems-level analyses of gene-expression programmes.

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ORIGINAL RESEARCH PAPER

Lackner, D. H. *et al.* A network of multiple regulatory layers shapes gene expression in fission yeast. *Mol. Cell* **26**, 145–155 (2007)

WEB SITE

The Wellcome Trust Sanger Institute Fission Yeast Functional Genomics web site: http://www.sanger.ac.uk/PostGenomics/S_pombe