GENE EXPRESSION

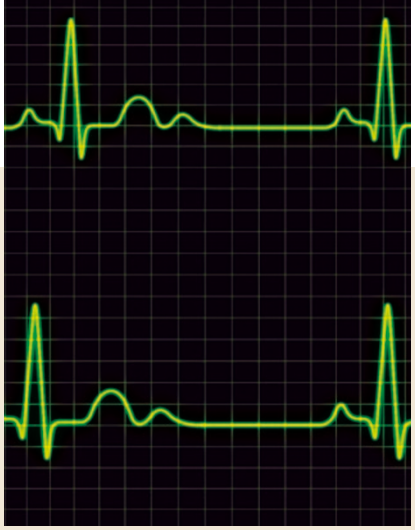
The restless resting phase of the cell cycle

New work from Holstege and colleagues reveals that 'resting phase' is something of a misnomer. Their results in *Saccharomyces cerevisiae* show that many genes are actively transcribed during this time and that, contrary to the current view, RNA polymerase II remains associated with DNA, poised for transcription on exit from the resting phase.

The authors used nutrient-starved *S. cerevisiae* as a model for the resting phase of the eukaryotic cell cycle. Over a period of 9 days, they carried out poly(A) RNA dot-blot hybridization and microarray analysis to look at gene expression during the stationary phase — the yeast equivalent of resting phase — in a single experiment. Previous work indicated that a general shutdown of transcription occurs at this stage of the cell cycle. Unexpectedly, the authors saw that although most transcription does stop, several transcripts become upregulated specifically during the stationary phase.

The dynamics of transcription in the stationary phase is not simple; for example, the authors saw three peaks of RNA accumulation. They also showed that exit from the stationary phase is followed by a strikingly rapid burst of transcription. Prompted by this observation, and the fact that even in the stationary phase genes can become activated in response to environmental changes, the authors used genome-wide chromatin immunoprecipitation to show that RNA polymerase II predominantly resides in intergenic regions, upstream of open reading frames. This contrasts with the current view that the polymerase needs to be recruited to DNA on activation.

Understanding the resting phase, and how a cell might switch from this state to undergo cell division, has important implications, for example, in cancer and ageing. This work prompts us to re-examine our thinking about the so-called quiescent phase of the cell cycle and about the regulation of gene transcription. Importantly, it also paves the way for future, more detailed studies of what really happens in the nucleus during what is the longest stage of a cell's life.



Magdalena Skipper

References and links

ORIGINAL RESEARCH PAPER Radonjic, M. & Andrau, J.-C. *et al.* Genome-wide analyses reveal RNA polymerase II located upstream of genes poised for rapid response upon *S. cerevisiae* stationary phase exit. *Mol. Cell* **18**, 171–183 (2005)

WEB SITE

University Medical Centre Utrecht — Genomics Lab: http://www.genomics.med.uu.nl/home/index.php

METAGENOMICS

Compare and contrast

A recent study published in *Science* has established an exciting new direction in environmental genomics — comparative metagenomic analysis.

For many years, environmental genomic studies were hindered by the fact that most environmental microorganisms cannot be cultured in the laboratory. This hurdle began to be overcome with the development of cultivation-independent techniques to characterize these organisms and, in the past 2–3 years, the development of metagenomics — the analysis of microbial community genome sequence data recovered directly from the environment — has provided the field with a new impetus. In this latest study, Susannah Tringe, Christian von Mering and colleagues set out to characterize several disparate microbial communities present in three deep-sea whale carcasses and an agricultural soil sample.

One of the key issues in metagenomics is obtaining ecologically and metabolically relevant data from the complex environments analysed. For the two niches examined in this work, it was estimated that for soil, $2–5 \times 10^9$ bp of sequence would be required to obtain a draft sequence of the most abundant genome, and for the whale carcasses, an estimated 100–700 Mb would be required. Given this obstacle to obtaining whole-genome sequences, Tringe *et al.* proceeded using a 'gene-centric', comparative approach. The aim is to identify a subset of genes that are present in a microbial habitat and use these to understand the genomic diversity between environmental samples, without the need to have a full genome sequence or even know which specific species are being analysed.

The authors generated shotgun libraries derived from each sample, then sequenced and annotated the genes present on the small DNA fragments. Comparing these so-called environmental genome tags (EGTs) with published metagenomic data obtained from an acid-mine drainage site and the Sargasso Sea demonstrated that the predicted protein complement in each niche differed in ways that would be expected given the different nutrients present. Gene-content analysis of pooled samples from the different environments provided evidence of environmental specialization — for example, genes that convert light into energy were found in the marine samples but not in the soil communities. The relative abundance of particular functional gene clusters (operons) also provided evidence for specialization: soil samples were enriched in genes required for potassium transport, which reflects the enrichment of this ion in this habitat.

The results of this study indicate that it might be possible to use sequence data in the form of EGTs to generate 'environmental fingerprints' that could be used to glean details of different environmental niches and provide a greater understanding of the interactions between microbial communities and their environments.

Sheilagh Molloy, Associate Editor,
Nature Reviews Microbiology

References and links

ORIGINAL RESEARCH PAPER Tringe, S. G. *et al.* Comparative metagenomics of microbial communities. *Science* **308**, 554–557 (2005)

FURTHER READING Tyson, G. W. *et al.* Community structure and metabolism through reconstruction of microbial genomes from the environment. *Nature* **428**, 37–43 (2004) | Venter, J. C. *et al.* Environmental genome shotgun sequencing of the Sargasso Sea. *Science* **304**, 66–74 (2004)