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GENE EXPRESSION

Dynamic omics responses

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Quantitative 'omics' tools are providing unprecedented global insights into gene expression. A study that characterized the transcriptome and proteome of cycling and quiescent fission yeast has now provided insight into poorly understood aspects of mRNA and protein dynamics.

Marguerat *et al.* used high-throughput RNA sequencing (RNA-seq) and mass spectrometry to characterize absolute molecule numbers across the transcriptome and proteome. In cycling *Schizosaccharomyces pombe* cells, most genes were expressed at both the mRNA and protein levels, but most RNAs were found at a low abundance (with a median of 2.4 mRNA copies per cell). Importantly, the authors found that low-abundance mRNAs can still be functionally relevant, as the vast majority of mRNAs present at ≥1 copy per cell were translated into detectable proteins. However, such a low abundance might make the presence or absence of these RNAs among cells highly susceptible to stochastic fluctuations in expression. Proteins were more abundant: a median of 3,919 copies of each protein was present per cell.

Globally, the levels of mRNAs and their corresponding proteins showed limited correlation ($R^2 = 0.55$ in cycling cells), indicating that although transcriptomic analyses can broadly reflect the resultant proteomes, translation provides an important layer of amplification and regulation.

However, for processes involving protein–RNA interactions, it seems that protein and RNA levels are coordinately regulated. For example, the number of molecules of ribosomal RNAs and ribosomal proteins was similar, as was the number of spliceosomal proteins and intron-containing genes.

The authors found intriguing differences in how the transcriptome and proteome changed in the quiescent state. mRNAs were globally downregulated but without extensive changes in the relative abundance among mRNAs. By contrast, the quiescent proteome retained a similar size but exhibited substantial remodelling. For example, proteins for mitochondrial respiration were downregulated and proteins for stress and nutrient responses were upregulated, thus reflecting the new metabolic and signalling needs of the quiescent cells.

To investigate this apparent discrepancy, the authors carried out gene expression analyses over a time course during quiescence, concluding that the observed global repression of mRNAs is preceded by a transient induction of stress-responsive mRNAs that accounts for the observed effects on the proteome.

This study thus highlights the intricate and dynamic interplay between the transcriptome and proteome to control gene expression.

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ORIGINAL RESEARCH PAPER Marguerat, S. *et al.* Quantitative analysis of fission yeast transcriptomes and proteomes in proliferating and quiescent cells. *Cell* **151**, 671–683 (2012)