Genome-wide messenger RNA stability in eukaryotes: Yielding hard facts with microarrays

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Abstract:

Messenger RNA stability is a major determinant of the relative transcript levels and varies widely among different genes and species. Unlike transcriptional regulation, mRNA stability and turnover has only recently come into closer focus as a determining factor in gene regulation.

I will outline and exemplify a general strategy for using microarrays to study how genetic perturbations affect overall patterns of mRNA stability and decay. Experimentally, the system involves comparing relative transcript abundances between unperturbed and perturbed conditions over a time course, following chemical inhibition of gene transcription. Computationally, it identifies biological categories of genes whose transcript stabilities are most affected by evaluating their expression profiles on genomewide databases using nonparametric statistics.

The mRNA turnover major pathways are preserved among eukaryotes and can be studied conveniently in the model organism Saccharomyces cerevisiae (baker's yeast). We examined the effects on relative transcript stabilities of mutations in the deadenylases Ccr4p, Pan2p, and in the mRNA-binding proteins Pub1p and Puf4p. Our results suggest that Ccr4p preferentially degrades transcripts encoding ribosomal proteins and other ribosome biogenesis factors and, surprisingly, we show that it is a mediator of a large portion of the yeast stress response to heat shock. The extension of this system to the study of human mRNA stability and further methods to infer gene functions from microarray expression data in statistically rigorous and biologically informative ways will be outlined.