Comparative Dynamic Transcriptome Analysis (cDTA) reveals mutual feedback between mRNA synthesis and degradation

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We present comparative Dynamic Transcriptome Analysis (cDTA), a technique for the quantitative monitoring of absolute cellular mRNA synthesis and decay rates on a genome-wide scale. cDTA is based on non-perturbing metabolic RNA labeling in mutant and wild-type *Saccharomyces cerevisiae* (*Sc*) cells, and the use of fission yeast (*Sp*) cells as an internal normalization standard. cDTA reveals that *Sc* and *Sp* transcripts encoding orthologous proteins have similar synthesis rates, whereas decay rates are five-fold lower in Sp, resulting in similar mRNA concentrations despite the larger Sp cell volume. cDTA of Sc mutants reveals that a eukaryote can buffer mRNA levels. *Sc* cells expressing a well-defined Pol II point mutant that elongates mRNA slowly *in vitro* showed that mRNA elongation is a critical determinant for cellular mRNA synthesis *in vivo*, and that cells compensate for low synthesis rates by lowering their decay rates. Vice versa, impairment of mRNA degradation by deleting subunits of the Ccr4-Not deadenylase results in decreased decay rates as expected, but also in decreased synthesis rates. According to kinetic modeling of our cDTA data, the factors involved in the feedback loop include a transcription inhibitor and a degradation activator, or a single factor with both activities.