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TRANSCRIPTION

Interference from near and far

Various mechanisms exist by which transcripts can regulate the expression of other transcripts, such as through RNA interference (RNAi) in *trans* or through local effects in *cis* when transcripts are expressed from proximal or overlapping loci. Although rare in mammals, convergent gene pairs — sense–antisense transcript pairs that have overlapping 3′ untranslated regions (3′ UTRs) — are common in many species, including yeast, flies and nematodes. In *Saccharomyces cerevisiae*, mutual repression between convergent gene pairs is typically attributed to collisions between the converging transcriptional machineries, but a new study identifies an additional repressive mechanism involving 3′ UTRs acting in *trans*.

Wang *et al.* mined genome and transcriptome data from *S. cerevisiae*; they found that ~20% of genes were arranged as convergent gene pairs and that the paired genes had negatively

correlated expression patterns, which indicates mutual repression.

The authors then carried out a more detailed functional analysis of four of the gene pairs. Mutual repression was suggested in various settings; for example, when one of the genes in a pair was known to be regulated by nutrient stress or by the cell cycle phase, its paired gene showed opposite changes in expression. Crucially, moving a gene to be ectopically overexpressed from a separate genomic location still resulted in repression of its paired gene at the original locus. This phenomenon occurred even when the 3′ UTR alone was ectopically overexpressed, thus repression can occur in *trans* through a mechanism involving 3′ UTRs that is independent of transcriptional collisions.

Further mechanistic characterization revealed that the repression occurs transcriptionally, rather than

post-transcriptionally, as levels of both nascent and mature transcripts were repressed. As various RNAi components are absent in *S. cerevisiae*, the repression is unlikely to be mediated through small RNAs derived from the transcripts, but mechanisms involving the hybridization of 3′ UTRs to the paired gene transcripts or genomic loci to physically hinder transcription remain possible.

It will be interesting to dissect the relative importance of this 3′ UTR-mediated mechanism versus transcriptional collisions for repression between convergent gene pairs that are expressed from endogenous loci at physiological levels. Furthermore, it is possible that 3′ UTR complementarity might point to long-range regulatory relationships between genes that are not currently known to interact.

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ORIGINAL RESEARCH PAPER Wang, L. *et al.* 3′ untranslated regions mediate transcriptional interference between convergent genes both locally and ectopically in *Saccharomyces cerevisiae*. *PLoS Genet.* **10**, e1004021 (2014)