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IN BRIEF

SYSTEMS BIOLOGY

Metabolically constrained regulatory networks

Cellular networks interact to result in the organismal phenotype, yet these networks have so far been difficult to integrate. Chandrasekaran and Price have developed an approach — Gene Expression and Metabolism Integrated for Network Interference (GEMINI) — that is able to constrain predicted gene regulatory networks on the basis of metabolic data in yeast. They used GEMINI to build a network in *Saccharomyces cerevisiae* and used it to predict phenotypes such as growth effects after transcription factor knockout in new conditions. This will be a valuable tool in synthetic biology.

ORIGINAL RESEARCH PAPER Chandrasekaran, S. & Price, N. D. Metabolic constraint-based refinement of transcriptional regulatory networks. *PLoS Genet.* **9**, e1003370 (2013)

EPIGENETICS

Mapping occluded genes

Cell fusion can be used to define a class of genes termed occluded genes, the expression of which remains silent despite the presence of *trans*-activating factors. By fusing mouse fibroblasts with a dozen of different rat cell types, the authors of this study were able to map occluded genes and characterize their epigenetic marks. They find that these genes are highly prevalent in somatic cells and are enriched for developmental regulators, which indicates a role for occluded genes in cellular identity.

ORIGINAL RESEARCH PAPER Looney T. J. *et al.* Systematic mapping of occluded genes by cell fusion reveals prevalence and stability of *cis*-mediated silencing in somatic cells. *Genome Res.* http://dx.doi.org/10.1101/gr.143891.112 (2013)

MOLECULAR EVOLUTION

Evolving demands on tRNAs

In this study, the authors investigate how the translational machinery adapts to genetic or environmental changes. They deleted a $tRNA^{Arg}$ gene in a *Saccharomyces cerevisiae* strain and found that when the strain evolved, the gene of a more commonly used tRNA evolved to match the missing anticodon, thus restoring a wild-type rate of cell growth. Further experiments showed that the evolved strains maintained some tRNAs at low levels, so that translation rate is optimal for proteins that are difficult to fold. Furthermore, analyses in various species indicate that the codon switching mechanism is a common form of molecular evolution across the tree of life.

ORIGINAL RESEARCH PAPER. Yona, A. H. *et al.* tRNA genes rapidly change in evolution to meet novel translational demands. *eLife* **2**, e01339 (2013)

SMALL RNAS

Insights into siRNA-triggered heterochromatin

Endogenous small interfering RNAs (siRNAs) contribute to heterochromatin formation at repetitive DNA loci, but the control mechanisms that prevent spurious silencing of additional loci are unclear. Using *Schizosaccharomyces pombe*, Yu *et al.* identified pervasive bidirectional transcription across various heterochromatic and euchromatic loci that can potentially generate double-stranded RNAs as precursors of siRNAs. However, the heterochromatic loci were selectively colocalized with Dicer 1 at the nuclear periphery to favour the processing of heterochromatic transcripts into siRNAs. Furthermore, signals in the 3′ untranslated regions of euchromatic genes were found to inhibit siRNA-mediated heterochromatin formation.

ORIGINAL RESEARCH PAPER Yu, R. *et al.* Determinants of heterochromatic siRNA biogenesis and function. *Mol. Cell* http://dx.doi.org/10.1016/j.molcel.2013.11.014 (2013)