These results show that the differences in transcript levels between the small- and large-fruit alleles of *fw2.2* are both quantitative (with the small-fruit allele being more abundantly expressed) and qualitative (as evident from the difference in their expression timing). Importantly, these findings provide empirical evidence that heterochronic regulatory changes in gene expression can bring about phenotypic, and probably evolutionary, change in plants. But how *fw2.2* actually modulates cell division remains unknown.

Jane Alfred

References and links

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FURTHER READING Dekkers, J. C. M. & Hospital, F. The use of molecular genetics in the improvement of agricultural populations. *Nature Rev. Genet.* **3**, 22–32 (2002)

WEB SITE

Steven Tanksley's laboratory: http://www.plbr.cornell.edu/PBBweb/Tanksley.html

feeding, lack of OSM-3 blocks antagonistic signals that normally inhibit this behaviour. Indeed, removing *osm-3* function restores social feeding in *odr-4* or *ocr-2* mutants. So, as with the body cavity neurons, nociceptive neurons might be involved in a system of antagonism between signals that promote and suppress aggregation.

As these neurons are required for responses to stressful or aversive stimuli, de Bono *et al.* propose that aggregation is a response to an aversive stimulus that is produced by bacteria. But what the aversive stimulus that promotes aggregation is and how the different control systems interact to regulate when social feeding occurs remains unknown.

Rachel Jones, Senior Editor,
Nature Reviews Neuroscience

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FUNCTIONAL GENOMICS

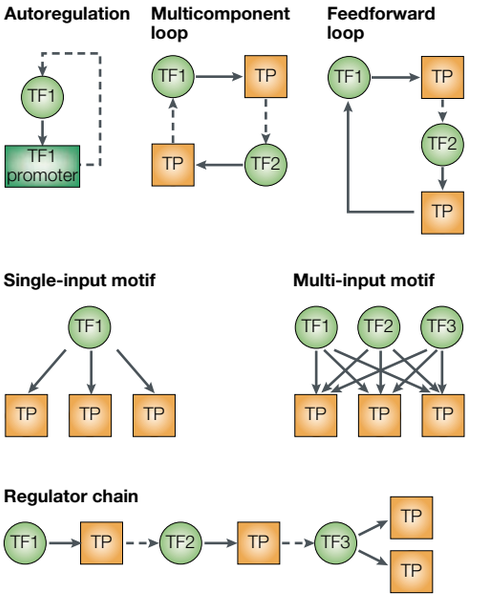
The importance of networking

For many, defining a single pathway was once the ultimate goal. No longer satisfied with understanding individual pathways, researchers now seek to understand how they interact with each other to bring about changes in living organisms. Lee *et al.* now present their *tour de force* approach to mapping transcriptional regulatory networks in the budding yeast. By using genome-wide location analysis (GWLA), they define regulatory motifs, which when combined with global gene expression data allow them to construct a complete regulatory network.

Driven by the desire to know how gene expression is regulated on a global scale, the authors reasoned that they would ultimately need to understand how transcription is regulated. To this end, they used GWLA — a method they previously developed and that allows them to find out which transcription factors (TFs) bind to which promoters. GWLA involves crosslinking TFs that are bound to their target promoters (TPs), recovering the DNA and identifying the TPs by using genomic DNA as a reference. The analysis was done under three growth conditions for 106 out of 141 TFs that could be found in the Yeast Proteome Database.

Lee *et al.* found that many yeast promoters were bound by more than two TFs — a feature that had been thought to be limited to higher eukaryotes. The 4,000 or so interactions fell into six basic regulatory motifs, which the authors consider to be building blocks of larger regulatory networks. They classify these networks as autoregulation, multicomponent loops, feedforward loops, single-input motifs, multi-input motifs and regulator chains (see figure). For example, autoregulation is thought to be important in quick responses to the changing environment, and therefore it is associated with a selective growth advantage. The authors show that 10% of yeast TFs autoregulate; by contrast, in prokaryotes, this figure is thought to be between 52% and 74%. The structure of the feedforward loop suggests that it might be important in response to a sustained rather than a transient signal. It might also provide a way for temporal control.

The authors wondered whether they could use these building blocks to construct a network of interactions. They decided to build a network for regulators involved in the yeast cell cycle because the large amount of information available for this process would make their theoretical model easily testable. To construct their network, the authors used an algorithm that combines the GWLA data with gene expression data. As core regulators that share the same spatial and temporal expression patterns were defined, more regulators with the same expression pattern were added, and so the network grew.



Modified with permission from Lee, T. I. *et al*. *Science* **298**, 799–804 © (2002) American Association for the Advancement of Science.

Astonishingly, the algorithm — which was automated and required no previous knowledge of biology — assigned all the regulators to the correct cell-cycle stages. Moreover, those regulators that had been poorly characterized were now placed in a particular position of the network, which can now be tested experimentally.

All of the interactions are testable, and the approach is applicable to any organism for which good genomic and expression data are available. One important observation that emerges from this work is that the control of cellular processes involves transcriptional regulation of other regulators. This has important implications for mutation analysis — if expression profiling is used to characterize a mutation, it is as likely to reveal direct targets of a mutated regulator as it is to reveal the effects of network disruption.

Magdalena Skipper

References and links

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