GENE EXPRESSION

Let's do the twist

Specific gene-expression patterns define morphogenetic movements during development. Emmanuel Farge now reports, in *Current Biology*, that the reverse is also true — gene expression can be modulated by the mechanical strains of morphogenetic movements.

To study the effects of mechanical stress on gene regulation, Farge used micromanipulation to induce a unilateral 10% deformation for 5 minutes in the early *Drosophila* embryo and then tested the expression of early patterning genes. Expression of the dorsal–ventral gene *Twist* was induced around the dorsal–ventral axis, which resulted in the ventralization of the embryo.

Farge then showed that mechanical deformation caused the translocation of Armadillo to the nucleus. This dual-function protein — a transcription factor and a component of the cadherin adhesion complex at the plasma membrane — was a possible candidate for mediating *Twist* expression. Indeed, the expression of a dominant-negative form of dTCF/Pangolin (a co-factor that is necessary for Armadillo-dependent transcription) prevented expression of *Twist* in response to the shape change. So, Armadillo somehow mediates the mechanical induction of *Twist* expression.

When cells of the stomodeal primordium are compressed during the first phase of germ-band extension, which leads to anterior-gut formation, *Twist* expression increases eightfold. To test whether this effect is the result of mechanical strain caused by germ-band extension, Farge analysed mutant embryos that did not undergo this morphogenetic process. The level of *Twist* expression in the mutants was similar to that before germ-band extension, but manual mechanical compression could rescue *Twist* expression in stomodeal cells.

Mutant embryos also had no Armadillo in the nucleus, but, again, this could be rescued by applying mechanical pressure to the stomodeal cells. So, the expression of *Twist* depends on the mechanically induced nuclear translocation of Armadillo.

The dorsal epithelium is normally subjected to pressure that is exerted by the extending germ band at the posterior pole and is transmitted to the anterior pole, thereby compressing the stomodeal cells against the invaginations of the mesoderm and foregut. Photoablation of the dorsal epithelium mechanically disconnects this tissue from the posterior pole

FUNCTIONAL GENOMICS

Total interconnectedness of everything

The advent of genome sequencing has generated a shift in the way in which researchers approach problems in biology — instead of analysing one gene at a time, studies are increasingly focused on whole pathways or gene networks. Joshua Stuart, Eran Segal and their colleagues bring us a prime example — by using microarray data from humans, flies, worms and yeast, they identify clusters of functionally related genes that have been conserved in evolution. The resulting gene co-expression network has uncovered new functional and evolutionary relationships.

Genes that have related functions often share expression patterns, so microarray data can be used to investigate functional relationships between genes. Stuart, Segal and colleagues constructed a gene co-expression network using pre-existing microarray data from four species; the assumption being that evolutionarily conserved co-expression is an indicator of its functional significance.

To make the network, the authors first associated genes from one organism with their orthologues from the others, using all-against-all BLAST. Based on the highest BLAST scores, they identified 'meta-genes' that corresponded to sets of orthologues from the organisms used in the study. They came up with 6,307 meta-genes that correspond to 6,591 human genes, 5,180 worm genes and so on.

The next task was to identify pairs of meta-genes that were co-expressed in many organisms across different experimental conditions. The authors looked for correlation of expression in data from 3,182 DNA microarray experiments from humans, worms, flies and yeast. Using a probabilistic model, the authors selected interactions that did not occur by chance alone and combined them into a network of meta-gene co-expression.

So, what does this network of 3,416 meta-genes and 22,163 interactions tell us about biology? When the network is viewed as a three-dimensional map, the highly interconnected areas appear as peaks, which correspond to clusters of specific gene–gene interactions. As the authors show, most of the components of each peak are involved in similar biological processes. For example, peak 5 is made up of interactions between cell-cycle genes. Importantly, out of the 241 meta-genes in this peak, 131 have no known function. Thanks to the network, their candidate role in the cell cycle can now be tested.

The network can also tell us about the evolution and conservation of genetic interactions. For example, peak 1, which is enriched in meta-genes that are involved in signalling pathways, is enriched in animal-specific genes and has a lower degree of evolutionary conservation.

So, the co-expression network turns out to be an extremely useful tool with which to explore the functional relationships between already characterized genes, and also to implicate new players in given biological processes and inform us about the evolution of the underlying molecular complexity. No doubt we will hear from these authors with more interesting results of further analysis of this network.

Magdalena Skipper

References and links

ORIGINAL RESEARCH PAPER Stuart, J. M., Segal, E. *et al.* A gene coexpression network for global discovery of conserved genetic modules. *Science* 21 August 2003 (10.1126/science.1087447)

WEB SITE

Supplementary data:
http://cmgm.stanford.edu/~kimlab/multiplespecies