DEVELOPMENTAL GENETICS

How not to go for the jugular

We used to think that differences in blood flow determined whether a blood vessel developed as an artery or a vein, but recently it became clear that this decision is genetically predetermined through vascular endothelial growth factor (Vegf) signalling. Using transgenic zebrafish, Nathan Lawson and colleagues have now identified *plcg1* as a key gene, downstream of Vegf, which directs endothelial cells along the arterial developmental pathway.

In a classic forward-genetic approach, Lawson *et al.* screened a zebrafish line, which had fluorescently labelled blood vessels, for developing embryos that lacked blood vessels between the somites — blocks of cells that give rise to the backbone and body muscle. In this way they identified a mutant (*y10*) with defects in the development of arteries but not veins, and reduced expression of artery-specific genes in the embryonic dorsal aorta.

The *y10* mutant mimicked mouse and zebrafish Vegf-knockout phenotypes but mapped to a location distinct from that of *vegf* or its receptor. Segregation analysis of mutant and wild-type embryos allowed Lawson *et al.* to place it in a region in which several zebrafish ESTs similar to rat *Plcg1* also mapped.

Linkage and expression analyses of *plcg1* provided strong indirect evidence that it was a mutant in this gene that led to the *y10* phenotype. Subsequent sequence analysis of *plcg1* in mutant and and wild-type embryos identified a G-to-A transition that eliminated a splice acceptor site as the putative causal mutation.

The authors then used an antisense morpholino to the intron–exon junction to mimic the effects of the putative mutation. The reduced number of segmental vessel sprouts in embryos that were injected with this morpholino corresponded to the *y10* phenotype. The clincher came when they showed that injection of wild-type *plcg1* mRNA could rescue *y10* mutants, which nailed down the zebrafish homologue of *PLCG1* as the gene involved.

However, the most significant aspect of this work is that by showing that the *y10* mutant phenotype could not be rescued by injecting wild-type *vegf* it provides the first definitive *in vivo* evidence that plcg1 acts downstream of Vegf. Moreover, because mice that lack *Plcg1* also have severe defects in blood-vessel formation it seems that this developmental pathway might be conserved throughout vertebrates.

Given this apparent conservation, the zebrafish, with its unique developmental characteristics, a genome sequence on the way and a growing arsenal of genetic tools, might just be the future model of choice for dissecting blood-vessel development and the diseases that are associated with it.

Nick Campbell

References and links

ORIGINAL RESEARCH PAPER Lawson, N. *et al.* *phospholipase C γ-1* is required downstream of *vascular endothelial growth factor* during arterial development. *Genes Dev.* **17**, 1346–1351 (2003)

FURTHER READING Lawson, N. & Weinstein, B. Arteries and veins: making a difference with zebrafish. *Nature Rev. Genet.* **3**, 674–682 (2002)

WEB SITES

Brant Weinstein's laboratory:
http://dir.nichd.nih.gov/lmg/uvo/WEINSLAB.html

Nathan Lawson's laboratory:
http://www.umassmed.edu/pgfe/faculty/lawson.cfm?start=0

IN BRIEF

GM ORGANISMS

Fitness effects of transgenic disease resistance in sunflowers.

Burke, J. M. & Reiseberg, L. H. *Science* **300**, 1250 (2003)

Could transgenes that escape from GM crops into wild populations confer a fitness advantage and spread quickly? Burke and Reiseberg crossed the transgene that confers resistance to white mold into wild sunflowers, to simulate the early stage of gene escape. The transgene provided protection against infection, but had no effect on seed output after inoculation with white mold. So, this particular transgene would diffuse neutrally after its escape.

TECHNOLOGY

Chips and solution detection of DNA hybridization using a luminescent zwitterionic polythiophene derivative.

Nilsson, K. P. R. & Inganäs, O. *Nature Mater.* **2**, 419–424 (2003)

Most methods for mutation detection rely on labelling of a nucleic acid or probe. This new technique removes the need for labelling, by detecting SNPs through the fluorescent signal that is produced when they interact with an electronic polymer. Unlike similar methods, this approach is still effective when the polymer is deposited and patterned on a surface, making it ideal for the development of high-throughput SNP detection microarrays.

GENOMICS

The male-specific region of the human Y chromosome is a mosaic of discrete sequence classes.

Skaletsky, H. *et al. Nature* **423**, 825–837 (2003)

Abundant gene conversion between palindromes in human and ape Y chromosomes.

Rozen, S. *et al. Nature* **423**, 873–876 (2003)

The full sequence of the male-specific region of the Y chromosome (MSY) has revealed an unanticipated number and diversity of genes. MSY euchromatic sequences are a mosaic of three classes: those closely related to the X chromosome, remnants of the autosomes from which the X and Y evolved and gene-rich groups of repeated sequences. The last class has eight large palindromes that contain many testis-specific genes and have arms with a minimum of 99.94% sequence identity. Recurrent gene conversion in the Y is responsible for maintaining intra-palindromic similarity.

EVOLUTION

Stress-induced mutagenesis in bacteria.

Bjedov, I. *et al. Science* **300**, 1404–1409 (2003)

Using conditions that mimic the stresses encountered by bacteria in natural environments, this study shows that mutation rates increased in most of the 787 natural isolates of ageing *E. coli* colonies studied. It is still unclear what mechanisms are responsible for stress-induced mutations, but, regardless, they are likely to have an important influence on adaptive evolution in bacteria.