TECHNOLOGY

Targeting the worm

Caenorhabditis elegans — affectionately known as 'the worm' — has just joined the list of model organisms in which targeted gene disruption is possible; all this, thanks to the work of Barrett and colleagues, who in the latest issue of *Nature Genetics* report a method based on transposon-mediated gene conversion.

Homologous-recombination-based gene targeting, so successful in the mouse, has not been generally possible in the worm owing to the low frequency of homologous recombination. Until now, researchers who wanted to generate mutations in their gene of interest had to rely on transposon insertions or on chemical or radiation-based mutagenesis. In both cases, the desired mutation is isolated in a PCR screen.

Frustrated by their lack of success with the transposon-insertion method, these authors investigated the possibility of using gene conversion to engineer a deletion in a gene of interest. Knowing that transposon excision generates dsDNA breaks, and that this lesion could be repaired in a template-directed manner by gene conversion, the authors set to work. That gene conversion works in the worm had already been shown, but the process was never adapted to a reverse genetic approach owing to the low frequency of this event. Barrett *et al.* found a way around this problem using a 'mutator' strain, in which transposons are highly active, therefore generating many dsDNA breaks. Into this strain, they introduced a plasmid that carried a transgene with a deletion in their gene of choice, in a genomic context. To facilitate homology search during gene conversion, one end of the deletion was placed near the site of transposon insertion. PCR testing with specifically designed primers identified worms in which the deletion made it to the chromosomal location.

Barrett *et al.* also used the same approach to make an insertion-replacement allele — in this case, the introduced transgene consisted of a translational fusion of GFP sequences and a coding sequence of a gene of interest. Although this replacement was also detected by PCR, the authors point out that, depending on the construct, the screening here could be done visually instead.

So the authors have created a truly valuable tool — especially given their frequency of 1–3 conversions in 45 populations — and have demonstrated nicely how to turn an initial failure into a success story.

Magdalena Skipper

References and links

ORIGINAL RESEARCH PAPER Barrett, P. L. *et al.* Targeted gene alteration in *Caenorhabditis elegans* by gene conversion. *Nature Genetics* **36**, 1231–1237 (2004)

FURTHER READING Jorgensen, E. M. & Mango, S. E. The art and design of genetic screens: *Caenorhabditis elegans*. *Nature Rev. Genet.* **3**, 356–369 (2002)

IN BRIEF

FUNCTIONAL GENOMICS

Megabase deletions of gene deserts result in viable mice.

Nóbrega, M. A. *et al. Nature* **431**, 988–992 (2004)

In mammals, most of the genome does not code for protein products, raising intriguing questions about its function. The debate intensified recently when ultraconserved noncoding regions were discovered in mammalian genomes; however, without functional data, no answers were forthcoming. Nóbrega *et al.* report that large-scale deletions of so-called gene deserts, which include highly conserved noncoding regions, have no adverse effects in mice that are homozygous for these deletions.

MOLECULAR EVOLUTION

Rate of molecular evolution of the seminal protein gene *SEMG2* correlates with levels of female promiscuity.

Dorus, S. *et al. Nature Genet.* December 2004 (doi:10.1038/ng1471)

One of the effects of female promiscuity is increased sperm competition, which in turn is believed to drive the rapid evolution of reproduction-related genes (and physiology). The authors discover that female promiscuity can also affect molecular evolution, therefore demonstrating a link between sexual and molecular evolution. They used *SEMG2*, which encodes a component of semen coagulum, as an example to show that its molecular evolution is faster in primate species with promiscuous versus faithful females.

GENE EXPRESSION

Special issue: Genes in action

Science **306**, 557–760 (2004)

How is gene expression controlled? How do we study it? And how is this control altered in disease? The 22 October, 2004 issue of *Science* tackled these topics and more in a special issue that contains news stories, viewpoints, review articles and research papers. Further articles available on the *Science*-companion online sites — the Signal Transduction Knowledge Environment (STKE), Science of Aging Knowledge Environment (SAGEKE) and the Science Functional Genomics web sites — discuss the application and future of microarray and other technologies, and provide links to useful resources.

TECHNOLOGY

The generation of cloned *Drosophila melanogaster.*

Haigh, A. J. *et al. Genetics*, 16 October 2004 (doi:10.1534/genetics.104.035113)

Although cloning organisms by nuclear transfer has been successful in amphibians, fish and mammals, this paper reports the first successful attempt to use the same approach to clone an insect, *Drosophila melanogaster*. The procedure involved injecting the nucleus taken from an early fly embryo into a fertilized fly egg; out of 820 injections, only 5 clones survived to adulthood. The authors hope that this experiment will help them to pinpoint the genes that are required for successful nuclear reprogramming, so that this knowledge can be used for therapeutic applications in humans.