HIGHLIGHTS

GENOMICS

Netting zebrafish genes

Among the favoured animals for studying the genetic basis of development through mutagenesis is the zebrafish *Danio rerio*. As in all vertebrates, however, identifying and cloning mutated genes is often a painstaking process. In the past few years, Nancy Hopkins and colleagues have proposed that retroviral insertional mutagenesis can markedly reduce the time that this requires. Reporting in *Nature Genetics*, Hopkins' group now describe the first fruits of their effort to identify many of the genes that are required for the development of the zebrafish embryo.

The ambitious goal of this screen — the logistics of which have been previously published — is to identify 450–500 retrovirally mutated genes that cause visible embryonic phenotypes. (From the results of previous chemical mutagenesis screens, they estimate that this number of mutations should hit ~20% of the genes that can be mutated to give a visible phenotype.) More than 500 insertional mutants have been produced so far, and Golling *et al.* now report the first 75 genes to be isolated from the screen. Thanks to the retroviral tags, most were fished out in as little as two weeks.

What can we infer from this list of mutant embryos and genes? The range of phenotypes resembles those observed in the Boston and Tübingen ENU mutagenesis screens, with many developmental defects occurring in specific tissues or structures. Mutants with more general defects discarded in the previous screens were kept by Golling *et al.* to generate an unbiased view of the 'genetic construction kit' of a vertebrate embryo.

As for the genes, ~20% cannot be assigned a function from their sequence, suggesting that a substantial fraction of the genes required for vertebrate development do not obviously fall into known groups. Among the many genes that are associated with specific developmental defects and that have a predictable function are those that encode the expected transcription factors, receptors and ligands, but various other proteins too. Those associated with the non-specific phenotypes include genes that encode putative helicases, chaperones, organellar proteins and metabolic enzymes, the study of which should help to integrate cell physiology with development.

The screen is still a work in progress, but a few things are clear. As is the case for ENU-based mutagenesis, retroviruses do not mutate all genes with equal frequency. However, this approach should allow the rapid cloning of many mutated genes by a single laboratory and from any genetically tractable organism whose genome is susceptible to retroviral integration. Most importantly, these mutants and genes constitute a superb community resource that will keep developmental geneticists busy for years to come.

Alan Packer, Associate Editor,
Nature Genetics

References and links

ORIGINAL RESEARCH PAPER Golling, G. *et al.* Insertional mutagenesis in zebrafish rapidly identifies the genes essential for early vertebrate development. *Nature Genet.* 13 May 2002 (10.1038/ng896)

FURTHER READING Patton, E. E. & Zon, L. I. The art and design of genetic screens: zebrafish. *Nature Rev. Genet.* **2**, 956–966 (2001)

WEB SITE
Nancy Hopkins' lab: http://web.mit.edu/biology/www/facultyareas/facresearch/hopkins.shtml