locus hit frequency of $0.2-2 \times 10^{-3}$ (similar to that found in mice) have been established.

The efficiency of mutagenesis was assessed by two criteria. First, new mutations at previously known loci affecting pigmentation were scored. Second, after inbreeding, new recessive lethal mutations were identified by simple visual inspection of embryos during early development; screening the equivalent of 240 F_2 lines yielded a total of 296 ENU-induced mutations, equivalent to a rate of 1.2 lethal hits per genome. Taken together with the single-locus hit rate estimated from the new pigmentation mutant alleles, these results yield a crude estimate of 600–1,500 as the number of genes that will mutate to give a visible phenotype. The two laboratories have therefore set out to screen 3,000 to 4,000 F_2 families each, and the hundreds of mutants found should reveal about 90 per cent of all embryonic lethal genes. Given the logistics now in operation, the screen should be completed within only two years.

The catch of mutants will be good, but what will it hold? Nüsslein-Volhard's group reports a phenotypic classification of the mutants isolated in a pilot screen.

Most (70 per cent) of them exhibit rather nondescript defects, such as swollen heart cavities or other general abnormalities. The remaining 30 per cent are more promising: some show defects in specific structures that arise early in development, such as the notochord, suggesting that the genes responsible may be involved in early patterning events, whereas others affect the later differentiation of structures such as eyes, ears, jaws or heart. Even in the absence of any molecular characterization of the mutated genes, such embryonic lethal mutants can serve as powerful tools in the analysis of early development. The ability to generate genetic mosaics by cell transplantation between wild-type and mutant embryos has provided insights into the cellular basis of processes such as cell migration and inductive interactions, as exemplified by studies of the *spadetail* and *cyclops* mutants^{8,9}. Ultimately, however, the goal must be to understand these processes at the molecular level, and for this purpose the cloning of the mutated genes will be essential.

A step in that direction has now been taken by John Postlethwait and co-workers at the University of Oregon⁵. Following strategies developed in plant genome analysis, several hundred dec-

mers were screened for their ability to PCR amplify sequences specific to either of two zebrafish strains, AB and Darjeeling. Postlethwait's group thereby identified 402 randomly amplified polymorphic DNA (RAPD) sequences and examined their segregation in 94 haploid offspring of an AB/Darjeeling female. These data were used to construct the first linkage map of the zebrafish genome. The ability to produce haploid offspring proved crucial in this exercise because it circumvents the need for inbreeding in inferring genotype from phenotype. The molecular basis for RAPD polymorphisms is uncertain, and so difficulties in reproducing adequate conditions for PCR using decamers may impede the use of the map as it stands. But cloning RAPD sequences should allow the design of longer primers with higher specificity to convert them into sequence-tagged amplified regions.

Using this same strategy, the Oregon group have mapped a recessive pigmentation mutation, *brass*, again exploiting the ability to genotype haploid embryos directly. They analysed the segregation of RAPD sequences between phenotypically mutant and wild-type haploid offspring of a heterozygous *brass*/Darjeeling female, and identified several markers that are closely linked to the mutation. Such mapping can be done quite quickly, and Postlethwait and colleagues estimate that, using 1,000 primer sets, any mutation can potentially be mapped to within 0.5 centimorgan of a molecular marker (which, according to their estimates, means to within 300 kilobases). Such closely linked markers can then be used as starting points for cloning the mutant gene by chromosomal walking. A physical map of the zebrafish genome similar to that developed for humans would greatly increase the speed of this step.

Given the success of the systematic genetics approach in *Drosophila*, expectations of the zebrafish screens are high. Many unknowns remain, but the development of large-scale screens and of the genetic linkage map surely mark the dawning of zebrafish genetics. □

Jean-Paul Concordet and Philip Ingham are in the Molecular Embryology Laboratory, ICRF Developmental Biology Unit, South Parks Road, Oxford OX1 3PS, UK.

In the wake of Columbus

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

Mary Evans/Explorer

If only Christopher Columbus had trailed a thermometer behind the *Santa María* instead of a tender, he could have extended oceanographic temperature records by several centuries. The lack of decent time series is one of the great problems for oceanographic science; today's detailed, worldwide monitoring is a fairly recent development. But Columbus's voyage of discovery in 1492 was at least of indirect benefit to oceanographic science — celebratory voyages along the route taken by the *Pinta*, *Niña* and *Santa María* (shown above) make it one of the most thoroughly sampled ocean transects. On page 48 of this issue, Gregorio Parrilla and co-workers add the results of a 1992 Atlantic crossing, made as part of the 500th anniversary celebrations, to those of two oceanographic expeditions in 1957 and 1981. In combination, the three records show a persistent warming between depths of 800 and 2,500 m, together with intriguing hints of large-scale spatial variation. Could this be a signal of climate change? Alas, things are unlikely to be quite that simple, because global warming would be expected to manifest itself in the surface waters rather than at depth.

Lindsay Matthews

1. Streisinger, G. C., Walker, C., Dower, N., Knauber, D. & Singer, F. *Nature* **291**, 293–296 (1981).
2. Slack, J. M. W., Holland, P. W. H. & Graham, C. F. *Nature* **361**, 490–492 (1993).
3. Mullins, M. C., Hammerschmidt, M., Häffter, P. & Nüsslein-Volhard, C. *Curr. Biol.* **4**, 189–202 (1994).
4. Solnica-Krezel, L., Schier, A. F. & Driever, W. *Genetics* **136**, 1401–1420 (1994).
5. Postlethwait, J. H. *et al.* *Science* **264**, 699–703 (1994).
6. Nüsslein-Volhard, C. & Wieschaus, E. *Nature* **287**, 795–801 (1980).
7. Mayer, U., Torres Ruis, R. A., Berleth, T., Misera, S. & Jürgens, G. *Nature* **353**, 402–407 (1991).
8. Ho, R. & Kane, D. *Nature* **348**, 728–730 (1990).
9. Hatta, K., Kimmel, C., Ho, R. & Walker, C. *Nature* **350**, 339–341 (1991).