

show expression of this gene. This is a seminal observation, since it suggests that cells can differentially express regulatory genes in a position-dependent manner and that positional information may regulate the expression patterns of some homeobox genes.

### Epilogue

The zebrafish has a glorious future ahead. With the isolation of newer mutations and development of molecular techniques for cloning genes rapidly, a lot more will be learnt about the riddles of vertebrate development; the development of the nervous system in particular. Several laboratories have been successful in generating stable lines of transgenic fish. This raises the possibility that we may soon have 'insertional mutagenesis' and enhancer detection methods refined in zebrafish. A simple sequence repeat map of the entire

zebrafish genome may soon become available<sup>10</sup>. Simple sequence repeats have been shown to be abundant and quite polymorphic between different zebrafish strains. Such a molecular map will be a boon in mapping mutations and may provide starting points for chromosomal walks and jumps. Unfortunately however, the zebrafish has 25 chromosomes and 10<sup>9</sup> bp of DNA; demanding several years of hard work before a map may become available. Be it as it may, it is time we welcome this novel developmental paradigm to our own laboratories, considering the exciting avenues it promises.

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## COMMENTARY

### Need for genetic and molecular biological research in Indian fish

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Many countries have taken up a conscious policy decision to participate in genome analysis programmes, i.e. the molecular mapping and sequencing of the genetic material in human and other organisms. For instance, China has embarked on a 15-year project on the sequencing of the entire rice genome, under the direction of G. F. Hong of the Shanghai Institute of Biochemistry. The anticipated benefits of this project are expected to be much greater than their present investment. Realizing the importance of gene therapy and the possible accruing economic benefits, the Americans and French have gone ahead with human genome project; their findings are to be patented, and may not be available to a country like India. Hence, there have been many arguments for and against launching an Indian human genome project with ear-

marked funds (e.g. J. Gowrishankar, *Curr. Sci.*, 1993, **63**, 705; P. M. Bhargava and Lalji Singh, *Curr. Sci.*, 1993, **65**, 663). A massive human genome programme is not only cost-intensive but involves many other issues, including ethical and social problems.

Much of our understanding of basic human biology comes from research work on organisms, which do not involve the practical, ethical and social problems of experimenting on human being. Such surrogate organisms used in research are few in number and the most widely used ones are the bacterium *Escherichia coli*, yeasts, nematode worms, fruitflies, zebrafish, clawed toads and house mice (P. Little, *Nature*, 1993, **366**, 204). However, most of these surrogate organisms do not possess all the specialized functions of mammals, and the genome of mouse is

as large as human with much of nongenic DNA, such as repeats, pseudogenes and other noncoding sequences, which make the technology of genome analysis difficult, and laborious as well as cost-intensive. Therefore, Sydney Brenner and his associates (including an Indian young scientist, at the Institute of Molecular and Cell Biology, National University, Singapore) made search for a better surrogate vertebrate, which has a 'small and perfectly formed genome, with small introns and high relative content of exon information'; hence, sequencing a part or even all this component genome would be an effective way of discovering vertebrate genes and provide relevant access to the human genome'.

Brenner is already known for introducing the surrogate nematode worm *Caenorhabditis elegans*. Undertaking elegant

genome research work in the pufferfish *Fugu rubripes rubripes*, Brenner *et al.* (*Nature*, 1993, 366, 265) made the following seminal contributions.

(1) A given *Fugu* DNA fragment was detected once in 24,625 phages, with an insert size of 16.5 Kb indicating a total genome size of 404 Mb.

(2) Of 127,831 base pairs of *Fugu* DNA sequenced, 1,011 i.e. 0.79% code for proteins, compared to 0.10% coding sequences of human. Hence, the coding sequences of the *Fugu* genome (including small introns of 80 bp median size) are about 7.68 times enriched than that of human or mouse. Briefly, the *Fugu* genome is unexpanded and has never acquired large quantities of 'junk' DNA. Correspondingly, one will have to put in about one seventh less laboratory work than required for human genome.

(3) The gene order in *Fugu* is more conserved than that of human. According to Little, the *Fugu* surrogate could be put to dramatic study on positional cloning strategies, if the observed conservation of short-range linkage extends to clusters of 5 or 6 genes. Therefore, the pufferfish *Fugu* can serve as an excellent surrogate vertebrate for undertaking rapid genome research.

*Fugu* occurs in Japanese seas and are not amenable for rearing. India has about 20 species of pufferfish and 7 species (e.g. *Tetrodon travancoricus*, P. K. Talwar and A. Jhingran, *Inland Fishes in India*, Oxford & IBH, 1991) occur in freshwater also and can therefore be reared in the laboratory. The DNA content of *T. fluviatilis* is 0.4 pg/haploid genome and the genome size is in the range of 380

Mb (R. Hinegardner and D. E. Rosen, *Am. Nat.*, 1972, 106, 621). On the whole, Indian molecular biologists have an excellent opportunity to work on the *Fugu*-like pufferfish, a surrogate vertebrate and to make the entry into human genome research much more effectively, and rapidly at a relatively low cost.

Independent of these academic exercises, genetic and molecular biological research work on Indian fish are becoming increasingly and urgently required, as it may lead to the production of faster growing strains and transgenic fish. Most Western countries harvest more cereals and fish than their present requirement. Therefore, production of transgenic plants and fish at a more efficient and/or faster rate using transgenic technology is not a pressing need, as it may reduce the price level of these food materials below the cost of production. Justifiably, Western scientists use transgenic techniques more for understanding the process of molecular basis of gene expression and control of development than for economic exploitation.

Thanks to developments in plant breeding and genetics, many Asian countries like India have achieved self-sufficiency in the production of cereals and other food materials, excepting meat and fish. As more than 40% of India's land area is under cultivation, any strategy to increase meat production will ultimately lead to further deforestation. On the other hand aquaculture opens up a new avenue for food, especially protein production. Secondly, many orthodox Hindus, who otherwise practice strict vegetarianism, will eat fish as water lily, i.e. *Jalapush-pam*. Even orthodox Muslims, to whom

*halal* meat alone is acceptable, readily accept fish. For reasons of environmental protection and social acceptability, India has much to be benefited by investing in aquaculture in a big way.

As in the case of the green revolution, researches in breeding and genetics may help India and other developing countries to achieve self-sufficiency in fish production. It is in this context that the production of transgenic fish, containing genes responsible for desirable traits and their transfer to broodstocks may provide a quantum leap over traditional selection and breeding methods. Realizing the importance of this potential, China has extended much support and built a strong network of fish biotechnologists and molecular biologists. This has resulted not only in the production of new fish strains but also a large number of research publications. For instance, more than 30 Chinese scientists from 8 institutions presented 15 research papers in the 'World Congress of Fish Genetics' held in 1993. Regrettably, not even a single abstract was presented from India, indicating that India's expertise in molecular genetics of fish and transgenic biology is meagre. Agencies like the Department of Biotechnology, Government of India, must initiate a national coordinated project to develop manpower in the area of molecular biological studies on fish with the goal of increasing fish production and research.

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