ties and strengthen its provisions on patient rights. Qiu says that the authorities have promised to consult geneticists in defining which genetic diseases should be covered by the law. But Yang Huanming, director of the Human Genome Center at the Chinese Academy of Sciences' Institute of Genetics, is dubious. "Scientists have a small voice in forming such regulations," he says.

One point of scientific consensus is that such laws won't reduce the prevalence of recessive disease genes in the population. "Population genetics shows [that eugenics] doesn't work," says Walter Bodmer, a British geneticist and former director-general of the Imperial Cancer Research Fund. Yet, researchers are concerned that the public, including many health care providers, may not understand that point. Mao, who was formerly at the West China University of Medical Sciences in Chengdu, says a 1994 international survey of genetic counselors found that all Chinese respondents thought the purpose of genetic counseling was to reduce the bad genes in the population, while few Western counselors gave that answer. Government officials quoted in the official Xinhua News Agency about the law echoed those sentiments. But others note that the problem of misunderstanding the possibilities and limitations of genetic technologies is not confined to China. "The overriding responsibility we have as geneticists is public education in genetics and its potential benefits," Bodmer says.

–DENNIS NORMILE

With additional reporting by Li Hui.

EVOLUTIONARY BIOLOGY

Doubled Genes May Explain Fish Diversity

MONT ROLLAND, QUEBEC—Take a dive to visit the rainbow-hued denizens of a coral reef and you will find it easy to accept that the ray-finned fishes—which include everything from goldfish to sea horses to flounder—are the most diverse group of vertebrates. Now, a new study of the genome of the zebrafish may explain how the 25,000 ray-finned species came to evolve such diverse forms.

In an early ancestor of the zebrafish—a common aquarium-dweller and research model—the entire genome doubled, according to John Postlethwait of the University of Oregon in Eugene, who presented his case at a recent evolution meeting.* He suggests that the ray-finned fish put their extra copies of genes to diverse uses and so evolved a wealth of different body shapes, for example, using an extra fin-bud gene to make the stinging fins of the lionfish "mane." The genome duplication also has implications for the zebrafish's role as a model organism, perhaps allowing researchers to spot dual functions of genes that would be hard to discern in species that have only one copy. "It's very exciting," says geneticist and hematologist Leonard Zon of Children's Hospital in Boston. "It's likely that, because of the duplication, otherwise hidden gene functions will be revealed."

Fishy forms. Ray-finned fish include pufferfish *(top)*, anglerfish *(middle)*, and butterfly fish *(above)*.

Postlethwait's analysis could upset the common explanation for why ray-finned fish seem to have extra copies of certain proteins and genes when compared to mammals. For years, many biologists have assumed that a mammalian ancestor had lost the extra copies.

Postlethwait and his colleagues focused on the developmental genes called Hox genes, which control some of the earliest patterns in a developing embryo. Most vertebrates, including mammals, have four Hox clusters, suggesting that two genome duplications occurred since these lineages split from the invertebrates, which typically have only one Hox cluster.

But after sequencing and mapping all the Hox genes they could find in zebrafish, Postlethwait, graduate student Allan Force, and postdoc Angel Amores and their colleagues found that the fish have seven Hox clusters on seven different chromosomes. Two clusters closely resemble the mammalian Hoxa, two resemble Hoxb, and two resemble Hoxc. Both mammals and fish have only a single copy of the Hoxd genes. Although zebrafish have two copies of the Hoxd chromosome, one is missing the Hox gene segment. Because the team found duplicates of all four chromosome regions, they believe the extra genes are not simply due to occasional gene duplications but stem from an event in which the entire genome was duplicated, with some genes then lost.

That conclusion is strengthened by the team's reanalysis of the published arrangement of Hox genes in the puffer fish, or fugu. Unlike the zebrafish, the fugu has an especially small genome, apparently with only four groups of Hox genes. The first three look very similar to mammalian Hoxa, -b, and -c, and the researchers who mapped the genes originally thought the fourth might be a much-remodeled Hoxd. But the leader of that effort, developmental geneticist Samuel Aparicio of the Wellcome/CRC Institute for Cancer and Developmental Biology in Cambridge, U.K., says Postlethwait's new analysis makes a clear case that this fourth Hox group is really a second copy of Hoxa. The researchers suspect that a fugu ancestor, too, once duplicated its genome, most of which was later lost.

Since the last common ancestor of fugu and zebrafish lived more than 200 million years ago, Aparicio says, the doubling might have occurred very early in the ray-fin lineage. That fits with having the extra genes power the great fish radiation of about 300 million years ago, he notes.

But geneticist Chris Amemiya of Boston University School of Medicine says he's waiting for more solid evidence. "They are the most successful group of vertebrates on

*The annual meeting of the Canadian Institute for Advanced Research Program in Evolutionary Biology, 25–29 July.

Earth," he says of ray-finned fishes, but "I'm not sure it's because of genome duplication. ... It's something that really needs to be shown empirically." And proving it will be tough, Postlethwait admits, requiring evidence that duplicate copies of genes have given rise to specific new traits such as the huge jaws of the anglerfish, or the lean body of the trumpetfish. But ongoing efforts to sequence genes from other fishes, including salmon and swordtail, will also help to test the theory, Postlethwait says. He is also analyzing the Hox genes of more primitive fishes such as sturgeon to better estimate the timing of the duplication.

DENNIS NORMILE

As more and more "extra" zebrafish genes were discovered, they were initially seen as a major blow for the fish's status as a model of mammalian development. Researchers induce mutations in the fish with chemicals, then observe the effects on the transparent embryos. But they feared that duplicate genes might mask the effects of mutations, or that if an extra fish gene had evolved a new function, it might not model mammals.

But Postlethwait and other zebrafish researchers say the doubling may be a benefit. For example, the *engrailed-1* gene in mammals is expressed in both the hindbrain and the limb buds. In zebrafish, however, there are two copies of this gene, and each specializes in a different region—one is expressed in the hindbrain and one in the earliest stages of fin development.

If this division of labor is common, says Zon, zebrafish mutants may reveal functions that would go undetected in mice. For example, if a gene is crucial for early development but also has a later function, knocking it out will kill embryos before the second role is revealed. But knocking out each gene separately in zebrafish would reveal both functions. Far from being a discouragement, Zon says, "I see it as good news all over."

–GRETCHEN VOGEL

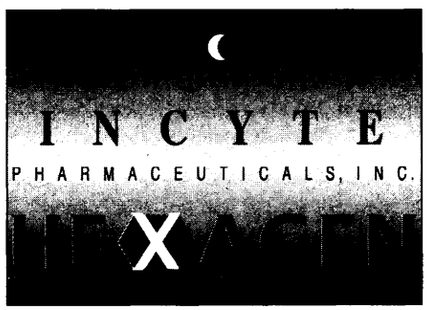
GENOMICS

A Second Private Genome Project

It's hard to imagine competition in the human genetics research business getting much hotter, but this week the temperature rose a notch. Incyte Pharmaceuticals Inc., a genetic data company in Palo Alto, California, announced that it plans to invest $200 million over the next 2 years to sequence the protein-coding regions of the human genome. It will also hunt for simple variations in the genetic code—also known as single nucleotide polymorphisms, or SNPs—and locate them and about 100,000 human genes on a computerized map. These data will be kept in a proprietary trove, available only to those willing to pay Incyte's stiff fees. Researchers expect to use SNPs to trace patterns of inherited vulnerability to disease and develop new drugs targeted for individuals likely to benefit from them.

As part of this new hunt for SNPs, Incyte said on 17 August that it will acquire a small British company, Hexagen Inc. of Cambridge, U.K., which developed a proprietary method for identifying variant genes in the mouse. Judging by the proposed budget, this project could rival the controversial sequencing and SNP-collection effort announced earlier this year by Perkin-Elmer Corp. of Norwalk, Connecticut, and J. Craig Venter of The Institute for Genomic Research (*Science*, 15 May, p. 994). And it will produce a SNP collection possibly larger—and much earlier—than a fast-moving public project funded by the U.S. National Human Genome Research Institute (*Science*, 19 December 1997, p. 2046).

"Incyte is going to focus on genes and polymorphisms of interest for pharmaceutical development," says Randall Scott, the company's chief scientific officer. He will head a new division that expects to receive "$20 million to $30 million in cash" from



Incyte as start-up money. It will raise the remainder, according to Scott, from the sale of new stock, subscriptions to its database, and partnership deals with drug companies. This is a risky undertaking, since SNPs have not proved their commercial value. Scott says: "There wasn't any clear-cut pharmaceutical interest 2 years ago, but we've seen a dramatic change just over the last 6 months." Now, he insists, "There's a huge interest."

Other genetic researchers were impressed by Incyte's investment but were cautious about the likely payoff. Fred Ledley, CEO of a SNP-based pharmaceutical company called Variagenics of Cambridge, Massachusetts, said "it won't be easy" to find SNPs or make them useful in drug research, but added that "Randy Scott has a record of taking on ambitious projects and succeeding." Says Eric Lander, director of the MIT Whitehead Center for Genome Research: "More data is good; I'm just sorry it isn't going to be available to the public."

–ELIOT MARSHALL

ScienceScope

CHINA RAMPS UP GENOME EFFORT

China has unveiled a new Human Genome Center in Beijing that it hopes will boost its contribution to international genome research. Completion of the facility, part of the Chinese Academy of Sciences' Institute of Genetics, was hustled along so that researchers in town for the 18th International Congress of Genetics could attend the 11 August opening ceremony.

Chinese geneticists celebrate new center.

Director Yang Huanming, who plans to hire 30 researchers and technicians within a year, says the center will hunt for disease genes more prevalent in Chinese populations and carry out large-scale sequencing of up to 2 megabases per year. Maynard Olson, a geneticist at the University of Washington in Seattle, says the center's focus on China's vast genetic diversity will be a "major benefit."

CONVICT DNA BANK UNCONSTITUTIONAL?

Gene-wielding crime fighters across the nation are keeping a close eye on the fate of an apparently unprecedented Massachusetts ruling declaring the state's prisoner DNA bank unconstitutional. Last week, a state judge shut down the bank, which stores blood samples drawn from convicts, ruling that the state can't force prisoners to give blood. The samples stored in Massachusetts and dozens of similar vaults worldwide yield genetic data that have helped investigators crack unsolved crimes.

The ruling—which the state plans to appeal—found that officials violated prisoners' constitutional rights to privacy. It could mark a turning point in efforts to force similar banks to change their practices, says John Roberts, director of the Massachusetts chapter of the American Civil Liberties Union, which brought the suit. But Dawn Herkenham, who heads the Federal Bureau of Investigation's Forensic Science Systems Unit, doubts the decision will stand. "I wouldn't say I'm alarmed," she says, noting that other states have successfully defended the legality of their banks.