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

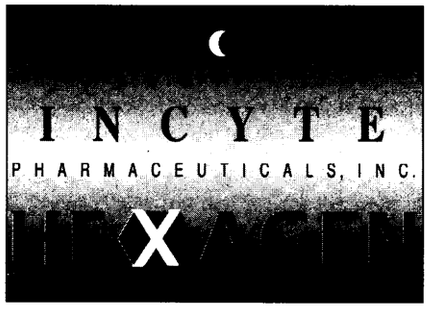
GENOMICS

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.

MUNN *ET AL.*

PHOTO, RIGHT: NASA

Target. The micrograph shows an embryo coming under immune attack after the mother was treated with an IDO inhibitor.

an enzyme known as indoleamine 2,3-dioxygenase (IDO), which destroys an amino acid, tryptophan, that the mother's immune sentries, known as T cells, need to do their job. Immunologist Phillipa Marrack of the National Jewish Hospital in Denver, Colorado, describes the observations as "very striking, interesting, and provocative."

In addition to explaining, as Mellor puts it, "why we, as mammals, survive gestation," the results—if they hold up—might help women with a history of spontaneous miscarriages. If those miscarriages are due to failure of the fetal cells to produce enough IDO, then drugs might be developed that mimic the enzyme's T cell–dampening effects. Such drugs might even be useful for preventing transplant rejection and treating autoimmune diseases. And conversely, compounds that inhibit IDO might lead to abortifacients that work by boosting the mother's innate rejection response.

Munn, a pediatric oncologist, did not set out to determine what protects the fetus from immune attack. He was searching for ways in which immune cells known as macrophages might activate the tumor cell–killing potential of T cells. Instead, Munn's team found that in their cell culture system, the macrophages were sedating the T cells, apparently because they were somehow destroying tryptophan. Since T cells, like other human cells, can't make their own tryptophan—it has to be supplied in the diet—they were unable to replicate, as they usually do when activated. To try to figure out whether tryptophan depletion might have a role in living animals, the oncologist teamed up with Mellor, a reproductive immunologist, and together the two groups showed that the amino acid declined in the cultures because the macrophages were making IDO.

Other researchers had shown in the early 1990s that the enzyme, in addition to being made by macrophages, is also produced in the placenta by fetus-derived cells called syncytiotrophoblasts. That finding suggested another possibility. We hypothesized, Mellor recalls, "that IDO prevents the maternal T cell response to [genetically foreign] fetuses, and inhibiting the enzyme would cause the mothers to abort."

That is exactly what the researchers have now found. For their experiments, Munn, Mellor, and their colleagues used two groups of pregnant mice. One set had been bred to genetically identical fathers of the same inbred strain while the other was bred to fathers from a genetically different strain. When the researchers implanted time-release capsules containing either the IDO inhibitor 1-methyl-tryptophan or a control substance under the skin of the pregnant animals, they found fetal rejection in only one group: mice that had been given the inhibitor and were carrying genetically foreign fetuses. The embryos developed normally at first, but then inflammatory cells moved in and extensive hemorrhaging occurred around the embryos. "The mother is rejecting the placenta and eventually the embryo chokes off and dies," Munn says.

Other experiments pointed to the mothers' T cells as instigators of the attack. The researchers mated mice that were genetically identical, except that the males had been engineered to carry a gene for an immune system protein that induces potent T cell responses. Treating the pregnant females with 1-methyl-tryptophan caused them to reject their fetuses, indicating that that single antigen was all it took to get the response. More direct proof for T cell involvement came when the researchers added T cells that recognize the antigen to mice that can't produce T or B cells and found that this could restore the response to the inhibitor.

From these results, Munn and Mellor propose that once the embryo implants and begins establishing connections with the mother's blood supply, fetal-derived cells located in the placenta begin making IDO. By destroying tryptophan, the enzyme then suppresses the activity of maternal T cells that would otherwise make their way through the placenta and attack the fetal blood supply.

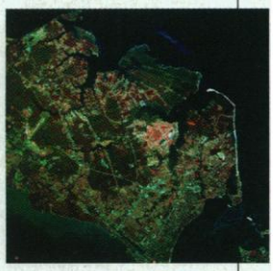
Some researchers have reservations about this scenario. As immunologist Joan Hunt of the University of Kansas in Kansas City points out, for example, since the embryo can't make the tryptophan it needs to

ScienceScope

EARTH PROBES EARTHBOUND

It is proving harder for NASA to explore Earth than to send spacecraft millions of kilometers to Jupiter. Launches of two Earth observation satellites are again on hold due to technical problems, hobbling researchers' efforts to gather data on everything from land-use changes to the carbon cycle.

Landsat 7 and EOS-AM1 were slated for launch earlier this summer, but NASA officials now say neither will be ready for orbit until next year. During a recent thermal vacuum test, key components failed on the $444 million Landsat 7, according to James Irons, the project's deputy scientist. Meanwhile, problems with the flight operations software for the $1.2 billion EOS-AM1, the first major spacecraft in the Earth Observing System series, likely will set that launch back until next summer, according to agency officials.



Landsat image of Virginia.

INTERNET'S FAST TRACK

The faster Internet being built by the federal government is supposed to help knit the research community more tightly together. But scientists working in academic outposts worry that it may actually make them second-class cybercitizens. That's because most rural researchers can't afford to pay the higher tolls needed to get onto the Internet's fast lane, says Joe Thompson of Mississippi State University, who has invited academic, government, and industry leaders to his campus next month to hash out the problem.

"Universities in nonurban states are at a significant disadvantage," says the engineer, who notes it can cost up to 10 times more for rural institutions to hook up to high-speed computer connections, which rely on infrastructure typically installed first in urban areas. Under pressure from Congress, the National Science Foundation last year began offering extra hookup funds to nonurban researchers (*Science*, 13 June 1997, p. 1639), but Thompson claims the bonus has proved "an order of magnitude too small" to cover real costs.

Contributors: Dennis Normile, Li Hui, Jennifer Couzin, Andrew Lawler, and David Malakoff