RANDOM SAMPLES

edited by CONSTANCE HOLDEN

Biotech Biggies Band for Protein Hunt

In a move uncharacteristic of the dog-eat-dog world of biotech, three big companies are teaming up this fall to exploit a new method of identifying the functions of thousands of proteins expressed by human genes. By joining forces, they hope to take a shortcut to the discovery of medical products—the pot of gold at the end of the genomics rainbow.

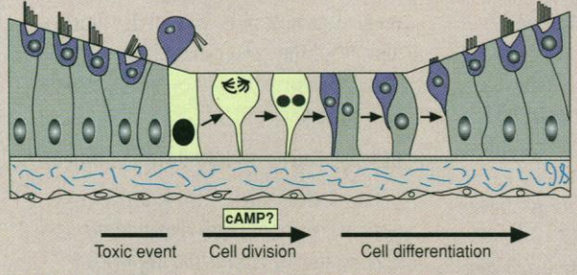
Leading this industrial trio is Genetics Institute (GI) of Cambridge, Massachusetts, which announced on 25 September that it has signed up two research partners: the Chiron Corporation of Emeryville, California, and Genentech Inc. of San Francisco. GI anticipates that other companies—and possibly some academic researchers—will also join the effort. GI's proposal is to share its library of genes and proteins with anyone who's willing to sign an agreement to share profits on commercial products on a 50-50 basis. GI says it will charge partners a relatively low fee for the use of its new yeast-based system, called DiscoverEase, that "traps" secreted human proteins (those active outside the cell, the best candidates for medical use). To spot genes that code for secreted proteins, scientists fuse human genes to a yeast gene that controls growth, and look for the ones that cause the yeast to grow. It is "an elegantly simple system for going through millions of clones and getting signal peptides," says Steven Clark, GI's senior vice president of research.

The goal, according to Clark, is to identify these proteins "as rapidly as possible, isolate full length clones for them, then express them and provide samples of expressed proteins for people to do biological assays." Clark says GI has already identified 5000 partial genes that express secreted proteins and has full-length clones in hand for 250 proteins. Nailing down each protein's function will be a massive task, however—more than any single company can handle.

This new collaboration of biotech behemoths, says industry analyst Samuel Isaly of the New York firm of Mehta and Isaly, shows that the race to extract commercial value out of genomics research is intensifying. GI may gain more by sharing than by hoarding its new technology, for "speed has become more important" than exclusive control of data, says Isaly, especially now that the "huge jigsaw puzzle" of human genetics is coming together faster than was expected just a few years ago.

Green Thumbs for Ear's Hair Cells

When hearing fades, it's often because the ear's so-called hair cells—cells with hairlike projections that translate sound waves into nerve signals—have died or been destroyed. Neurobiologists considered this loss permanent until a few years ago when several research groups demonstrated that hair-cell regeneration, already known to occur in birds, might also be possible in mammals (*Science*, 12 March 1993, pp. 1616, 1619).



Back to Life. Phases of hair cell regeneration.

Now the search for ways to trigger that regrowth has begun to pay off. Biochemists at the University of Pennsylvania School of Medicine in Philadelphia have found a new trigger in chickens. Adding substances that rev up the production of cyclic AMP—a common signaling molecule inside cells—to a bird's cochlea stimulates the proliferation of the support cells that underlie hair cells, says team leader J. Carl Oberholtzer. And some of those new cells eventually differentiate into replacement hair cells, his team reports in the October *Nature Medicine*.

"In most systems the addition of cyclic AMP inhibits cell proliferation," says Oberholtzer. But his team decided to look into that substance because they had found, in comparing damaged and undamaged cochlea cells, that certain enzymes in the cyclic AMP pathway were active during cell regeneration. By adding forskolin, a chemical that stimulates cyclic AMP production, to undamaged cochlea "we can induce a fairly vigorous response" leading to the formation of new support cells and hair cells in a few days, Oberholzter reports. Such proliferation does not usually occur in undamaged cochlea. They then demonstrated that they could retard the regrowth of hair cells that occurs after a bird cochlea is damaged by inhibiting an enzyme activated by cyclic AMP.

"[The work] suggests what may be a novel approach toward trying to make hair cells regenerate in mammals," says Edwin Rubel, a developmental neurobiologist at the University of Washington in Seattle. But he cautions that the behavior of cyclic AMP in birds may not be a reliable indicator of what it will do in mammals. It still isn't certain hair-cell regeneration is even possible in the mammalian cochlea, he adds: almost all the hair cell regeneration achieved in mammals has been in a different organ, the utricle (important for balance). But at the very least, Rubel says, the work "will stimulate a lot of good research."

Lasker Awards

In biomedicine, the Lasker awards are considered the next best thing to a Nobel Prize in prestige, if not money (the biggest award is $25,000). Fittingly, they are announced just days before the Nobels. The Albert and Mary Lasker Foundation presented this year's awards on 4 October to pioneers in the discovery of nitric oxide's role in the body, vaccine development, and the deciphering of the genetic code.

Zamecnik

Two scientists who helped discover that the toxic chemical nitric oxide also serves as a messenger between cells share the basic medical research award: Robert Furchgott, distinguished professor emeritus at the State University of New York Health Science Center at Brooklyn, and Ferid Murad, former president and CEO of Molecular Geriatrics Corporation in Lake Bluff, Illinois.

Four scientists from two teams share the clinical medical research award for work that led to a vaccine against *Hemophilus influenzae* type b (Hib), the agent for bacterial meningitis, which causes death, deafness and retardation among children. Porter Warren Anderson, Jr., professor emeritus of pediatrics at the University of Rochester, and David Smith, president of the David H. Smith Foundation and founder of Praxis Biologics, share the award with John Robbins and Rachel Schneerson, both immunologists at the National Institute of Child Health and Human Development. The scientists were instrumental in both developing the vaccine in the laboratory and producing it commercially.

A new award, for special achievement in medical science, goes to Paul Zamecnik, a mo-

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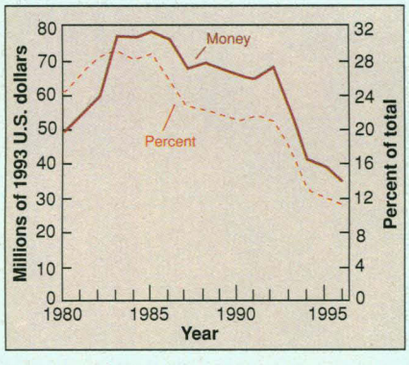
lecular biologist at the Worcester Foundation for Biomedical Research in Shrewsbury, MA, for work that led to the deciphering of the genetic code. Zamecnik doesn't have the name recognition of Watson and Crick, but the Lasker award committee calls him a scientist of "unique magnitude and immeasurable influence" who helped discover some of the first hard evidence for transfer RNA, the molecules that help translate genetic information into proteins. He also was one of the first to propose using anti-sense DNA to inhibit gene expression. Michael Yarus, a molecular biologist at the University of Colorado, calls Zamecnik's work "one of the foundation blocks of the edifice of molecular biology."

Foreign Research Aid Pays Off in U.S. Ag

The United States has been steadily slashing its support for the global network of agricultural research centers called the Consultative Group on International Agricultural Research (CGIAR), which develop improved strains of crops (see chart). Yet according to a new study, U.S. taxpayers as well as the world's hungry reap rewards from this investment—huge ones in the case of wheat.

US aid to the CGIAR centers, which has fallen (in 1993 dollars) from $78 million in 1985 to $37 million this year, "was never meant to pay for itself in the US," says economist Julian Alston of the University of California, Davis. "But we get some incidental benefits" from the varieties developed by CGIAR. To size up those benefits, economist Phil Pardey of the International Food Policy Research Institute in Washington, D.C., Alston, and their colleagues looked at the U.S. benefit-to-cost ratio of research on wheat and rice. First, they estimated the dollar value of increases in yields since 1970 due to new strains of grains. Then they traced what share of the ancestry of these strains came from varieties developed at two CGIAR centers, in Mexico and the Philippines.

The researchers used several methods to estimate the contribution of CGIAR innovations such as semi-dwarf traits, which mean more seed production per plant, to gains in yields. Some gave less credit to traits introduced early in the grain's pedigree; another considered the contributions of all ancestors to be equal. They then compared those gains to total US aid to the two CGIAR centers—$134 million since 1960. For rice, a minor crop in the U.S., the benefit-cost ratio ranged from 0.6:1 to 17:1. Gains for wheat were astounding, with ratios ranging from 48:1 to 190:1. "I was surprised," Alston says. "I've been skeptical of these studies in the past. Now I'm convinced."



Flagging. U.S. share of the budget for CGIAR, 1980–1996.

Keith Fuglie, an economic analyst with the U.S. Department of Agriculture, says "trying to partition out the contributions is fairly new," but the Pardey team's methods appear to be "a very fair way" of doing it.

Taxpaying Over the PC

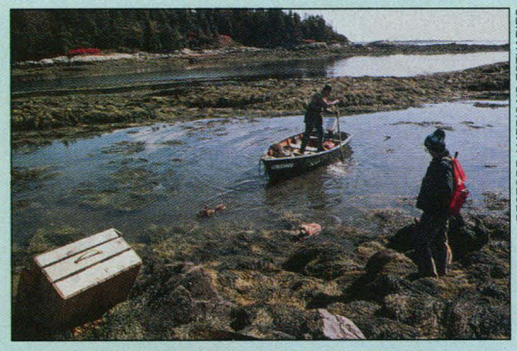
Cyber-citizens won't be able to file their taxes directly over the Internet any time soon. After spending $17.1 million, the Internal Revenue Service (IRS) has indefinitely halted its Cyberfile project following a blistering series of reports from the Government Accounting Office (GAO), which lambasted the program for poor management and security flaws.

While designing and building a system to accept tax forms over the Internet is a large undertaking, "it's not the human genome problem, and it's not putting a man on the moon," says Rona Stillman, GAO's chief scientist for computers and telecommunications. Stillman, author of the latest report on the project, says the technology is available to build a secure, efficient system. But she says project managers never fully analyzed the security hazards of the Internet, and "really didn't know what they wanted" when they launched the project in August 1995.

The IRS already has a system in place to accept electronic filings, but taxpayers must go through a private company, which forwards the information to the IRS for a fee. Cyberfile, which would have enabled taxpayers to file electronically without a middleman, was originally slated to go online early this year, in time for citizens to file their 1995 taxes. That timetable, says Stillman, was unrealistic and, among other problems, led to cost overruns. A GAO inspection last March found dozens of security and safety flaws ranging from faulty locks on doors to communications lines that crossed those of another agency.

After spending most of the $22 million originally budgeted for the project, the IRS decided to pull the plug earlier this summer. No one involved in the Cyberfile project is talking to the press about it. IRS spokesperson Jodi Patterson says the agency is "fully committed to the concept of from-home filing." But it won't have a timetable—and won't know how much of the $17 million can be salvaged—until an internal review of the project is completed.

Rescuing Estuaries. Estuaries like this one in the Gulf of Maine—ecologically rich coastal areas where rivers and oceans mingle—are increasingly threatened by development and pollution. Federal laws protect some ecosystems under the Clean Water Act and the National Wildlife Refuge system, but most government efforts focus on protecting a single feature, such as water quality or a particular species. Last month a group called Restore America's Estuaries (http://www.estuaries.org/), a coalition of eight regional environmental organizations, launched a campaign to restore whole habitats. The group has drafted an "Estuary Habitat Restoration Act" that would put $100 million a year into grants and incentives for community-based, comprehensive restoration efforts, including cutting pollution or removing dikes that block tidal swells. The goal is to restore 405,000 hectares (1 million acres) by 2010, says director Naki Stevens. Group members say they have met with several members of Congress who, they hope, will introduce the measure next year.



RESTORE AMERICA'S ESTUARIES

John Callaway, assistant director of the Pacific Estuarine Research Laboratory at San Diego State University, says that so far, most wetlands restoration has been done by commercial interests in response to Environmental Protection Agency regulations. "If a group like this has the funds and can set goals based on habitat needs, that would be great," he says.