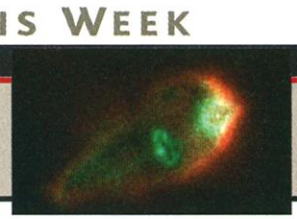

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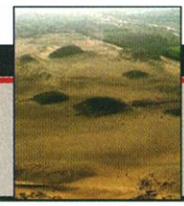
How planets get it together



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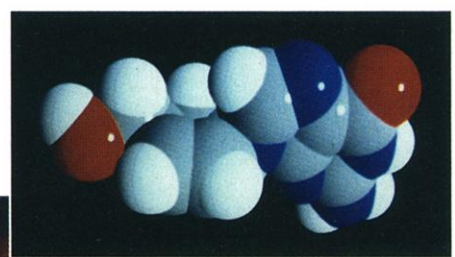
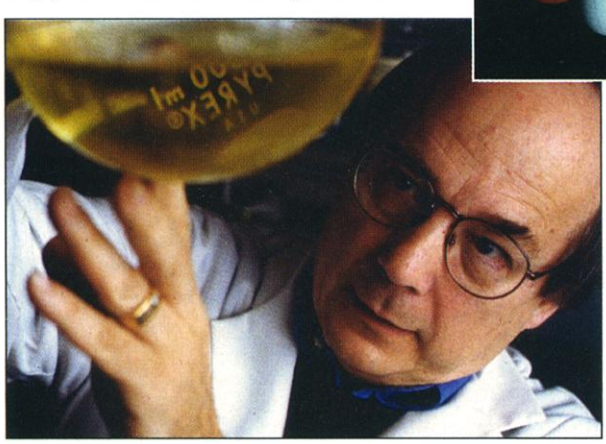
The first New World city?

DRUG PATENTS

Universities, NIH Hear the Price Isn't Right on Essential Drugs

When the University of Minnesota won a drug patent fight in 1999, its president, Mark Yudof, said it was "like winning the lottery." Now that lottery prize, worth as much as $300 million over time, has put Minnesota into the middle of an international debate over whether the public should get back some of the profits generated by biomedical research it has funded. A major driving force has been the cost and availability of AIDS drugs in developing countries—an issue on which advocates of limiting drug profits claimed a victory last week in South Africa. And the U.S. National Institutes of Health is being drawn reluctantly into the fray by a congressional directive to identify big moneymaking drugs derived from NIH-funded research.





Research rewards. Minnesota's Robert Vince and his very valuable antiviral molecule, carbovir (*inset*).

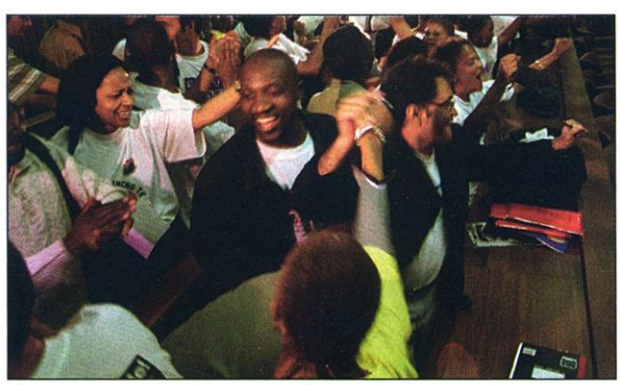
What's at stake is the process by which drug companies develop and bring new products to market. Much of the underlying research for new drugs stems from university-based work, typically funded by the government. Under a series of laws passed since 1980, publicly funded researchers and their institutions are encouraged to patent and commercialize discoveries. But billion-dollar sales and high profit margins on certain drugs created in part with public monies have led some to ask whether the government deserves a slice of the revenues. Universities are also nervous about being seen as greedy.

The public is starting to "look askance" at academic biomedicine's interest in profits, says Stanford University's dean of medicine, Eugene Bauer. Speaking last week at the National Academy of Sciences, Bauer warned that "we are perhaps entering into an era of distrust" about faculty patents and spin-off corporations. He suggested that medical schools need to build public confidence with clear conflict-of-interest rules. At the same time, faculty patent holders are bewildered by the mixed signals they're getting. Says Robert Vince, a medicinal chemist and drug inventor at Minnesota's Twin Cities campus: "I like to think that what we did was useful. … All of a sudden, we're bad guys because we developed an AIDS drug."

Two years ago, Minnesota managed to convince Glaxo Wellcome, now GlaxoSmithKline, that Vince and his colleague Mei Hua, who had filed patents on nucleoside analogs, were partial inventors of Ziagen (abacavir), a drug approved for AIDS therapy in December 1998. But this month, a group of Minnesota students staged a teach-in to pressure the university to forgo some of these royalties and not enforce its Ziagen patent in poor countries. These demands echo a campaign 10,000 kilometers away in South Africa, where activists are cheering a decision last week by 39 companies to withdraw from a suit to protect their patent rights. And activists at Yale University won another concession: They persuaded the university to rewrite a license agreement with Bristol-Myers Squibb Co. for the AIDS drug d4T so that generic knock-offs could be sold with impunity in South Africa.

The debate is most acute in Africa, but U.S. politicians are getting involved, too. Last December, the U.S. Senate asked NIH to keep tabs on "blockbuster" drugs that arise from government-sponsored research and to draw up a plan to recapture some of the money. The proposal was advanced by Senator Ron Wyden (D–OR), who has long been concerned about government research "walking out the door" without an adequate return to taxpayers, one observer says. A decade ago, as a member of the House, Wyden investigated the NIH-funded discovery of Taxol, the toxic compound derived from the Pacific yew that was developed into an anticancer compound by Bristol-Myers Squibb. Wyden failed last fall to attach his proposal to an NIH spending bill, but his colleagues agreed to include it in an accompanying report on the bill.

With the goal of "securing an appropriate return on the NIH investment in basic research," the report asks NIH to draw up a list of FDA-approved drugs with annual U.S. sales of $500 million that also received NIH backing and to prepare a plan to "ensure that taxpayers' interests are protected." The report is due in July, but the high threshold could limit it to one or two drugs.



Legal victory. Activists in South Africa cheer companies' decision to drop a suit on drug patents.

CREDITS: (TOP TO BOTTOM) COURTESY OF ROBERT VINCE; UNIVERSITY OF MINNESOTA; LORI WASALCHUK/AP

NIH officials declined to comment, saying only that they are working on the report.

Back in the Twin Cities, meanwhile, the University of Minnesota is holding firm. Christine Maziar, vice president for research, says the university "applauds" Glaxo's plans to reduce the cost of other drugs and "would welcome" a price reduction of Ziagen in sub-Saharan Africa, "despite a potential reduction in royalties." But the university will not abandon its intellectual property: "As a public institution, we are not able to give away a public asset," Maziar says about the patent on Ziagen. "If a farmer were to donate land, we wouldn't be able to give that away, either."

Amanda Swarr, a graduate student in women's studies at Minnesota and leader of the Ziagen protest, argues that "negligible" revenues are at stake in Africa. Besides, she says, "the university needs to put people's lives over patents."

Vince says he's trying to do exactly that by putting his share of the Ziagen money to work on three potential new AIDS drugs and a drug design center. Those dreams, however, rest on the expected royalties from university-owned patents. **–ELIOT MARSHALL**

AIDS ORIGINS

Disputed AIDS Theory Dies Its Final Death

At an unusual Royal Society meeting in London last September, a controversial theory that a contaminated polio vaccine triggered the AIDS epidemic was all but pronounced dead. Now, a paper in this issue (see p. 743) and three more in this week's issue of *Nature* collectively declare that—to paraphrase the Munchkin coroner in *The Wizard of Oz*—the theory is not only merely dead, it's really most sincerely dead.

The Royal Society meeting (*Science*, 15 September 2000, p. 1850) and these new studies are a response to a hotly debated 1999 book, *The River*. In it, British writer Edward Hooper links the first known cases of AIDS to tests of an oral polio vaccine in 1 million Africans more than 40 years ago. Hooper contends that in the manufacturing process, scientists accidentally introduced a precursor of HIV, a chimpanzee virus known as SIVcpz, into the vaccine. Specifically, Hooper asserts that the scientists grew the poliovirus vaccine in cells taken from chimps infected with SIVcpz. The scientists, led by Hilary Koprowski, former director of the Wistar Institute in Philadelphia, denied the charge, asserting that they grew the vaccine virus in monkey, not chimp, cells. They further contended that no evidence supported the notion that SIVcpz or HIV had contaminated any batches of the vaccine.

Preliminary data presented at the Royal Society meeting challenged each of Hooper's main claims, and these four new papers now formally dismiss them. Three of the four papers—including the one in this issue by Hendrik Poinar and colleagues at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany—examined old samples of Koprowski's vaccine and found that none contained DNA from chimpanzee cells. Each lab also found evidence of monkey DNA. Two of the labs further looked for genetic material from HIV or SIVcpz but found none.

The fourth paper, by evolutionary biologist Edward Holmes and co-workers at Oxford University, analyzed an altogether different contention made by Hooper: that the odd shape of the evolutionary tree formed by different strains of HIV supports the contaminated polio vaccine theory. Hooper highlighted the fact that the various subtypes of HIV seemed to appear simultaneously, forming clusters called "starbursts"; these theoretically could have occurred if this massive human trial used an SIVcpz-contaminated vaccine. In Hooper's hypothetical scenario, the vaccine would have contained a range of viral subtypes, which either existed in one chimp or came together when scientists pooled cells from several chimps.

By studying 197 HIV isolates obtained in 1997 in the Congo—where the bulk of these polio vaccine tests took place—Holmes and co-workers found that the HIV tree does not show the distinctive subtypes that are seen in previously constructed trees from the entire world. "The starburst is no longer there," says Holmes. Rather than all of the subtypes originating first in chimps, these data suggest that the subtypes evolved in humans. "A set of people want HIV and AIDS to be a unique thing—it's so unexplainable that they think that somebody must be responsible," says Holmes. "But it's actually like any other virus. It differs in that what it does to us is so horrendous." (Hooper did not respond to an interview request.)

Most sincerely dead. Like the Wicked Witch of the East, the theory that AIDS was spread by a polio vaccine has been discounted.

To Holmes, these studies have, in the absence of new evidence, thoroughly dismissed Hooper's theory. "Hooper's evidence was always flimsy, and now it's untenable," says Holmes. "It's time to move on."

–JON COHEN

DEVELOPMENTAL BIOLOGY

Stem Cells Are Coaxed To Produce Insulin

In a boost for scientists who hope to turn the potential of undifferentiated stem cells into medical miracles, researchers have found a way to produce insulin-producing cells from mouse embryonic stem (ES) cells.

There is ready-made demand for anyone who can achieve such alchemy in human cells: millions of patients with diabetes. Doctors have reported promising results in transplanting pancreatic cells from cadavers into diabetic patients, enabling a handful of recipients to stop insulin injections indefinitely. But the demand for cells is far greater than the supply. An unlimited source of cells that can produce insulin in response to the body's cues would thus be a hot commodity.

But although scientists have transformed ES cells into a range of cell types