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

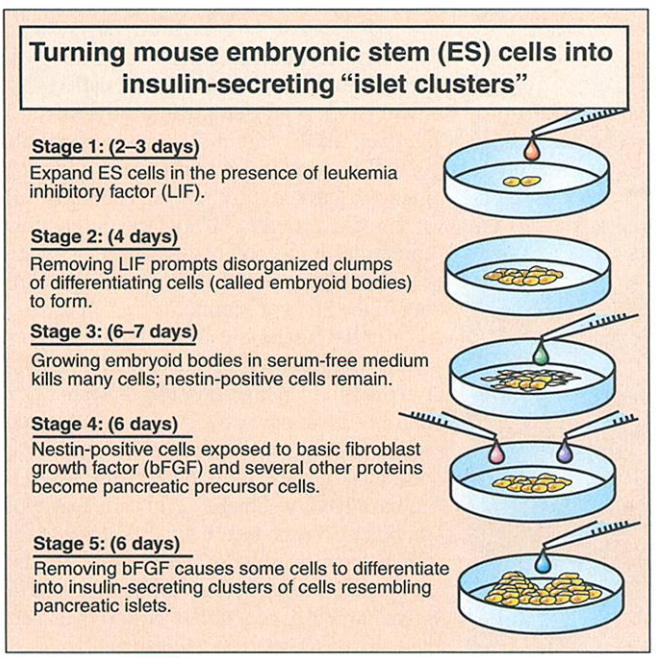
In a boost for scientists who hope to turn the potential of undifferentiated stem cells into medical miracles, researchers have found a way to produce insulin-producing cells from mouse embryonic stem (ES) cells.

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

such as neurons and muscle, pancreatic beta cells—the cells that produce insulin—have been an elusive target. Scientists know relatively little about the genes that control development of the endoderm, the layer of cells in the early embryo that gives rise to many of the internal organs. Nor do they know why ES cells left to differentiate in culture spontaneously produce cells resembling muscle, neurons, and even intestine—but only rarely pancreatic cells.

In a paper published online today by *Science* (www.sciencexpress.org), Nadya Lumelsky, Ron McKay, and their colleagues at the National Institute of Neurological Disorders and Stroke in Bethesda, Maryland, describe a five-step culturing technique that can turn mouse ES cells into cell clusters that resemble pancreatic islets. The cells produce small amounts of insulin and seem to behave similarly to normal pancreas cells. "The percentage of cells that become insulin positive is remarkable and way above what others have reported," says developmental biologist Palle Serup, who studies pancreas development at the Hagedorn Research Institute in Gentofte, Denmark.



CREDITS: (TOP TO BOTTOM) TOM BRAKEFIELD/CORBIS; ILLUSTRATION BY C. SLAYDEN

McKay's team usually focuses on brain development but was drawn to this area by recent papers showing similarities between neural and pancreatic development. For example, Serup and his colleague Ole Madsen demonstrated last year that pancreas cells and neurons use some of the same genetic pathways during differentiation. And two other teams recently reported that some pancreas cells express nestin, a protein typical of developing neural cells.

The members of McKay's team already knew how to encourage mouse ES cells to express nestin. They wondered if they could coax their nestin-positive cells to take on characteristics of pancreas cells. When they briefly exposed nestin-positive cells to a growth factor, the cells differentiated not only into neural cells but also into clusters that resemble the insulin-producing islets in the pancreas. The clusters' inner cells produced insulin, while outer cells produced glucagon and somatostatin, two proteins typical of pancreas cells. "It really looks as if you're getting bits of the animal—groups of cells that are assembled together," McKay says. He says he and his team have grown nestin-positive cells from mouse bone marrow, but they have different properties. They have not yet tried this protocol with these adult cells.

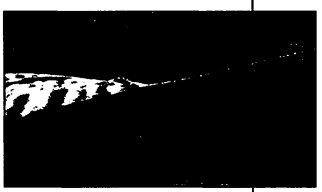
The ES-derived cells produce insulin in response to glucose—the fundamental role of beta cells—and they increase their insulin production when exposed to chemicals that prompt insulin secretion in normal pancreas cells.

Important caveats remain, however. The clusters produce only about 2% as much insulin as normal islets do. And when the cells were implanted into diabetic mice, the animals' blood sugar did not return to normal, although transplanted mice survived longer than control animals. Moreover, the cells failed to produce insulin in response to a 5-millimolar concentration of glucose, a level that typically triggers a response in beta cells. "The cells are clearly not behaving as normal beta cells," says Serup, who also notes that the gene *PDX1*, a hallmark of mature beta cells, is expressed only at low levels.

The low insulin production does not discourage researchers such as molecular biologist Ken Zaret of the Fox Chase Cancer Center in Philadelphia. "The glass is 1/50th full," says Zaret, who predicts that refinements in the culture technique or drug manipulation will boost insulin production. "The amount of insulin they produce is less than it should be if they're mature beta cells," agrees developmental biologist Douglas Melton of Harvard University. But he is nevertheless eager to see whether the technique works with human cells. McKay has shared the protocol with him, he says, and he is trying it with human ES cells in his lab. —GRETCHEN VOGEL

ScienceScope

At Sea, at Risk The smalltooth sawfish may soon become the first marine fish living in U.S. waters to be listed as an endangered species. The National Marine Fisheries Service (NMFS) last week concluded that the sawfish (below), a shark relative, is in "in danger of extinction" due to fish net entanglements and habitat loss. Scientists believe the U.S. population has declined by as much as 99%, with survivors confined to a few areas off Florida.



NMFS has listed just one other totally marine fish, a tropical species that lives off Mexico, as endangered (*Science*, 25 July 1997, p. 486). Sonja Fordham of the Center for Marine Conservation, which asked for the sawfish's listing, says NMFS's move, due to be finalized later this year, "sends an important warning that marine fish can indeed be threatened by human activities."

Fast Track Should NASA or the National Science Foundation control U.S. astronomy research? At the White House's request, a blue-ribbon panel under the auspices of the National Academy of Sciences is gearing up to answer that controversial question. The 12-person panel named 21 April includes a mixture of science policy heavyweights, such as retired aerospace manager Norman Augustine and former presidential science adviser D. Allan Bromley, as well as researchers from universities and nonprofits. The panel's work kicks off 10 May with a private phone conference, followed by three public meetings this summer. A final report is due 1 September.

Arsenic Punt After yanking a new rule for arsenic in drinking water that she felt was issued too hastily, Environmental Protection Agency chief Christie Whitman has now tossed the matter to the National Academy of Sciences (NAS).

The withdrawn Clinton-era rule would have lowered the acceptable level of arsenic, a carcinogen, from the current 50 parts per billion to 10 ppb. Whitman wants the NAS panel to examine the health impacts of levels between 3 and 20 ppb by August. An academy staffer explains, however, that the panel will not recommend the best level—that's not its role—but review recent research in updating a 1999 NAS study which urged only that the standard be tightened.