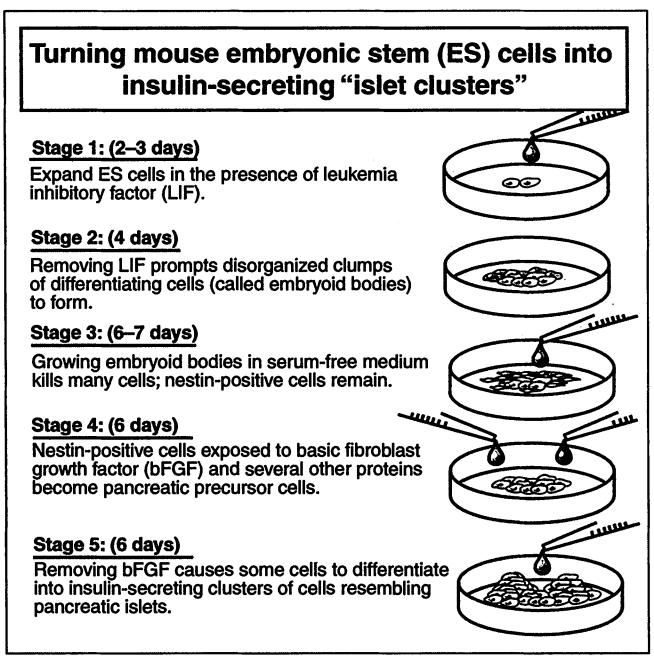
such as neurons and muscle, pancreatic beta cells—the cells that produce insulin—have been an elusive target. Scientists know relatively little about the genes that control development of the endoderm, the layer of cells in the early embryo that gives rise to many of the internal organs. Nor do they 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."

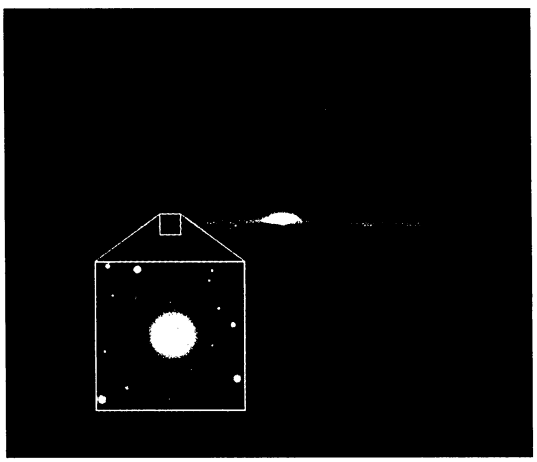
Fast Track Should NASA or the National Science Foundation control U.S. astronomy research? At the White House's request, a blue-ribbon panel under the auspices of the National Academy of Sciences is gearing up to answer that controversial question. The 12-person panel named 21 April includes a mixture 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.

like Milky Way. But there is a possible catch: Their survey covered a nearby part of the galactic disk in which disk residents mingle with halo stars that just happen to be passing through. Indirect observations show that almost all of the galaxy's dark matter is native to the halo, making disk stars nearly useless for explaining it.

In principle, disk and halo dwarfs are easy to tell apart. Disk dwarfs are whirling around the galactic center at an average speed of 220 km/s, the same as the sun; halo dwarfs are, on average, standing still. Applying that test to separate out halo dwarfs and then extrapolating their density to the entire galactic halo, Oppenheimer and his collaborators estimated that white dwarfs could account for at least 2% of the dark matter known to make up 90% of the halo's mass. Suspected halo dwarfs currently too faint to be seen could boost their estimate to as much as a third of the dark matter.



Mixed message. Near the sun, mingled stars from our galaxy's disk (white) and halo (red) complicate the quest for dark matter.

Shortly after their paper appeared on *Science* Express, however, several scientists fired back a barrage of electronic critiques. On 5 April, a team led by astronomer Neill Reid of the Space Telescope Science Institute in Baltimore posted a paper destined for the *Astrophysical Journal Letters* on the LANL server. Reid and collaborators argued that Oppenheimer's criterion was not stringent enough to remove all of the disk white dwarfs from his sample. In Reid's view, the white dwarfs are not dark matter at all, but merely a part of a previously known population of stars in the galactic disk. "It is a gaping hole in their argument," Reid says.

A week later, astrophysicist David Graff of Ohio State University in Columbus made a similar argument in an LANL posting that was also submitted to *Science* as a Technical Comment. And on 16 April, in another paper posted on the LANL server and submitted to *Science* as a Technical Comment, astronomers Brad Gibson of Swinburne University in Australia and Chris Flynn of the Tuorla Observatory in Finland pointed out typographical errors in Oppenheimer's online paper. (The printed version of the paper in this issue includes minor corrections.)

Oppenheimer says he welcomes the criticism but that public release of the preprints before they had been peer reviewed distorted the debate. "Our paper went through the standard channels of scrutiny, with two referee reports that were very favorable," he says. "None of these comments or papers have been properly refereed." And rapid-fire online publication, he says, left no time to make a considered response. As a result, Oppenheimer says, "the playing field was unfair."

On 20 April, editors at *Science* asked the authors of the two Technical Comments to withdraw their preprints from the LANL server until they appeared in the journal. Gibson and Flynn complied with the request, although they say that it disrupts the normal flow of scientific discussion. "I'm quite stunned that *Science* is more concerned with being first than they are with being correct," Gibson says.

But the proverbial cat is out of the bag. Every one of the several experts *Science* contacted was already intimately familiar with the preprints in question. And their consensus on the white dwarf controversy is that the new survey has turned up some dark matter, but maybe not as much as the team claims. "I'd say that the Oppenheimer team makes a few assumptions that tend to increase the number of their white dwarfs attributed to the halo," says astrophysicist Dave Bennett of the University of Notre Dame in South Bend, Indiana. "The Reid team does the opposite." Astrophysicist Brad Hansen of Princeton University agrees. "Bottom line, these white dwarfs are definitely interesting, and I'm not sure anyone has the right picture yet."

–MARK SINCELL

Mark Sincell is a science writer in Houston.

MIDDLE EAST

Two Pledges Boost SESAME Project

ANKARA—A long-planned synchrotron project for the Middle East took a major step forward last month after its Jordanian hosts pledged the money to house the instrument and its German donors agreed to ship it.

SESAME (Synchrotron Radiation for Experimental Science and Applications in the Middle East) was founded in 1999 to implement Germany's donation of BESSY-I,

ScienceScope

Appealing Case A state court judge has delivered a surprising setback to a Harvard researcher hoping to prove job discrimination. After a 3-week trial, a Massachusetts jury last month found in favor of biomathematician Tamara Awerbuch-Friedlander, who claimed that Harvard's School of Public Health denied her a promised slot on the tenure track and then retaliated against her for complaining (*Science*, 23 February, p. 1466). But before the jury could set damages, Judge Diane Kottmyer surprised both sides by dismissing the case, ruling that Awerbuch-Friedlander's 1994 complaint missed a filing deadline. Harvard officials declined comment. But Awerbuch-Friedlander says she will appeal, arguing that the timing issue is moot because Harvard actively dissuaded her from filing the complaint.

Fined Example Spurred by a government fine for violating pollution laws, the Massachusetts Institute of Technology (MIT) plans to become a model environmental citizen. The Environmental Protection Agency (EPA) has been battling the Cambridge, Massachusetts, university since 1998 over sloppy hazardous waste handling at more than 200 of its 2200 labs, and on 18 April the agency fined the school $150,000. But the same day, MIT announced that it will spend an additional $405,000 to build a Web-based "environmental campus" which will demonstrate how other schools can cope with complex environmental laws. Funds will also go to an education program at Cambridge public schools and a biofiltration storm water management system.

In a letter to MIT President Charles Vest, EPA official Sam Silverman wrote that MIT's plan "to go beyond its compliance obligations by taking on far-reaching green initiatives is laudable."

Italian Living Researchers worried about the future of science aboard the international space station got some good news on 19 April. A month after NASA said it would cancel a planned crew quarters module to save money (*Science*, 9 March, p. 1883), the Italian Space Agency said it might take on the project in return for greater access to the station for its astronauts and scientists. Researchers say the quarters are essential, because they will house the larger crew needed to run planned experiments. NASA and Italian officials warn that it may take months to nail down a deal.

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