tential drugs in a variety of cells, but they rarely use healthy human liver cells, says Strom, who is a liver expert, because the cells are very hard to obtain. Now, he says, "we have to be cognizant that we might miss some things. There is not really much in these preclinical studies [of TRAIL] that could have been done differently."

Strom did not set out to study TRAIL's role as a cancer drug. With graduate student Minji Jo and their colleagues, he was trying to find the molecular players that bring about liver cell death in diseases such as hepatitis and alcoholic cirrhosis. Previous work had shown that TRAIL kills cancer cells by triggering a form of cell suicide called apoptosis, and the team wanted to find out whether TRAIL-induced apoptosis might also be involved in the premature death of diseased liver cells.

Much to their surprise, the researchers found that TRAIL readily induces apoptosis in cultured liver cells from both sick individuals and healthy liver donors. Because the protein had never before been shown to trigger death in animal liver cells, "we thought [the result] was a fluke," perhaps an artifact of the team's culture conditions, recalls Strom.

Further work ruled out that possibility. For example, the team found that TRAIL also induces apoptosis in cells anchored in liver slices. And, in accord with previous findings, the researchers found no effect of TRAIL on cultured human epithelial cells derived from liver tissue or on rat, mouse, or monkey liver cells. "The animal cells are resistant in the culture dish, in whole livers, and in the live animal," Strom sums up. "This was not a culture artifact."

So why do human liver cells remain susceptible to TRAIL when other normal cells appear to fend the molecule off? Work a few years ago suggested that tumor cells succumb because they, unlike normal cells, fail to make a so-called decoy receptor that sops up TRAIL and prevents it from triggering the receptor that, in turn, programs cell suicide (*Science*, 8 August 1997, pp. 768, 815, and 818). But Strom and his colleagues found no differences between human liver cells and others in the production of either the decoy or regular TRAIL receptors. "This is very difficult to explain," says Nagata, whose own work focuses on apoptosis. "Perhaps, some factor is produced by mouse or monkey hepatocytes but not humans' that can inhibit TRAIL."

Researchers at Immunex and Genentech think there might be a simpler and, from their view, more favorable explanation for the Pittsburgh team's findings. Often, especially in the standard bench-top purification method used by Strom's group, TRAIL proteins clump together, forming "multimers" that are more toxic to cells than more natural preparations, says Douglas Williams, executive vice president and chief technology officer at Immunex. "The studies being reported are interesting," he adds, "but they have not been performed with the material we have been producing here at Immunex and Genentech."

To see whether that accounts for the discrepancy between the current observations and those made previously, Strom and the Immunex-Genentech workers will exchange their TRAIL preparations, and each group will redo the tests with the other's material. Until the results are in, TRAIL's fate will hang in the balance. "There is no magic drug for cancer at the moment," Nagata says.

–TRISHA GURA

Trisha Gura is a science writer in Cleveland, Ohio.

ADVANCED TECHNOLOGY PROGRAM

Grants Evoke Squeals Of Delight and Anger

It's easy to understand why the "Three Little Pigs" is David Ayares's favorite children's story. On 14 March Ayares's company, PPL Therapeutics Inc. of Midlothian, Scotland, surprised the scientific community by announcing that it had successfully cloned a pig from an adult cell, taking a small but vital step toward its goal of mass-producing organs to be transplanted into humans.

Corporate pork? ATP-funded research by PPL Therapeutics led to these cloned pigs.

Last week Ayares told a version of the story to an audience at the U.S. National Academy of Sciences, recounting how a $2 million grant last fall from a beleaguered federal research program had rescued his U.S.-based project. The grant came just in the nick of time, he said, as the company was ready to pull the plug because success seemed too far away. But unbeknownst to Ayares, at the very moment he was relating his story, a Big Bad Wolf on Capitol Hill

ScienceScope

Genome Club The zebrafish may soon join the elite list of organisms honored by having their entire genome sequenced. The Wellcome Trust's Sanger Centre is expected to make the little striped swimmer the target of a new large-scale sequencing project, Philip Ingham, a developmental geneticist at the U.K.'s University of Sheffield, announced last week at the Cold

Spring Harbor Laboratory in New York. Ingham told a meeting of developmental biologists—who value the species for its transparent embryos—that he is "99% certain" that Wellcome trustees will approve the project.

As the Sanger Centre winds down its work on the human genome in October, Ingham said, it will have the capacity to start sequencing the fish. He estimated that the center could complete a rough draft of the 1.8-billion-base-pair genome in 2 years. As with human data, the center plans to release its newest fish sequences nightly to a public database. "I am ecstatic," said geneticist Stephen Johnson of Washington University in St. Louis. "If Sanger does it, we are going to get a fantastic product."

Russian Roulette The U.S. government must step up efforts to prevent former Soviet weapons scientists from selling their services to hostile nations, experts say. Meeting in Washington last week, members of an outside task force reviewing the Department of Energy's (DOE's) beleaguered nonproliferation programs took the department to task for not taking the threat seriously enough. "Future generations are going to look back on this period and wonder why we didn't do more," said former representative Butler Derrick (D–SC), now a lobbyist.

The State Department estimates that DOE, State, and Defense Department assistance programs, funded to the tune of about $175 million this year, have helped fewer than 15,000 of Russia's 50,000 nuclear, biological, and chemical weaponeers find civilian work. To improve on that record, the task force plans to give DOE advice on how to persuade Congress—which is skeptical that the conversion programs work—to go for a big boost in the 2002 budget.

Contributors: Michael Baker, Michael Hagmann, Gretchen Vogel, Richard Stone

CREDITS: (TOP TO BOTTOM) STEPHEN L. JOHNSON/WASHINGTON UNIVERSITY; PPL THERAPEUTICS

was trying to blow his house down.

What Ayares was praising, and what Representative James Sensenbrenner (R–WI) was criticizing, was the Advanced Technology Program (ATP) run by the National Institute of Standards and Technology (NIST). Created by a 1988 law aimed at making U.S. companies more competitive in global markets by funding innovative research with potentially high payoffs, ATP for the last decade has been a $1.5 billion political litmus test for whether the government should subsidize corporate research. A hard-earned truce in recent years has left ATP with an annual budget of about $200 million, far below what the Clinton Administration has requested in most years but much more than many Republicans say it deserves.

Last week Sensenbrenner, chair of the House Science Committee, tried to shatter that truce by releasing a report (GAO/RCED-00-114) questioning ATP's ability to plow new ground. ATP is violating its mission by backing projects that "addressed similar research goals to those already being funded by the private sector," the Government Accounting Office (GAO) concluded after examining three ATP awards. Although the auditors concede that company scientists pursued "unique technological approaches" in carrying out the funded work, Sensenbrenner complained in a press release that ATP was "duplicating private research and shortchanging taxpayers."

ATP supporters say that the report's methodology and conclusions are badly flawed. NIST Director Ray Kammer says its definition of "similar research" is so broad that "by that doubtful criterion we would shut down federal research on cures for a host of diseases" and many nonmedical projects. One participant in last week's academy meeting saw the report as old wine in new bottles: "It's part of a continuing battle by those who dislike ATP."

For Ayares, PPL's vice president for research, the idea that his ATP grant is duplicative ignores both the formidable technological challenges his pig xenograft team faced and the fact that the company was ready to jettison the project. "We were going down," Ayares told his audience. The company laid off a third of its research staff in Blacksburg, Virginia, and shut down complementary projects there involving cows and rabbits. Ayares could read the writing on the wall: "My house was on the market," he confesses.

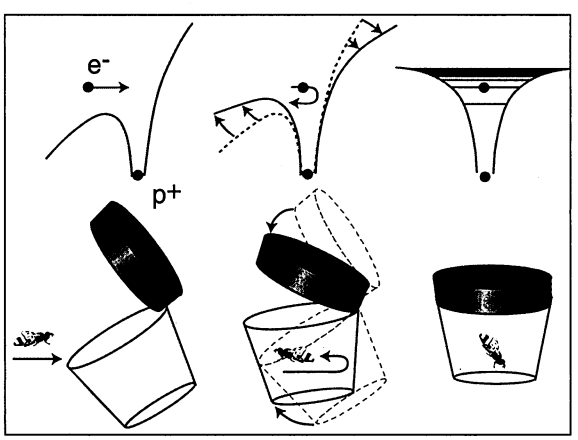
Instead, 5 months after receiving the grant, the company announced the Caesarian birth of five piglets cloned from adult cells. Big Pharma companies and venture capitalists that had once shunned the work as too speculative are now calling him on the phone and begging him to do a deal, Ayares says. The company's board of directors "now agrees to support us for as long as it takes" to find support for clinical trials and commercialization of the technology, he crows. "Without ATP," he says, "there would be no cloned pigs, only 4 years of intellectual property." –JEFFREY MERVIS

ANTIMATTER

Coaxing Shy Particles Into an Atomic Jar

One major frustration the universe inflicts on physicists is a serious shortage of antimatter. It should be fascinating stuff—looking-glass atoms with negatively charged nuclei surrounded by clouds of positive charge, and with who knows what bizarre properties—but no one has ever made enough of it to tell.

That could change, thanks to a new method a Dutch-American team has demonstrated for recombining free electrons with ions to form atoms. In the 24 April *Physical Review Letters*, researchers led by Bart Noordam of the FOM Institute for Atomic and Molecular Physics (AMOLF) in Amsterdam describe how they enabled rubidium ions to trap electrons by applying a pulsed electric field in a series of steps similar to the way a child traps an insect in a jar. The team claims the technique can be used to produce atoms of antihydrogen, the simplest form of antimatter, in greater numbers than ever before.



Atom trap. Like a child catching a wasp, shifting electric fields stop a speeding electron, then block its escape.

"So far there is no proven way to make these atoms, so any additional suggestion is certainly welcome," says Theodor Hänsch of the Max Planck Institute for Quantum Optics in Garching, Germany. Thomas Gallagher of the University of Virginia in Charlottesville agrees wholeheartedly. "A few years ago, I would have thought this is completely nuts," he says. "I think it is a nifty trick."

To create antihydrogen, scientists must nudge a positron—the antiparticle of an electron—into a quantum-mechanical dance around a negatively charged antiproton. Between 1995 and 1997, physicists at CERN, the European particle physics laboratory near Geneva, and at the Fermi National Accelerator Laboratory near Chicago forged 108 atoms of antihydrogen in particle accelerators, but all perished in collisions with accelerator walls within billionths of a second. Because of the short life-span, Noordam says, "this was not a method that ever could lead to antimatter that we actually could study."

Researchers tried to extend the longevity of antihydrogen by catching it in Penning traps, devices that slow down and confine atomic particles through an interplay of electric and magnetic fields. In 1996, physicists at CERN tried bringing together antiprotons and positrons in such a trap, but the energetic positrons just flew past the antiprotons without forming atoms. "You can compare this to the flyby of a spacecraft around a planet," Noordam says. If the spacecraft is moving too fast, it will swerve past the planet and out into space. To put it into orbit, you must first reduce its energy.

Scientists are investigating several braking maneuvers for a positron approaching an antiproton. Hänsch and colleagues plan to use laser light to stimulate the positron to emit a photon, jettisoning enough energy for the antiproton to capture it. Another team, led by Gerald Gabrielse at Harvard University, is investigating a method called three-body recombination, in which the positron transfers some of its energy to another, onlooking positron. Researchers plan to test those methods and others when CERN's new Antiproton Decelerator becomes available for experiments later this year, but the yield of antiatoms is still expected to be very small.

Noordam and Kees Wesdorp at AMOLF think their new technique can do much better. As stand-ins for positrons and antiprotons, they shoot electrons into tiny clouds of rubidium ions. The speeding electrons swerve toward the oppositely charged rubidium ions. Before the electrons can swing past the ions and escape, an electric field decelerates them and turns them back. Then, suddenly, the field is switched off, leaving some of the stalled electrons easy prey for the rubidium ions to capture into wide orbits. Researchers compare the method to the way a child coaxes a wasp into a jar, then clamps on the lid just as the wasp turns around to escape.

The AMOLF team obtained three atoms for every 1000 free ions, more than 100 times better than other methods, Noordam says. "This is very efficient, and this is impressive," says Hänsch's collaborator, Joachim Walz.

SOURCE: FOM/AMOLF