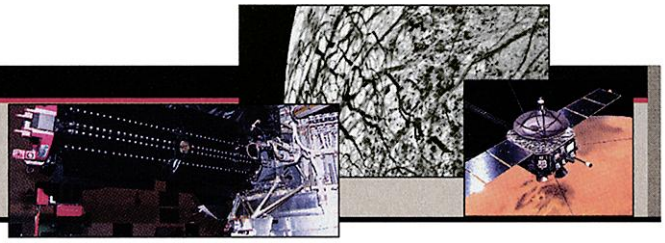
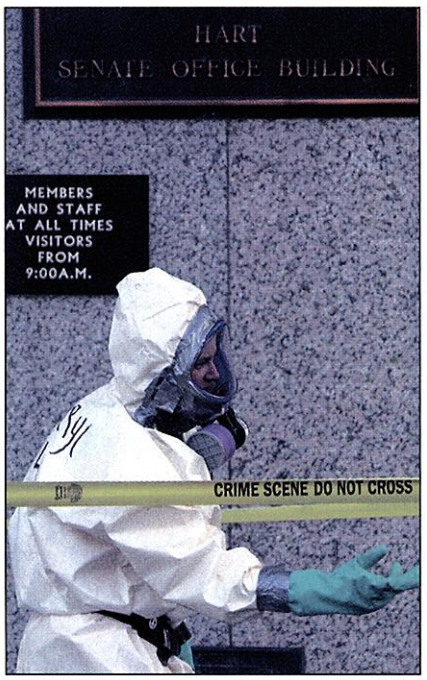


restores a cut of nearly $150 million that the Administration had proposed for Department of Energy programs aimed at securing Russian nuclear materials and keeping ex-Soviet scientists from taking their talents to enemy nations. And it includes some goodies for NIH as well: The National Institute of Allergy and Infectious Diseases will get $85 million for bioterrorism-related research and $70 million to build an ultrasecure laboratory for working with dangerous pathogens.

Bioterrorism security. At the last minute, lawmakers removed language from the defense spending bill that would have tightened security requirements for researchers working with potential bioweapons. The American Society for Microbiology and other groups had scrambled to help Congress craft workable regulations on worker screening and registering of pathogens, and some of those measures were attached to the Senate's version of the spending bill. After House leaders objected to using an appropriations bill to pass the new rules, however, the two bodies agreed to finalize separate bioterrorism security legislation early next year.



Fighting terrorism. NIH gets a new lab to work with dangerous pathogens and the government beefs up security.

Science education. The science education community got its heart broken by congressional appropriators. On 18 December, science education lobbyists celebrated completion of a highly publicized reform of federal funding for elementary and secondary education. Among many other provisions, the new law authorizes the Department of Education to spend up to $450 million a year on partnerships between universities and local school districts to improve math and science. Later that day, however, the committee that actually hands out the money approved a paltry $12.5 million for the program. "We're still recovering from the shock," says a disheartened Jodi Peterson of the National Science Teachers Association.

"It's kind of interesting that in the midst of all this talk about improving education, math and science are left out of the picture," says Representative Vernon Ehlers (R–MI), a long-time advocate for better science education. He also scolded scientists for not getting more involved sooner. "It was a question of too little, too late," he said. But Congress did provide at least a little solace: Earlier this year it gave the National Science Foundation $160 million to start a similar partnerships program.

NIST earmarks. The construction budget of the National Institute for Standards and Technology (NIST), approved in November, is larded with an unprecedented level of earmarks. Senator Judd Gregg (R–NH), the top Republican on the committee that oversees NIST's budget, managed to steer a staggering $18 million to his home state of New Hampshire, part of $41 million in earmarks for a $62 million account. NIST's overall budget rose 13%, to $674 million, due to the earmarks and a 27% increase, to $185 million, for the Advanced Technology Program. But NIST's $321 million core research budget edged up by only 3%. "I am amazed to see that we are more concerned about 'pork' than supporting world-class research facilities," says Senator John McCain (R–AZ), who regularly rails against the practice.

Researchers are already wondering about the effects of earmarks on next year's budget. The Bush Administration, which will release its 2003 budget proposal on 4 February, has said that rising security needs and a declining economy will leave little room for new research initiatives. But, while Bush has threatened to veto any bill that smells too strongly of bacon, Congress often holds the upper hand in budget battles.

–DAVID MALAKOFF

With reporting by Jeffrey Mervis.

CREDITS: (TOP TO BOTTOM) KENNETH LAMBERT/AP; RANDALL S. PRATHER

XENOTRANSPLANTATION

Cloned Pigs May Help Overcome Rejection

The cloning of Dolly the sheep nearly 5 years ago raised the hopes of transplant scientists looking for an endless supply of life-saving organs. It was a key step toward creating a line of identical animals genetically engineered so their organs could be used in people. Now, a team led by researchers at the University of Missouri, Columbia, has made another major advance—the creation of four cloned piglets that lack one copy of a gene that causes pig organs to be rejected by the human immune system.

"This is something that's been eagerly awaited," says immunologist Jeffrey Platt of the Mayo Clinic in Rochester, Minnesota, an expert in xenotransplantation, or animal-to-human transplants. The work, published online this week by *Science* (www.sciencexpress.org), brings researchers halfway to their goal of producing live pigs lacking both copies of the gene. It puts the Missouri group ahead of a pack of companies, one of which has just welcomed the birth of knockout pigs, that are pursuing the same goal.

Pigs are the most promising species for organ transplants because they are physiologically similar to humans and, unlike nonhuman primates, are in plentiful supply. But progress in the field has been slow for two reasons—the fear of new viruses being transmitted from pigs to humans and the almost certain rejection of the transplanted organ.

Pigs produce a sugar, a link between two galactoses, on the surface of their endothe-

Handling rejection. This piglet lacks one copy of a sugar-producing gene that makes humans reject pig organs.

lial cells that humans and Old World monkeys do not make. Primates' immune systems recognize this sugar as a foreign antigen and attack the pig cells, leading to "hyperacute rejection" and organ failure.

Researchers have addressed the problem by endowing transgenic pigs with protective proteins to counter the immune response, which has allowed the organs to function in primates for months rather than days. But the only complete solution is thought to be a pig lacking the gene for the enzyme galactosyltransferase that makes the sugar. Cloning technology raises the possibility of disrupting, or knocking out, this gene in cultured cells, then inserting the nucleus of the modified cells into an empty pig egg to create embryos.

The first cloned pigs were created in 2000 (*Science*, 18 August 2000, pp. 1118 and 1188). Now, animal scientist Randall Prather and his team at Missouri, along with collaborators at Immerge BioTherapeutics Inc. in Charlestown, Massachusetts, have knocked out the galtransferase gene in fetal cells used to make cloned piglets.

To disrupt the gene, the researchers used a "gene trap" vector, a piece of DNA containing snippets complementary to the target gene along with sequences for antibiotic resistance. They moved this vector across the cell membrane and into the nucleus by jiggling the cells with electricity. They then treated the cells with antibiotics to kill all but the cells that contained the inserted DNA, then screened for those that had it in the right location. This replaced gene causes the cell to make a truncated version of galtransferase. Because the odds of a successful insert were only 1 in 5 million, the team didn't expect to get any cells with both alleles knocked out.

The researchers then fused these modified fetal cells with oocytes from which the chromosomes had been removed by zapping the cells with electricity, which kick-started the process of cell division. They implanted these embryos into sows that had just come into heat.

Because fetal cells stop dividing after a few weeks in culture, the team had to move quickly. "We did a bunch of things in the lab differently" to speed up the modification and testing steps, Prather says. All the same, the team had to implant more than 3000 embryos in 28 surrogate sows to get seven live piglets born in September and October, a 0.2% success rate. "It's a rather heroic piece of work," says cattle cloning researcher George Seidel of Colorado State University, Fort Collins. And the work isn't over: The four surviving piglets, all females, still make the galactose link with their good copy of galtransferase.

At least two other companies are hot on the Missouri team's heels. Advanced Cell Technology of Worcester, Massachusetts, say they are close to announcing the birth of pigs lacking the galtransferase gene. And David Ayares of Scotland-based PPL Therapeutics's lab in Blacksburg, Virginia, told *Science* at press time that five pigs appearing to have the knockout allele were born on Christmas Day. Prather says the next step, which his group hopes to achieve within 18 months, is to produce double knockout pigs using conventional breeding methods.

–JOCELYN KAISER

ANTIBIOTIC RESISTANCE

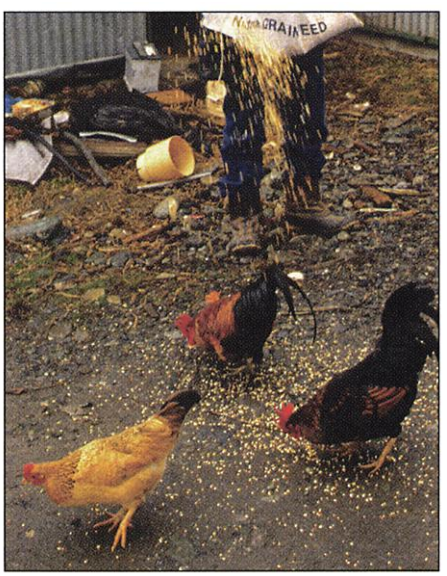
Livestock Feed Ban Preserves Drugs' Power

CHICAGO—It's no secret that livestock fed antibiotics breed drug-resistant bacteria that can cause dangerous infections in people. But a new study suggests that the process is reversible. Banning a drug called avoparcin from animal feed dramatically reduced the chances that potentially dangerous gut microbes in hospital patients would be resistant to an important, related drug, Belgian researchers reported last month at a meeting* sponsored by the American Society for Microbiology.

The results are the first to show that cutting antibiotic use on the farm leads to reduced resistance in hospital patients—those who need antibiotics the most, says microbiologist Stuart Levy of Tufts University School of Medicine in Boston. "This says there's a strong connection between what's done in animals and what you see in people," he says.

Farmers mix low doses of antibiotics into

* The Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, 16–19 December 2001.



Just say no. Cutting antibiotics from chicken feed reduces microbes' drug resistance in people.

CREDIT: PHIL SCHERMEISTER/CORBIS

ScienceScope

THE YEAR AHEAD

Weather forecasting models may not be reliable beyond a few days out, but ScienceScope is willing to stick out its neck for an entire year. Here are some likely science-related developments in 2002:

New Faces at NIH A director will finally arrive—and immediately face questions about the best way to adapt to slower budget growth. A report from a congressionally ordered panel due out within a year of the new director's appointment is rumored to be looking at merging several institutes as part of a perennial quest to make the Bethesda biomedical behemoth more efficient.

ITER Inches Ahead Plans for a multibillion-dollar international fusion reactor will continue to crawl forward, with the United States making noises about rejoining the project. The Bush Administration is mulling requests to send observers to planning meetings—although other partners say they don't want the United States present unless it is ready to pony up some cash. In 1998 U.S. officials pulled out of a more costly version of the project.

Kyoto Clash The Bush Administration is still working on an alternative to the Kyoto climate change treaty. In the meantime, dozens of other nations may implement a carbon emissions–trading scheme that would allow some countries to emit more of the gas in exchange for undertaking projects—such as tree planting—to soak up carbon.

To Clone ... Or Not? The U.S. Senate will debate a controversial bill to ban human cloning early in the year, while nations from Germany to China continue to discuss how to regulate their own cloning and stem cell research. Some researchers fear that talent and resources will flow to countries with the most permissive laws.

Deep Dreams Scientists hoping to convert an abandoned gold mine in South Dakota into the world's deepest laboratory will find out whether National Science Foundation (NSF) reviewers think the idea is a good one. Backers haven't waited for NSF's blessing to move ahead with the $300 million project, however. Senate Majority Leader Tom Daschle (D–SD) last month tucked language into a defense spending bill that makes the mine state property, opening the way to future renovations.