among the microbes used in the attacks and other representatives of the Ames strain. At the meeting, Keim reported an advance that may help federal investigators home in on the bioterrorists who sent the anthrax letters last fall. With a new marker discovered in his lab last year and dubbed Homomeric-1 (HM1), Keim says he's able to tell apart five different Ames strains, four collected from research laboratories and one from a goat that died in Texas in 1997.

At the HM1 locus, *B. anthracis* has between 12 and 35 copies of adenine, one of DNA's building blocks, and the number varies for all five isolates. If the strain used in the mail attacks matches one of the strains obtained from laboratories, it could tell investigators where to focus their attention. But Keim, following FBI orders, declines to say which four labs the strains came from, or whether he had checked the Florida isolate for the same marker. **–MARTIN ENSERINK**

CLONING

Carbon-Copy Clone Is the Real Thing

"While the cloning of companion animals is not yet possible, Advanced Cell Technology is currently able to store cells from your animal now."

—ACT Web site, 15 February 2002.

ACT needs to update its Web site. Last week, scientists in Texas unveiled the first clone of a pet—a kitten named CC, short for Copy Cat (also Carbon Copy). The kitty is the fruit of a privately funded initiative, Operation CopyCat, started a year ago by Mark Westhusin and colleagues at Texas A&M University, College Station. It's actually part of a larger and much more difficult project that aims to clone a dog.

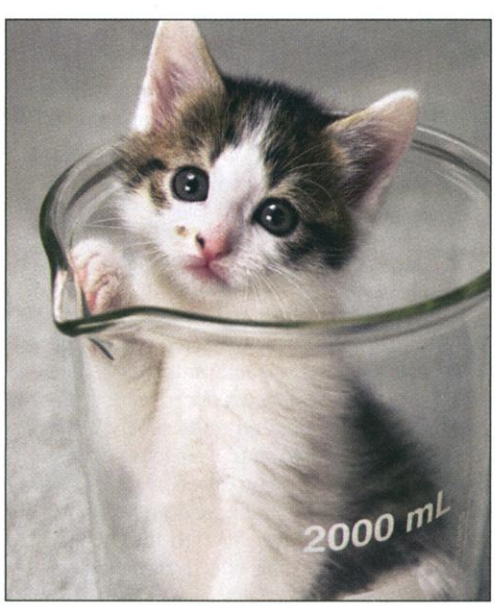
The researchers, who report their feat in the 21 February issue of *Nature*, say cat cloning is just about as efficient (or inefficient) as duplicating mice, cows, sheep, goats, or pigs. Westhusin's team first attempted to use skin fibroblast cells, inserting their nuclei into enucleated cat eggs. Although 82 cloned embryos were implanted into seven surrogate mother cats, only one pregnancy resulted, and the fetus died. In their next try, the scientists created embryos using nuclei from the cumulus cells surrounding the ova of a calico research cat named Rainbow. They implanted five embryos in a surrogate mother—three from cumulus cells and two from the oral mucosa cells. This time, one of the embryos from a cumulus cell made it to term. That puts the success rate at one out of 87.

Born by cesarean section on 22 December 2001, CC is a lively, normal-looking feline, the researchers say. She's not an exact copy of her calico progenitor because these coat markings result partly from random events during development. "I'm not at all surprised at the success of the Texas A&M team; they're an excellent group of scientists," says Robert Lanza, medical director of ACT. He says ACT is moving away from pet cloning and has licensed its technology to the Texas group and others.

CC is the first creation to emerge from the Missyplicity Project. The project was launched 5 years ago by 81-year-old Arizona financier John Sperling, who wants to be able to replace his husky–border collie mix, Missy, when her time is up (*Science*, 4 September 1998, p. 1443). So far, Sperling has put $3.7 million into the Texas A&M group's cloning efforts through a new company called Genetic Savings and Clone, based in College Station, Texas, and Sausalito, California.

Dog clones, however, are still a long way off, Westhusin cautions. "Assisted reproduction technology in cats has all been worked out," he says. And "you can get them to come into heat when you want." But dogs come into heat more rarely and unpredictably. Dogs also release immature eggs from their ovaries, and researchers have found it very difficult to get them to ripen in a test tube. The focus in this area, says Westhusin, is still "how do you get viable ova."

The public appears willing to wait for dog cloning—and probably to pay $20,000 or so for it. Lou Hawthorne, CEO of Genetic Savings and Clone—which stores tissue for possible future pet cloning and is gearing up to open its own lab—says the start-up was formed in response to public demand. "When we launched [it] 2 years ago, we got thousands of calls within the first 24 hours," he says. The company hopes to be offering

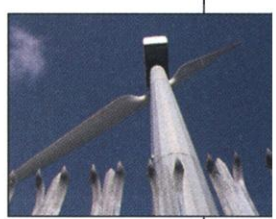


Copied cat. Two-month-old CC seems normal so far.

CREDITS: (TOP TO BOTTOM) NEIL BEER/CORBIS; RICHARD OLSENIUS

ScienceScope

Energetic Discussion U.K. researchers have mixed reactions to a call for a new national energy research center. A government panel reviewing energy policy last week recommended that a new center is needed to energize studies of power use, production, and environmental and social issues. Chemist David King of the University of Cambridge, the government's chief scientist and head of a subpanel that looked at energy research, says the center would help pull together a "broad menu" of new energy technology studies.



But Ian Fells, an energy expert at the University of Newcastle, favors a more decentralized approach that would boost energy research at "half a dozen" local research centers. That is just one funding model currently being studied by the U.K.'s research councils, which oversee government science spending.

No final decision is expected soon. The energy panel's recommendations are now open for public comment, and a final long-term strategic plan is due later this year.

Oversight Overlords British researchers say pending legislation to prevent the export of sensitive technologies to hostile countries could give the government too much control over what research gets published. According to the lobby group Universities UK (UUK), a revised Export Control Bill now before the House of Lords would give the Department of Trade and Industry (DTI) the right to review new research before it is submitted for publication. DTI would also be able to impose controls on e-mails and instruction manuals covering topics deemed sensitive. The current law applies only to tangible objects and descriptions of certain military technologies.

DTI officials insist that the rules would pertain only to applied research and that additional legislation will define and exempt basic research from export control oversight. UUK, however, wants to see academic freedom enshrined in the export law itself and is seeking support for an amendment during debate next month.

Contributors: Andrew Lawler, Gretchen Vogel, David Malakoff, Adam Bostanci

cat cloning on a "case-by-case basis" by the end of the year, according to spokesperson Ben Carlson.

For now, at least, pet cloning is mainly of interest to sentimental animal lovers and not to serious dog and cat people. Currently, says Michael Brim, spokesperson for the Cat Fanciers' Association in Manasquan, New Jersey, a clone "wouldn't be registrable with us as a pedigreed cat" because of its irregular parentage. Cloning, says Brim, "would basically jump over all the genetic rules of breeding" and take all the sport out of cat fancying. Besides, the whole idea is to breed animals to approach a perfect ideal, so a clone would be a ready-made has-been.

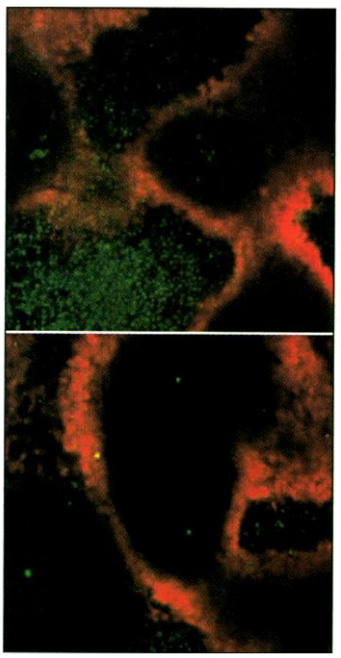
–CONSTANCE HOLDEN

CANCER RESEARCH

Obstacle for Promising Cancer Therapy

Cancer cells are wily. Drug therapies may temporarily halt tumor growth, but all too often the agents lose their effectiveness as the cells' genetic versatility allows them to become resistant. Researchers hoped that so-called antiangiogenesis therapies, which are aimed at preventing the growth of the new blood vessels needed to nourish tumors rather than at the tumors themselves, might circumvent this problem. But recent work suggests that tumors may be able to get around angiogenesis inhibitors, too.

The latest example comes from Joanne Yu, Robert Kerbel, and their colleagues at Sunnybrook and Women's College Health Sciences Centre in Toronto. They report on page 1526 that tumors in which the *p53* tumor suppressor gene has been inactivated—which happens in about 50% of human cancers—are much less responsive to angiogenesis inhibitors than comparable tumors in which the gene is still functional. Researchers already knew that cancer cells can counteract the inhibitors by pouring out more of the factors that promote new blood vessel growth. But loss of the *p53* gene apparently renders tumor cells better able to survive in the low-oxygen conditions present in tumors deprived of an ample blood supply.



Holding their breath. Cells without *p53* (*bottom*) withstand hypoxic conditions in tumors better than do those with the gene (*top*), whose death throes are indicated by green staining.

James Pluda—who has just left the National Cancer Institute, where he oversaw antiangiogenesis trials, for MedImmune Inc. in Gaithersburg, Maryland—describes the Kerbel team's experiments as "a very nice piece of work," one that will help researchers decipher results from clinical trials of angiogenesis inhibitors. Already, some 40 agents are being tested worldwide against a wide range of cancers. Neither Pluda nor others expect the new results to preclude development of the inhibitors. But, Pluda notes, the findings "give us something to look at if patients whose cancers initially respond then progress."

Some 12 years ago, Kerbel proposed that therapies based on inhibiting new blood vessel growth might not be prone to the resistance problem. But hints to the contrary have appeared in the literature, particularly when angiogenesis inhibitors are given alone. Two years ago, for example, Kerbel and his colleagues found that treating human tumors growing in mice with single antiangiogenesis drugs caused them to shrink—but after a month or two they began growing again. Kerbel wanted to know, he recalls, "why were we getting these relapses?"

A clue came last year when his team found that cells within a single tumor vary in their ability to withstand the low-oxygen (hypoxic) conditions that angiogenesis inhibitors create. Because work by other investigators had shown that *p53* loss makes cells more resistant to hypoxia, Kerbel, Yu, and their colleagues decided to test whether that genetic change could account for the reduced susceptibility to angiogenesis inhibitors.

They obtained two lines of human colon cancer cells from Bert Vogelstein's group at Johns Hopkins University School of Medicine in Baltimore, Maryland; the lines were identical except that in one, the *p53* gene had been inactivated. The Sunnybrook workers then transplanted either the unaltered cells or the $p53^{-/-}$ cells into mice. The tumors produced by the unaltered cells "responded quite nicely" to a combination of two antiangiogenic drugs, Kerbel says. But those produced by the $p53^{-/-}$ cells took longer to shrink, and the response was shorter lived, even though the therapy had shown long-lasting effectiveness in previous animal tests.

When the researchers then implanted equal mixtures of $p53^{+/+}$ and $p53^{-/-}$ cells in single mice, the proportion of $p53^{+/+}$ cells decreased dramatically after treatment with the angiogenesis inhibitors. This result also suggests that in natural tumors, which usually consist of genetically diverse cell mixtures, antiangiogenesis therapy might select for the growth of $p53^{-/-}$ cells.

As the Sunnybrook team suspected, the $p53^{-/-}$ cells survived better because they are more tolerant of hypoxia. In mixed tumors, the $p53^{+/+}$ cells tend to cluster around the oxygen-giving blood vessels, and those in the more hypoxic regions succumb to the cellular suicide known as apoptosis. In contrast, very few $p53^{-/-}$ cells died of apoptosis even in low-oxygen regions.

Although Kerbel concedes that the new results are a "bit of a downer," he maintains that "they don't negate the idea of exploiting antiangiogenesis therapy." Indeed, as angiogenesis pioneer Judah Folkman of Children's Hospital Boston points out, although tumors may be able to reduce their reliance on the vascular supply, "this paper should not be misinterpreted to mean that tumors can grow under completely [oxygen-free] conditions." This might be achieved by combining angiogenesis inhibitors with other drugs that destroy existing blood vessels.

Folkman and Kerbel outline additional strategies that might get around the problem of tumor resistance to antiangiogenesis therapy, such as upping the dose of the inhibitors or giving them with drugs that specifically target hypoxic cells. The trick to defeating cancer, this work shows once again, will be to outmaneuver the enemy.

–JEAN MARX

MICROBIOLOGY

Weight of the World On Microbes' Shoulders

Bacteria withstand stress far more gracefully than the rest of us. Sizzle them to above 110°C, freeze them to below –10°, douse them with salt or acid—and, if they had eyelashes, they'd barely bat any. Now a study takes stressful conditions to a new extreme, crushing microbes beneath the equivalent of a 160-kilometer column of water—and showing that, voilà, they survive. To some microbiologists this suggests that similar organisms might survive the high-pressure environments of other celestial bodies, like Jupiter's moon Europa.

To engineer this pressure, geochemist Anurag Sharma, microbiologist James Scott, and their colleagues at the Carnegie Institution of Washington in Washington, D.C., took a 50-year-old tool used by physicists and applied it to microbe physiology for the first time. The high-pressure device, called a diamond anvil cell, is created by

CREDIT: J. YU *ET AL.*