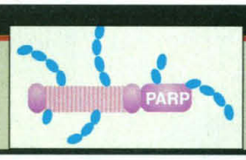

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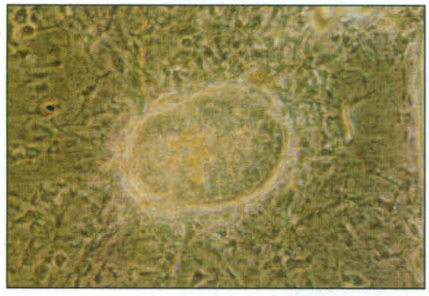
BIOTECHNOLOGY

Claim of Human-Cow Embryo Greeted With Skepticism

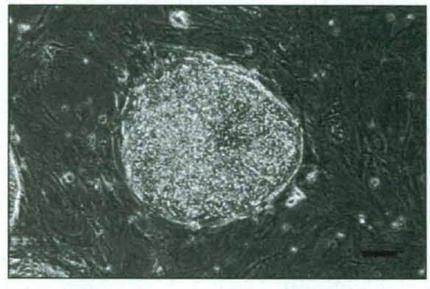
A small, privately held company in Worcester, Massachusetts—Advanced Cell Technology Inc.—startled the scientific world last week by announcing that it had fused human DNA with a cow's egg to create a new type of human cell. Company leaders say that a colony of these fused cells—created in 1996, kept alive for 2 weeks, and discarded—looked like a cluster of human embryo cells. On this basis, the company declared that it had "successfully developed a method for producing primitive human embryonic stem cells."



The claim, announced in a front-page news story in *The New York Times* on 12 November, came just 6 days after two groups of researchers reported in *Science* and the *Proceedings of the National Academy of Sciences* that they had used traditional techniques to culture human embryonic stem cells—"undifferentiated" cells that have the potential to grow into any cell type (*Science*, 6 November, pp. 1014 and 1145). It added to the concerns already raised among ethicists and government officials. On 14 November, President Clinton sent a letter to Harold Shapiro, chair of the National Bioethics Advisory Commission (NBAC), saying he is "deeply troubled" by news of the "mingling of human and nonhuman species." The president asked NBAC to give him "as soon as possible … a thorough review" of the medical and ethical considerations of attempts to develop human stem cells. And a Senate committee may review the company's claim at a hearing on stem cell technology planned for 1 December.

Scientists, however, were startled for another reason: They were amazed that Advanced Cell Technology (ACT) broadcast its claim so widely with so little evidence to support it. Some were puzzled that the company had tried to fuse human DNA and cow eggs without first publishing data on the fusion of DNA and eggs of experimental animals. Many doubted that ACT's scientists had created viable human embryonic stem cells. And most were left wondering why the company chose to go public now with this old experiment.

The company had inserted DNA from adult human cells into cow's eggs using a nuclear transfer technique similar to the one used to clone Dolly, the first mammal cloned from an adult cell. ACT's top researcher and co-founder—developmental biologist James Robl of the University of Massachusetts, Amherst—says an early version of the experiment was performed in his UMass lab "around 1990." A student carrying out nuclear DNA transfer in rabbits had run out of donor cells, Robl recalls, and, almost as a lark, took cheek cells from a technician and transferred their DNA into rabbit oocytes. "I didn't even know about it," Robl says. To everyone's surprise, the cells began to divide and look like embryos. "I got very nervous" on learning about it, Robl says, and shut down the experiment.



Scant evidence. Experts question whether the cells in ACT's circular colony *(top)* are really human embryonic stem cells, like those from James Thomson's lab *(bottom)*.

Robl and his former postdoc Jose Cibelli, now a staffer at ACT, returned to this line of experimentation in 1995 to '96, when they were working with cow embryos on other projects. They remembered that the human DNA–animal oocyte combination worked before, and "we thought, 'Maybe we can get a cell line' " this way. Cibelli transferred nuclear DNA from 34 of his own cheek cells and 18 lymphocyte cells into cow oocytes from which the nuclei had been removed. Six colonies grew through four divisions, according to Cibelli, but only one cheek cell colony grew beyond that stage—reaching 16 to 400 cells. Robl says they didn't follow up on the work because "we had about 15 other things we were doing," and developing human stem cells was not at the top of the list. But the university did file for a patent on the technique, granting an exclusive license to ACT.

Robl concedes that the experiment did not yield publishable data. He says he classified the cells as human stem cells based on his experience of "look[ing] at hundreds and hundreds" of cell colonies. But Robl offered no other data to support this conclusion.

Other researchers agree that the cells may have had human qualities, because they continued to divide after the cow's nuclear DNA had been replaced with human DNA. But Robl and Cibelli didn't do any of the tests normally done to show that these cells were human or that they were stem cells, such as looking for expression of human proteins or growth of specialized tissues. James Thomson of the University of Wisconsin, Madison, lead author of the *Science* paper, says that ACT's cells "meet none of the criteria" for embryonic stem cells. And Gary Anderson of the University of California, Davis, who has isolated a line of embryonic pig cells, comments: "Just because someone says they're embryonic stem cells doesn't mean they are."

A few researchers—including Robert Wall, a geneticist at the U.S. Department of Agriculture in Beltsville, Maryland—were willing to suspend their disbelief, however, if only because they respect Robl. He is "a top-notch, very solid scientist," says Wall, who adds that anyone who has examined a large number of embryonic cells can distinguish real ones from impostors.

But others are less charitable. "This may be another Dr. Seed episode," says Brigid Hogan, an embryologist at Vanderbilt University in Nashville, Tennessee, referring to Chicago physicist Richard Seed, who caused a furor early this year when he announced that he planned to clone humans. Although Seed didn't have the means to carry out his

CREDITS: (TOP) ACT; (BOTTOM) J. THOMSON *ET AL.*

project, Congress quickly drafted a criminal ban on many types of cloning research. Congress set that debate aside last spring but indicated it might take it up again later (*Science*, 16 January, p. 315 and 20 February, p. 1123). Hogan, a member of a 1994 National Institutes of Health (NIH) panel that proposed guidelines for human embryo research, agrees that "it's theoretically possible" to do what ACT claims to have done. But the company's announcement reminds her of the Seed case because "it smells to me of sensationalism" and seems "likely to inflame an uninformed debate."

Why did ACT publicize this experiment now? Some observers think the company wanted to ride the PR bandwagon created by the 6 November announcements by the labs that had isolated human embryonic stem cells using more traditional culture techniques. One group, led by developmental geneticist John Gearhart at The Johns Hopkins University, extracted primordial germ line cells from fetal tissue and kept them growing through 20 passages (transfers from one plate to another) for more than 9 months. The other group, led by Thomson at the University of Wisconsin, established a culture of stem cells derived from early human embryos. Thomson, whose cell line has survived 32 passages over 8 months, published molecular data suggesting that the cells may continue dividing "indefinitely."

Michael West, president and chief executive officer of ACT since October, says it is "pure coincidence" that ACT's news came out within a week of these announcements. West—noting that ACT won't benefit immediately, for it doesn't sell public stock—says that after becoming ACT's CEO last month, "I learned about the work that had been done in 1996 … and I wanted to develop this technology." But he says he "didn't feel comfortable" moving ahead with nuclear DNA transfer experiments without getting a reading on how future U.S. laws and regulations might affect the field. "So I decided, 'Let's talk about the preliminary results,' " says West. "Let's get NBAC to help clear the air."

West notes that some information on ACT's mixing of human and cow cells was already public. In February, the World Intellectual Property Organization in Geneva had published Robl's application for a patent on "Embryonic or Stem-like Cell Lines Produced by Cross Species Nuclear Transplantation" (WO 98/07841). It describes the Robl-Cibelli experiment of 1996 and stakes broad claims to stem cell technology based on transferring human or animal DNA into an animal oocyte. After being approached by the staff of CBS's news show *48 Hours*, West says, he arranged to discuss the research in exclusive but simultaneous releases to *The New York Times* and CBS. The CBS report aired on 12 November.

Robl confirms it was West, and not the scientific staff at ACT, who initiated the announcements. "I wouldn't have had the guts to do it," Robl says, although he agrees it is important to debate ethical concerns that might impede the technology.

These ethical concerns may get an airing next month. Senator Arlen Specter (R–PA), chair of the appropriations subcommittee that approves the budget for NIH, is planning a hearing on 1 December. There, NIH director Harold Varmus and developers of new human cell technologies are expected to testify about federal restrictions on the use of embryonic and fetal tissue and their impact on biomedical research. That discussion may now be expanded to include questions about ACT's single experiment. **–ELIOT MARSHALL**

With reporting by Elizabeth Pennisi.

CREDIT: (TOP) SPACE RESEARCH INSTITUTE, RAS; SOURCE: (BOTTOM) ANSER

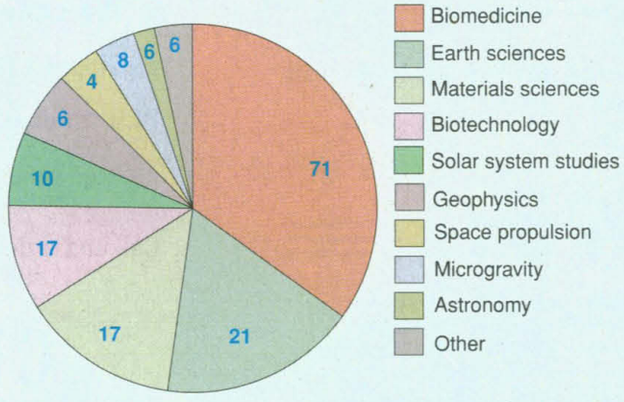
RUSSIAN SPACE SCIENCE

Station Launch Hides Lingering Woes

MOSCOW—Valery Bogomolov welcomes the scheduled launch today of the first piece of the international space station as a sign of the world's commitment to space exploration. But the launch is also a bitter reminder to Bogomolov, deputy director of Russia's premier space biology facility, the Institute for Biomedical Problems (IBMP), of his country's recent decision to sell NASA thousands of hours of station time earmarked for research by Russian cosmonauts for the $60 million needed to complete a key station component (*Science*, 9 October, p. 206). "It was very sad for us, and for Russian science," says Bogomolov, whose institute is scrambling to plan experiments on the ground that were meant to be done in space. "We had no warning."

Still grounded. Managers hope to get the Spectrum-X-Gamma mission into orbit by 2001.

As the rest of the space community readies its payloads for the $50 billion international space station, Bogomolov and his Russian colleagues must resign themselves to a limited role until at least 2003, when they will vie for a share of research time aboard the completed station. And the lost opportunity is only one of several continuing crises for Russian space science. The launch of the Russian-backed Spectrum-X-Gamma spacecraft, a $500 million international effort to study x-rays, is running almost a decade behind schedule. Even a last-ditch effort to postpone the dismantlement of the Mir space station, allowing some biology



Miraculous results. Biomedicine got the largest slice of Russia's $20 million of research on Mir, both in dollars and number of projects (in blue).