At 9:00 in the evening on January 29, just as President George W. Bush was about to begin his first State of the Union address, I gathered with three anxious scientists in a small, windowless laboratory in Worcester, Massachusetts. We were at Advanced Cell Technology—a privately owned biotechnology company that briefly made international headlines last fall by publishing the first scientific account of cloned human embryos. The significance of the achievement was debatable: the company's most successful embryo had reached only six cells before it stopped dividing (one other had reached four cells, another had reached two)—a fact that led to a widespread dismissal, in the media and the scientific community, of ACT's "breakthrough." The work was largely judged to be preliminary, inconsequential, and certainly not worthy of headlines. Many people in political and religious circles, however, had a decidedly different view. They deemed ACT's work an ethical transgression of the highest order and professed shock, indignation, and horror.

Nonetheless, ACT was pressing ahead—which was why I had come to the company's cloning lab that night in January. The door to the lab was locked; a surveillance camera mounted on the ceiling watched our every move; and the mood was at once urgent and tense. A human egg, retrieved just hours earlier from a young donor, was positioned under a microscope, its image glowing on a nearby video monitor. The egg's chromosomes would shortly be removed, and the scientists in the room would attempt to fuse what remained of the egg with a human skin cell. If the procedure succeeded, the result would be a cloned human embryo.

Skin cell to embryo—it's one of the most remarkable quick-change scenarios modern biology has to offer. It's also one of the most controversial. Since the announcement, in 1997, of the cloning of Dolly the sheep, attempts to use human cells for cloning have provoked heated debate in the United States, separating those who have faith in the promise of the new technology from those who envision its dark side and unintended consequences.

Crucial to the debate is the fact that human cloning research falls into two distinct categories: reproductive cloning, a widely frowned-on effort that aims to produce a fully formed child; and therapeutic cloning, a scientifically reputable procedure that takes place entirely at the microscopic level and is designed to advance medical therapies and cure human ailments. The two start out the same way—with a new embryo in a petri dish. But the scientists I was observing in the lab had no intention of creating a person. Instead they were embarking on an experiment that, if successful, would be a first step toward creating radical new cures for patients like the donor of the skin cell—Trevor Ross (not his real name), a two-year-old boy afflicted with a rare and devastating genetic disease.

The mood in the lab was tense in part because of the uncertain outcome of the experiment. But it was also tense because of concern over what President Bush might say about cloning in his address to the nation. A radio in one corner of the room was tuned to the broadcast as the scientists began their work, and they were listening carefully: in perhaps no other field of science are researchers as mindful of which way the political winds are blowing. The ACT scientists had good reason to be concerned—what they were doing that night might soon be made illegal.

On July 31 of last year, by a 100-vote margin, the U.S. House of Representatives passed the Human Cloning Prohibition Act of 2001, which would impose a ban on the creation of cloned human embryos for any purpose, whether reproductive or therapeutic. Both forms of cloning would be punishable by up to ten years in prison and a million-dollar fine. The House passed the measure over the objections of a long list of biomedical organizations (including the Association of American Medical Colleges and the American Society for Cell Biology) and patients' advocacy groups (including the Juvenile Diabetes Research Foundation International, the Alliance for Aging Research, the American Liver Foundation, and the Kidney Cancer Foundation). That same day House members overwhelmingly rejected an amendment, put forward by Congressmen James Greenwood, of Pennsylvania, and Peter Deutsch, of Florida, that would have preserved scientists' ability to use therapeutic-cloning techniques for medical research.
Politics and religion, it seemed, were trumping science. Therapeutic-cloning research was already ineligible for federal funding in the United States. In 1995 Congress had passed legislation barring the use of federal funds for any experiment in which a human embryo is either created or destroyed, thus making official a de facto ban that had been in existence since 1975. (Congress has renewed the federal-funding ban annually since 1995 as a provision of the Department of Health and Human Services appropriations bill.) As a result, the burden of moving many areas of important medical research forward has fallen on the private sector, a situation that by many accounts has severely hobbled research into treatments for infertility—and even disorders such as childhood cancer and birth defects. These research areas, like therapeutic-cloning research, demand the kind of long-term study and financial commitment that only the federal government can provide. This past summer human therapeutic cloning already fell squarely under the federal-funding ban, yet Congress was now going further, considering making that research illegal.

In the debate preceding the House vote in July, opponents of therapeutic cloning had warned against the "industrial exploitation of human life" and had conjured up images of "cloned human embryo farms" at which "human beings" would be manufactured as a source of raw material and then "killed" for parts—this despite the fact that researchers envisioned working with five-day-old embryos, balls of undifferentiated cells that could fit on the point of a pin. Congressman James Sensenbrenner, of Wisconsin, insisted that "those who are interested in values" should vote to ban therapeutic cloning. Tom DeLay, of Texas, the House majority whip, called the practice "monstrous science that lacks any reasonable consideration for the sanctity of human life." Congressman Chris Smith, of New Jersey, stated plainly, "Creating human embryos for research purposes is unethical, it is wrong, and it ought to be made illegal." The mood was summed up the following November by Congressman Dennis Kucinich, of Ohio, in the debate that followed ACT's announcement. Kucinich said, "The Creator that our founders referred to was not ACT."

During the debate about the House bill, a handful of speakers had risen to protest what one of them called "this papal event that we are having here today." Congresswoman Zoe Lofgren, of California, argued, "Our job in Congress is not to pick the most restrictive religious view of science and then impose that view upon federal law." Greenwood, who co-sponsored the amendment to keep therapeutic-cloning research legal, said, "I am not prepared as a politician to stand on the floor of the House and say, '... You cannot go there, Science, because it violates my religious belief.'" He added, "I think it violates the Constitution to take that position."

In August, President Bush made clear that he agreed with the restrictive position. He characterized therapeutic-cloning research as an attempt "essentially to grow another you, to be available in case you need another heart or lung or liver." He continued, "We recoil at the idea of growing human beings for spare body parts, or creating life for our convenience." The President's wording did nothing to clear up widespread ignorance of the difference between reproductive and therapeutic cloning. ("What's going to happen to those clones?" a caller to NPR asked last fall, with typical confusion. "I mean, do they just live in a closet for their whole life?")

Ever since the passage of the House bill, ACT had been waiting for the Senate to act. A vote had been expected in the fall, but the events of September 11 overshadowed the matter. As the winter recess approached, Tom Daschle, of South Dakota, the Senate's Democratic majority leader, signaled his intention to bring the cloning issue to a vote by the end of March. "We need to bring some scientific light on this subject," said Senator Arlen Specter, of Pennsylvania, a supporter of therapeutic-cloning research and the ranking Republican on a subcommittee hosting cloning hearings. "The scientific community is ready to put forward a very strong case, and I think that case will be persuasive to the Congress." In mid-January the prestigious National Academy of Sciences, created to advise Congress, reiterated its support for therapeutic-cloning research, a move that proponents of the technology were hoping would sway opinion in the Senate. The word on the Hill at the time, however, was that the vote on a ban could go either way.

Last fall, with the prospect of a Senate vote looming, I decided to take a considered look at cloning research. The time seemed right: it was a unique moment in what could be the development of a major new medical technology, an odd period of legislative limbo in which the first halting steps were being taken toward creating cloned human embryos just as such efforts were in imminent danger of being outlawed.

In particular, I wanted to investigate the work being done by ACT—the only group in the country openly pursuing human therapeutic-cloning research. I wanted to know what motivated ACT's scientists. I wanted to observe firsthand what was happening in their cloning lab. I wanted to meet ordinary people afflicted with illnesses for which therapeutic cloning represented a potential cure. And, perhaps most important, I wanted to understand what happens to scientific progress when the burdens of research and development in an ethically sensitive area like cloning fall on the private sector rather than on the government. My motives were very much in the spirit of a remark made by Senator Daschle last November, when he helped to prevent a hasty Senate vote on cloning. "Let's take a deep breath," he said. "Let's think about this."
"That's Trevor's cells," Jose Cibelli told me in the ACT cloning lab on January 23. Cibelli is the vice-president of research at ACT, and the scientist in charge of its therapeutic-cloning attempts. He's a gentle, compact man with dark hair, a trim moustache and goatee, and a vaguely worried expression. A native of Argentina, he speaks quietly and with a thick accent.

It was the first time I had been in the cloning lab, which had the distinct feel of a walk-in closet. Inside the room were a refrigerator, an incubator, a sink, a sterile lab hood, and three microscopes lined up on a black lab bench. Cibelli had just placed a small plastic dish on a microscope platform. Stuck to the bottom of the dish, below a few liquid millimeters of red culture medium, were millions of fibroblasts—living skin cells taken from Trevor Ross.

"The smaller ones just finished dividing," Cibelli explained as we peered at Trevor's cells. "So they're just in G1." G1 is a rest phase that cells enter before preparing to divide again. It's also the stage that ACT has found best for cloning. Through the microscope I looked at the smaller cells. In each of them a large round nucleus—the compartment housing a full copy of Trevor's forty-six chromosomes—was clearly visible. With this payload of DNA, each cell had all the genetic know-how it needed to build a cloned human embryo.

The cells had come from a round plug of Trevor's skin, three millimeters across, and had arrived at ACT just five days before. The Rosses' dermatologist had chosen a crease between Trevor's buttock and thigh, where a scar would not be likely to show, and had punched down with a circular razor blade—past the dead cells of the epidermis and into the dermis, where fibroblasts grow and thrive. The dermatologist had closed the biopsy site with a single stitch. "I was very brave," Trevor told his mother afterward. During the next several days the Rosses treated Trevor's wound with dabs of antibiotic ointment and covered it with tiny Winnie-the-Pooh Band-Aids.

Cibelli now had fibroblasts for potential therapeutic-cloning experiments stored away at ACT from five patients: one with a spinal-cord injury, one with diabetes, two with healthy but aging bodies, and Trevor. But skin cells are the easy part—they're plentiful, hardy, easy to obtain and work with. Eggs are much trickier, and Cibelli had thus started measuring the likelihood of progress not in years but in eggs. "When do I think we'll get this to work?" he asked me rhetorically. "About two hundred eggs from now."

"We've gotten a handful of eggs so far," he had earlier explained. "It's a whole different game when you're talking about animal embryology versus human embryology." In the cow-cloning lab next door, for example, ACT receives 1,400 eggs on a typical day. But whereas cow eggs are available in abundance from slaughterhouses, human eggs must be obtained from young women who have undergone two weeks of hormone injections, regular visits to a doctor, and a nontrivial surgical procedure. All told, it costs ACT about $22,000 to take an egg-donation procedure from start to finish. "And the number is so small," Cibelli added. "I mean, you get ten eggs! Instead of working with a hundred embryos, I'm working with one." From July to October of last year, ACT collected a total of seventy-one eggs from seven donors—of which only nineteen were designated for cloning. That didn't leave much room for error, or much chance to tinker with conditions that might improve the chances of success.

To make matters worse, the company hadn't had any luck cloning from fibroblasts, which it was hoping to use routinely. In three failed rounds of experiments from July to September not a single egg vested with the DNA of a fibroblast so much as divided from one cell into two. ACT's six-cell embryo, created in October, had been produced not with a skin cell but with an ovarian "cumulus" cell—a type of cell regularly used to clone mice. Unlike skin cells, however, human ovarian cumulus cells are rather difficult to obtain and, obviously, are not available for men.

Given the situation, I asked Cibelli what he would say to critics who might accuse ACT of promising the moon to desperate families like the Rosses long before the technology is ready for the clinic. "I'm not promising anyone anything," he responded, looking surprised. "I am saying that this has the potential to cure all these diseases. There are gaps in the research, but the gaps are getting smaller and smaller." One gap would start to close, of course, when a viable human embryo was created.

At five days of development a human embryo is smaller than a grain of sand. It's a perfectly round ball with a fluid-filled core. The internal architecture of the ball, however, is somewhat lopsided. Huddled against one wall of its interior is a group of cells known as the inner cell mass. The outside of the ball is destined to become the placenta and associated membranes; the inner cell mass is what forms a baby. But after only five days of development no cell's fate has yet been determined—it's impossible to tell which cells will become blood or muscle, skin or brain, gut or liver. All that is present is the simple raw material from which the more than 200 cell types in a human body will eventually be built.

If the inner cell mass of an embryo is removed at this early stage, it can yield cells known as human embryonic stem cells—which retain the ability to form any cell or tissue in the body. In a sense they are immortal, in that they can divide indefinitely in the lab, producing large quantities of cells. With the right coaxing those cells can theoretically be converted into an unlimited supply of
tissue for transplant: new heart muscle for heart-attack survivors; insulin-secreting cells for diabetics; neurons to treat those suffering from spinal-cord injuries, the effects of stroke, or Parkinson's disease. Tissue engineers hope someday to build even more complex structures from these stem cells: new blood vessels for bypass surgery, new liver tissue, even new kidneys—all from what began as a loose collection of cells in a lab dish. They dream of a future in which all kinds of organs and tissues can be custom made to replace those ravaged by disease, injury, or a lifetime of hard use.

Since 1998 human embryonic stem cells have been isolated dozens of times—most often from embryos left over after infertility treatments. Each of these embryos, however, had a unique genetic makeup, and the stem cells derived from it will not be a perfect match for anyone on earth. When transplanted into a patient, therapies created from these stem cells—like donated organs in a traditional transplant—run the risk of being rejected by the immune system.

ACT hopes to use cloning to get around the problem of rejection, by tailoring embryonic stem cells to the patient. The procedure would be as follows: Take a patient's skin cell and create a cloned embryo in the laboratory. Five days later derive stem cells from that embryo and grow them in the lab. Then turn those cells, en masse, into the cellular therapy a patient needs. These would be the patient's "own" cells—a perfect genetic match. Of course, before putting cells into a patient, ACT would need to satisfy the FDA.

The first goal was to prove that the procedure could be done—before the Senate vote, if at all possible. "There are senators who are willing to support this," Cibelli told me. "But we'll really make their work a lot easier if we can show that this is feasible."

So far, it had been slow going. Since ACT's October "success," experiments planned for November, December, and early January had all fallen through—pushed back when an egg donor's hormone regimen failed, when the surgical team slated to collect the eggs had scheduling conflicts, and when ACT was running so low on cash that it couldn't afford to proceed.

After showing me Trevor's cells, Cibelli checked the clock. "We're going to have to get going," he said. It was 5:00 P.M.—time to drive to a fertility clinic just outside of Boston, where the eggs for ACT's experiment that day were being retrieved. We left the lab and headed for Cibelli's car, carrying a portable thermoslike incubator that would be used to transport the eggs. Cibelli plugged the incubator into his car's cigarette lighter, and a row of lights on the incubator began to turn on, registering that it was warming up to body temperature inside.

An hour later, when we arrived at the clinic, the egg-retrieval procedure was still under way, so we went for a cup of coffee at the neighborhood Starbucks. Cibelli placed his cell phone in the middle of our table, and we waited anxiously, fully aware that the number of eggs obtained can vary widely. When the phone finally rang, Cibelli checked his caller ID and said, "This is it." He answered the phone and listened for a few seconds. Then his face fell.

"Zero," Cibelli said when he hung up the phone, looking crushed. "We've gotten as low as five, but never zero." On the long ride back to Worcester with his empty incubator, Cibelli called to let his team know what had happened. Everyone could go home, he said. They'd try again the following week.

A RADICAL HOPE

Adrienne and Ben Ross (all names of the family members have been changed) first came to ACT late last October, ten months after their son, Trevor, and two of his cousins had received a diagnosis of X-linked adrenoleuko-dystrophy (ALD), a relatively rare and underdiagnosed genetic disorder that can abruptly ravage the white matter of the brain, with devastating and often fatal results.

The first symptoms had appeared in Trevor's cousin Andrew, a bright boy who loved baseball, competed in spelling bees, and played the violin. Shortly after starting kindergarten, Andrew had been given a diagnosis of attention deficit hyperactivity disorder, but otherwise he seemed to be thriving. Within a few years, however, his cognitive abilities seemed to have changed. He would regularly ask the same questions again and again. By the time Andrew was eight years old, it was clear that something grave was at work. His karate teacher began to notice a dramatic and progressive loss of coordination. Andrew was having increasing difficulty following instructions or participating in the classroom. In December of 2000, after an MRI, his ALD was diagnosed; soon after, with alarming swiftness, Andrew went blind and deaf, and then lost motor and bowel control. At the age of nine he was in a nearly vegetative state, unable to speak or move.
Andrew had developed what is known as childhood cerebral onset of ALD, a condition that afflicts a third of the disease's victims—who, for genetic reasons, are almost always boys. Half of boys with childhood cerebral onset die by the age of nine. Boys with ALD who are lucky enough to escape childhood cerebral onset are almost certain to suffer a degeneration of the spinal cord in adulthood, which can lead to such symptoms as muscle spasms in the legs, loss of bladder control, and general weakness and stiffness. Although symptoms in adults can vary greatly in severity, a third of adults with the disease also develop brain involvement and are reduced to a vegetative state or die within three to four years of onset.

Within a week of Andrew's diagnosis the other boys in his extended family were tested for ALD, and a tragic pattern was revealed. Andrew's seven-year-old brother, Eric, had inherited the abnormal gene. So had Trevor, then barely a year old.

Currently, the best treatment for childhood cerebral onset of ALD is a bone-marrow or umbilical-cord-blood transplant from a healthy, well-matched donor. This procedure can halt or even reverse the progression of the disease, for reasons that aren't fully understood; it appears that some of the healthy transplanted cells travel to the brain, where they are able to prevent further damage. Compatible transplant donors are extraordinarily hard to find, however—and even when suitable donors are found, the transplants don't always take. Sometimes transplants don't work because a patient's immune system rejects the transplanted cells as foreign. In other cases mature immune cells in the transplanted material actually reject and attack their new host, a life-threatening condition known as graft-versus-host disease. Radiation and chemotherapy before a transplant—and immunosuppressive drugs afterward—can help to reduce the risks of rejection, but they also leave a patient vulnerable to serious infection. Overall, the odds aren't good: according to one expert, a quarter of the boys who receive a bone-marrow transplant to treat ALD die from complications related to the procedure.

In Andrew's case the diagnosis came too late for a transplant to have any effect. But for Trevor there still seemed to be time even to push experimental treatments forward, because his brain hadn't yet shown any evidence of deterioration. Only once have neurological symptoms of ALD been observed in a child under the age of three, and about half of boys with childhood cerebral onset develop normally until age seven. And it was conceivable that Trevor wouldn't develop symptoms until adulthood, so researchers might have a couple of decades to find a better cure for him.

The Rosses had sought out ACT with the radical hope that therapeutic cloning might someday allow doctors to create a transplant that would carry no risk of rejection. The work of a bone-marrow transplant is actually done by hematopoietic stem cells—cells in the marrow that restock our blood and immune systems throughout life, serving as a reservoir of new components as old ones wear out. HSCs are also the cells that have rescued patients with ALD. What the Rosses were exploring with ACT was the idea of coaxing human embryonic stem cells, taken from cloned embryos, into forming HSCs that might someday save Trevor.

When the Rosses first traveled to ACT to talk about Trevor's case, they met with Michael West, a dreamy, laid-back forty-eight-year-old with a lopsided grin. West is the company's president and chief executive officer, and a well-known figure in biotech circles. In 1990, at the age of thirty-six, with a Ph.D. in cell biology and one year of medical school completed, West founded a company in Menlo Park, California, called Geron Corporation, now the industry front-runner in human embryonic-stem-cell research. West's goal was to develop treatments for age-related disease. Five years later he launched a full-fledged effort to obtain human embryonic stem cells. "I was quite convinced of the power of these cells to do things that we've never been able to do before," he told me during one of our many recent conversations. "The whole intent was to get some new tools in the toolbox for physicians." West roamed the country, appearing on the doorsteps of top embryonic-stem-cell researchers (who were then working with animal cells) and offering them financial backing to work with human cells—money unavailable from government sources because of the federal-funding ban. These efforts paid off in 1998, when James Thomson, of the University of Wisconsin, with funding from Geron, successfully isolated the cells from human embryos for the first time. By then, however, amid growing friction with Geron's management team, West had left the company and joined ACT, in October of 1998. His intention was to apply ACT's cloning technology to human medicine.

At his meeting with the Rosses, West opened up a laptop computer and hit a key to start a video of the cloning procedure. "This is how it works," he told the Rosses. A magnified gray egg cell appeared on the screen. Adrienne and Ben leaned forward to get a better look. As they watched, a glass tool wielded by an invisible technician carefully sucked out the egg cell's chromosomes and then placed the egg in contact with a skin cell, in preparation for fusion. "This is bovine," West said—a reminder that he was showing the Rosses an example of cow cloning, not human cloning.

Creating cloned cow embryos had become routine at ACT, and the company's scientists were regularly nurturing them into blastocysts—balls of about 100 to 150 cells. The blastocyst stage of development is the point at which stem cells can be isolated. What West didn't mention to the Rosses is that despite months of effort, his scientists had not yet had any luck creating a human blastocyst. "We're working hard," he told them simply. "I'm not showing you the human data yet on purpose, because we haven't published it yet and we don't talk about human data." He wanted to emphasize the technology's promise, of course—an unlimited supply of tissue that matches a patient perfectly.
But Trevor needed something more: cloned cells in which the debilitating ALD mutation had been corrected. A leading experimental approach to correcting this kind of defect is a procedure known as gene therapy, which uses a modified virus to shuttle new genes into a patient's body cells. The virus infects a cell, carries a therapeutic gene to the nucleus, and inserts it into the DNA at a random location. Someday the procedure might be used to add a functional ALD gene to cells from Trevor's own bone marrow. This was another approach the Rosses were pursuing, but it's very experimental, and scientists are having difficulty modifying all the cells that need therapy in a patient, and difficulty ensuring reliable long-term expression of the new genes.

What therapeutic cloning should allow scientists to do, West explained, is provide a pure population of genetically modified cells. Use one modified cell for cloning, and the entire cloned embryo will then carry that modification. So will embryonic stem cells derived from it, and any therapeutic tissues they produce. Alternatively, scientists could do the modification in embryonic stem cells after cloning, and then grow a limitless supply of tissue from one properly modified cell. "We can give the patient cells that all have the same precise targeted modification," West said. "One hundred percent. We won't do that with gene therapy in our lifetime."

A therapy for Trevor isn't the only thing at stake. The stem cells derived from cloned embryos bearing an ALD mutation could be powerful research tools. In fact, scientists consider creating cloned embryos that match patients with a genetic predisposition to disease to be one of the most important therapeutic applications of the technology, because, for one thing, it would allow diseased tissues of all kinds to be created and studied in the lab. But such work is rarely discussed in the political debate about cloning.

As she listened to West spin out optimistic future scenarios, Adrienne began to wonder if they would be able to proceed—or if using Trevor's cells for cloning would be pushing the bounds of the law as well as of science. "Can you clarify for me?" she asked, interrupting West. "On the cloning side, if you're not using federal funds, can you do what you want?"

It's understandable that she would wonder. The House's anti-cloning legislation was designed to make everything Mike West and the Rosses were discussing that day illegal. If the Senate were to pass the bill, not only could ACT's scientists be prosecuted for attempting therapeutic cloning for Trevor but Adrienne and Ben could be prosecuted for participating in such an attempt. One provision of the legislation would make it illegal even to "import" a life-saving medical therapy developed elsewhere in the world through cloning.

Adrienne's question was a sore point for West. "Yeah, we're free to do what we want," he answered simply.

"But now they're looking to try to ban that?" Adrienne asked.

West hesitated. "Well, I don't know," he said. "The Senate at some point will take this up, and my honest, best read is, I don't believe the Senate will pass it." Still, he admitted, anything could happen. "We could lose," he said, "and that would be tragic."

For the moment, however, therapeutic-cloning research was legal—and the Rosses were ready to get started. "So," Ben said over lunch, pulling a ball-point pen and a scrap of paper from his pocket. "What's the checklist?" Scheduling Trevor's skin-punch biopsy went to the top. So did a reminder to send ACT the sequence of the ALD gene mutation afflicting the Ross family—and a healthy sequence that could be used to correct it.

"And are you just as happy with the eggs you have, or do you need eggs from us?" Adrienne asked. "I could mention to our ethics board that you're interested in donating egg cells," West answered. "We should set ourselves up for as much success as we can."

West was referring to a potential complication with therapeutic cloning. The procedure involves the transfer of a patient's cell nucleus into an egg from which the nuclear chromosomes have been removed. But those chromosomes are not the sum total of an egg's DNA. A small amount of DNA is located outside the nucleus, in energy-producing structures called mitochondria. The amount of genetic information they contain is tiny, involving only a few dozen functioning genes, as opposed to the tens of thousands found in a cell nucleus. Still, studies in mice and rats have shown that unfamiliar mitochondrial proteins can provoke an immune rejection response. If the differences in mitochondrial DNA between egg donor and patient are too great, the patient's body may reject the cloned tissue as foreign.

"If you took mitochondria from the maternal lineage of the patient," West told the Rosses, "then there's no conflict. You're home free." Mitochondria are passed exclusively from mother to child, so all relatives with the same maternal lineage have the same mitochondrial DNA. This meant that many women in Adrienne's family could donate eggs that would be a perfect mitochondrial match for Trevor's body tissues.
The science, however, still had a considerable way to go. Even if ACT were able to create cloned embryos and isolate stem cells, turning those cells into hematopoietic stem cells suitable for transplant could be difficult—at the time, scientists had yet to produce HSCs, even in animals, that could migrate to the bone marrow, take up residence there, and produce useful blood and immune-system cells over the long term.

Nevertheless, West was upbeat. "You guys should take encouragement," he told the Rosses. "This is doable. It's only a question of can we mobilize the people. It won't happen unless people work on it." Ben nodded his head. "Well, you let us know what we can do to help."

A PUBLIC-RELATIONS DISASTER

A few weeks later ACT took a risk that could have put the company out of business—and, worse, could have closed the door on the budding field of therapeutic-cloning research. On November 9 the company e-mailed a hastily written scientific paper to e-biomed: The Journal of Regenerative Medicine, an online publication known for its quick turnaround time. The paper announced dryly that in ACT's lab "three somatic cell-derived embryos developed beyond the pronuclear stage." Robert Lanza, ACT's vice-president of medical and scientific development, called before the report came out to give me a translation. "The news is going to be that we have the world's first cloned human embryos," he said. "I just want to give you a heads-up—because when we make this announcement, it might bump the war [on terrorism] off the front page."

On almost every level the announcement was premature. ACT's original goal had been to publish in a prestigious journal like Science or Nature, when the company had what it is really after: human embryonic stem cells derived from a cloned embryo. ACT had nothing like that—it had managed only to sustain a cloned embryo to the six-cell stage of development.

At first, ACT's scientists say, they were uncertain whether they should publish such preliminary data. But given that they were working in an ethically fraught area of science, they decided to be as open as possible about their progress.

After Lanza called me about the imminent publication of ACT's cloning paper, I traveled to his house, on an island in a pond in central Massachusetts, to discuss the announcement. Lanza is in his mid-forties, animated and boyish, with graying brown hair that sticks straight up from his head. He, West, and Cibelli form ACT's core triumvirate. As we sat at his kitchen table, Lanza told me that rumors in the scientific community were starting to make him nervous. Apparently the mavericks of the cloning world—those trying to produce a baby—were possibly on the verge of getting some preliminary results. "If they should come out and make some sort of an announcement first," Lanza said, "it could do severe damage. Because when it breaks, if their goal is reproductive cloning, all of the research will be banned. It will be killed—and it won't matter what we say, because no one's going to listen anymore." Last year, in fact, the outrage surrounding the mavericks' activities had directly contributed to the passage of the House anti-cloning bill.

But ACT itself also bore responsibility. On July 12, just weeks prior to the bill's passage, The Washington Post had broken the news that ACT was trying to create cloned human embryos as a source of stem cells—making it the only group in the country to acknowledge such plans publicly. The uproar that followed was still fresh in congressional minds at the time of the vote. Congressman Bart Stupak, of Michigan, one of the bill's co-sponsors, alluded on the day of the vote not only to the renegades but also to ACT. "The need for action is clear," he told his colleagues. "Research firms have announced their intentions to clone embryos for research purposes and then discard what is not needed."

A week before the publication of ACT's paper in The Journal of Regenerative Medicine, I called Thomas Okarma, the current chief executive officer of Geron, to get his views on ACT and its reputation. Despite his commitment to stem-cell and therapeutic-cloning research, Okarma was harshly critical of ACT. "They've done more harm to the field than good, I'm afraid," he told me. The most glaring example, he said, was ACT's announcement, just after Mike West joined the company, in the fall of 1998, that it was attempting to fuse human skin cells with cow eggs whose nuclear DNA had been removed. The motivation was sound: ACT was essentially hoping to do therapeutic cloning without the difficulty and expense of using human eggs—reviving experiments Jose Cibelli had started as a graduate student, in 1996, with his own cells. But, in the interest of "transparency" West released details to The New York Times and 48 Hours, and two days after the news broke, President Bill Clinton, "deeply troubled" by the work, asked the head of his National Bioethics Advisory Commission to investigate. By an unfortunate coincidence, one week before the 48 Hours broadcast, scientists had announced that they had derived human embryonic stem cells for the first time—news that made ACT's announcement seem like me-too publicity.

The cow-human embryos turned out to be "just plain duds," according to West, and ACT has never generated enough data for a significant scientific paper. (Members of the scientific community had predicted this outcome, although researchers in China have recently claimed success using rabbit eggs.) But the damage was done, because the public entirely misinterpreted the experiments. "Religious fundamentalists who, you know, are against reproductive and therapeutic cloning anyway, are using this example,"
Okarma told me. "'My God,' they say, 'these people are going to make chimeric creatures—mixing cows and humans.' It creates a fantasied negative scenario that casts an umbrella on all of us working in the field, and makes it harder for the field to advance. And it's well documented in the scientific literature that fusing cells from two such distantly related species will not work." Okarma was not alone in dismissing ACT: the company's "publication by press release" was widely attacked by other scientists as irresponsible and insubstantial.

He added, "It's not in the same category as the Raëlians"—a religious group, inspired by "revelations" from extraterrestrials, that is working on reproductive cloning—"because there are certainly legitimate scientists at ACT trying to do this work, okay? But from the perspective of the regulatory bodies, they are in the same spaceship."

**BACKLASH**

When Bob Lanza joined ACT, in March of 1999, not long after the cow-human cloning fiasco, it was a company bruised and embarrassed by recent events, and in need of building its scientific reputation. Lanza was a strong addition to the team.

He had gotten started young. When Lanza was just eighteen, he published his first research paper—in *Nature*, a journal many scientists strive a lifetime to publish in. The paper involved the results of biology experiments he had started in his parents' basement, in the Boston area, at the age of twelve. As a thirteen-year-old Lanza had gone to Harvard seeking advice and had stumbled on Stephen Kuffler, the chairman of the department of neurobiology. Kuffler (whom the boy initially mistook for a janitor) helped Lanza to finish his experiments and work toward publication. From then on Lanza bootstrapped his way along, invoking the name of one scientist to gain access to the next. He ended up accumulating an astonishing list of apprenticeships. He worked with Jonas Salk, the engineer of the polio vaccine; with the renowned behavioral psychologist B. F. Skinner; and with the Nobel laureates Gerald Edelman and Rodney Porter, who uncovered the structure of antibodies. Lanza did surgeries in South Africa with the pioneer of heart transplantation, Christiana Barnard, and while he was still in medical school he co-wrote the first textbook on heart transplantation, with Barnard and David Cooper.

One of the first things Lanza did after he joined ACT was to recruit sixty-seven Nobel laureates to sign a letter urging the Clinton Administration to support federal funding for human embryonic-stem-cell research. He tracked them down one by one, calling them and enlisting them in the cause. He sent a similar letter, carrying eighty signatures, to President Bush in February of last year. Lanza's efforts were part of a snowball effect. A month later the presidents of more than a hundred universities and colleges sent their own petition to the Secretary of Health and Human Services. By last summer even some pro-life conservatives, such as Senator Orrin Hatch, of Utah, had come out in favor of the research, as had former First Lady Nancy Reagan.

Lanza and his colleagues hoped to generate a similar effect with their cloning announcement. The press release that they prepared also referred readers to feature stories about their cloning "milestone" that would be appearing on the covers of *Scientific American* and *U.S. News & World Report*. The stories were written by journalists who had a long association with ACT, and the *Scientific American* article was in fact co-authored by the ACT scientists and written in their own voices. These articles ended up being scheduled to go online at exactly 9:00 A.M. EST on November 25—the precise moment that the *Journal of Regenerative Medicine* article itself was to appear online. Mike West was also scheduled for a 10:00 A.M. appearance on NBC's *Meet the Press* that day.

"You can see how things are lined up," Lanza told me about the articles. "We're getting our ammunition all in the barrel. At least people will understand that there is a legitimate medical use for this technology. And even though we may get beat up, I hope there's minimal damage."

When ACT's paper became public, on the Sunday of Thanksgiving weekend, the backlash was swift. The White House made it clear immediately that President Bush was "100 percent opposed to any type of cloning of human embryos." The following day, in a Rose Garden appearance, the President called ACT's work "morally wrong," and added, "We should not, as a society, grow life to destroy it. And that's exactly what's taking place." The Vatican issued a statement expressing "unequivocal condemnation" of therapeutic cloning, which it portrayed as tantamount to murder.

Conservative members of both houses of Congress, backed by anti-abortion and religious groups, joined the President in calling for immediate Senate action, warning that the "mad scientists" doing this "ghoulish work" must be stopped. When I spoke with Bob Lanza on the Friday after the announcement, protesters from pro-life groups were outside ACT's office building, which was being guarded by police cruisers. Its front doors—usually left open—were locked.

Earlier in the month Sam Brownback, of Kansas, the Senate's most vocal advocate of a total ban on cloning research, had struck a deal with the Senate's Democratic leadership, agreeing to delay action on human cloning legislation until February or March of this year. All had been quiet on the legislative front, with a thoughtful debate planned on the merits of the technology. But after ACT's announcement, that agreement went out the window. Brownback immediately resumed attempts to force a vote on a ban—
or, failing that, to impose a six-month moratorium on all human cloning research. "I have been warning this body for months that this day was going to be here. Now it's here," he said in the Senate. "We now have the first human clone."

"I was frankly horrified," Tom Okarma told me the week after the announcement. "This is precisely what the opposition has been waiting for. They can now mount a renewed offensive to proscribe or outlaw this technology, and there won't be any credible scientists who push back, because no value has been demonstrated by the experiment ACT published. It hasn't moved the field one millimeter. It's essentially negative results. And no legitimate scientist will stand behind that."

None did. Instead they pointed out that ACT's experiment didn't actually make clear whether creating a healthy cloned human embryo was even possible, since the researchers hadn't succeeded in nurturing an embryo beyond the six-cell stage. Human eggs are packed with factors that control the first few rounds of cell division, which meant that the cloned embryos created by ACT may simply have been cruising on autopilot, without the donor cells' DNA ever having taken over the controls. "It's a complete failure," George Seidel, a cloning expert at Colorado State University, in Fort Collins, told The New York Times about the experiment. Ian Wilmut, one of the researchers who cloned Dolly, told London's Independent newspaper, "In terms of what this says for human cloning, it is pretty irrelevant." John Gearhart, of the Johns Hopkins University School of Medicine, said in an interview aired on ABC that the research was so preliminary that "it should not have been published."

But it wasn't the preliminary nature of the research that had raised scientists' ire so much as the fanfare with which it had been published. In the 1960s and 70s, when Robert Edwards and Patrick Steptoe were attempting to create the first baby through in vitro fertilization, they similarly published the results of a number of steps along the way. Before they had even created a blastocyst, much less a pregnancy, they published reports in Nature of the first time human sperm cells penetrated human eggs in the lab dish, and of the first time such embryos faltered along to just sixteen cells. ACT's paper had done essentially the same thing.

The scientific consensus, though, was that ACT's public-relations campaign had raced far ahead of its data. "Important Milestone in Therapeutic Cloning," ACT had headlined its press release, which claimed in the opening paragraph that the experiment provided "the first proof that reprogrammed human cells can supply tissue for transplantation." Given that there were no human embryonic stem cells and no transplantable tissue in evidence, it had done no such thing. Although ACT did go on to qualify its results as "preliminary"—the first halting steps in an ongoing effort—it was clear that the company was trying to engineer front-page news out of what could be construed as a scientific non-event.

The announcement did indeed make headlines, but even the mainstream media quickly turned sour. "As pure business hype, the announcement of human cloning by a small biotech startup was a masterpiece," the San Francisco Chronicle editorialized. "In reality, the achievements ... are skimpy." The Washington Post concurred, calling the work "less than meets the eye." An article in the Los Angeles Times dismissed the "big breakthrough" as "a yawn." The New York Times was no less critical. "Unfortunately," an editorial in the paper read, "by rushing into print with such preliminary results, and orchestrating a media blitz to accompany the announcement, Advanced Cell Technology has invited legislative retaliation that could cripple the very research it is attempting to pioneer." In terms of ACT's credibility, it seemed to be the cow-human-embryo fiasco all over again.

One of the more bruising assessments came from Harold Varmus, a Nobel laureate and a former director of the National Institutes of Health. "So why did the company make its announcement?" Varmus wrote in The New York Times. "Although its executives claimed to be excited about the findings and said the information would promote educational debate, the actual reasons may be more self-serving. Biotechnology companies are dependent on investors, and investors like publicity."

In January, I asked Cibelli if he had any regrets about the announcement. "No," he said. "It brought the issue back to the table, and that's what we wanted. We predicted that we would be criticized by our peers. We took a calculated risk. Would I rather have had blastocysts? Sure. Was it thrilling to see at least six cells? Yeah." He paused, and then continued. "Now that the storm has died down, we've got to finish what we started. Mike has gotta get the money, and the rest of us have to finish the work."

"AN INCREDIBLE GIFT TO MANKIND"

Although ACT is adamant that commercial realities had not motivated the announcement, one thing was clear: last fall ACT was not far from going broke. Its scientists were tight-lipped about the situation. When I spoke with Mike West about it, he chose his words carefully. He described the state of affairs as "nerve-racking," and went on to talk about the difficulties of a situation "where you are not making any money, you are losing millions of dollars a year ... and trying to raise money when Congress is trying to criminalize your business."
ACT was running on fumes. It was making payroll at the last minute and funding its human cloning experiments with eleventh-hour investments from friends, or with money from its scientists' own pockets. By October the situation had reached crisis proportions. "The finances were such that much of our research had to be put on hold," Bob Lanza told me.

The company did have a small amount of cash trickling in from an agricultural subsidiary, however, including a round of investment that came in shortly before the November announcement. In the end the announcement did attract interest from venture-capital firms, but everything hinged on the Senate's upcoming decision, since no one was committing money to a business that might soon be outlawed.

Others in the field weren't particularly encouraging about the company's long-term prospects, even if the work remained legal. "We don't think this is a good business," William Haseltine, the chief executive officer of Human Genome Sciences, in Rockville, Maryland, told me when I asked him about ACT's viability. Haseltine is a pioneer in regenerative medicine (the field that includes human embryonic-stem-cell therapies) and also the editor in chief of The Journal of Regenerative Medicine. "I think the government should fund this work," he said. "Private companies can't do it justice ... Therapies using these cells are ten to fifteen years away, and most of these companies will probably be long gone by then. In my opinion, they can't sustain themselves for that long without sales." Tom Okarma is skeptical for a different reason. He thinks that therapeutic cloning is too inefficient and costly ever to achieve commercial success, and calls it a "nonstarter," because, among other reasons, each patient's cells would have to be put through FDA-mandated safety testing individually. (Geron is exploring several other potential solutions to the immune-rejection problem.)

All that said, when asked how the company plans to make money from therapeutic cloning, scientists at ACT are likely to give an impatient response. "I don't care about whether there's commercial value in it," Bob Lanza told me. "You know, the point is that if a mother can give her oocyte and cure her kid from a lifetime of suffering—if you can cure people, you know, screw whether it's commercially viable."

Mike West was confident, although not very specific, about the potential for profit. He told me, "I've heard the criticism, you know, that 'Mike West is just into trying to help people, he's not serious about business.' My philosophy is, cure diabetes and you'll make plenty of money. You see what I'm saying? Don't put the cart in front of the horse. Cure the disease and you'll make money."

The most frequent refrain among political opponents of therapeutic cloning, and of human embryonic-stem-cell research in general, is that adult stem cells are a better choice for the development of medical therapies. Like cells from cloned embryos, adult stem cells are a perfect genetic match for a patient. Unlike embryonic cells, however, they can be found in the tissues of the patient's own body—a fact that prompted Senator Brownback, after ACT's announcement, to insist on CNN that adult-stem-cell research is "a much better route to go." Opponents of therapeutic cloning wonder why there's a need to work with embryonic cells at all, since adult stem cells aren't rejected by the immune system, can produce a wide variety of body tissues, and do not require destroying embryos.

A report released by the NIH last July provided some answers, pointing out that most adult stem cells are rare, may be difficult or dangerous to harvest from patients, and have a limited capacity to divide in the laboratory, which means that they can't yet be grown in large enough quantities to be of therapeutic value. What's more, adult stem cells have not been found for all types of tissue.

Still, if any type of adult stem cell has proven its clinical promise, it is the HSCs in bone marrow—the same cells needed for Trevor Ross. Clinicians have been doing bone-marrow transplants involving these cells for more than thirty years, and have been able to help cancer patients, correct anemias, and even reprogram the immune system to provide reprieve from auto-immune diseases such as systemic lupus, multiple sclerosis, and rheumatoid arthritis. Some clinicians who work with adult HSCs on a daily basis, however, think that therapeutic cloning could do even better. One of them is Malcolm Moore, a specialist in blood-cell development at the Memorial Sloan-Kettering Institute, in Manhattan. Moore is among the scientists collaborating with ACT on therapeutic-cloning experiments in animals. "We want to improve the whole strategy of bone-marrow transplantation," he told me when I visited him in his office, which overlooks East Sixty-seventh Street. If anyone knows the promise of adult hematopoietic stem cells, it's Moore, who for thirty years has been working to optimize their use in treating cancer patients whose bone marrow has been destroyed by chemotherapy. But Moore points out that giving patients back their own adult stem cells is not always an ideal therapy. In cancer patients these cells are sometimes damaged by early rounds of chemotherapy or contaminated with cancer cells that are difficult to purify away. In a patient like Trevor the cells have a genetic defect that gene-therapy techniques are still far too experimental to treat effectively. And in all cases adult stem cells suffer from a major limitation: cellular aging.

It comes down to a simple fact about cell division: skin cells, heart cells, liver cells, even adult stem cells, can divide only so many times—perhaps fifty to a hundred—before burning themselves out. It's as if some biological counter were tallying rounds of cell division with the help of structures called telomeres. Telomeres are repeated sequences of DNA that cap and protect the ends of.
each of our chromosomes, much like the plastic tips that protect the ends of a shoelace. The problem is that each time a cell divides, its telomeres grow shorter. Eventually they grow so short that the cells reach a state of senescence in which they simply stop dividing or die. Cells in the reproductive lineage, however, including human embryonic stem cells, escape this fate. They have high levels of the enzyme telomerase, which extends and maintains telomeres as the cells divide, making them immortal in a cellular sense. Human embryonic stem cells can go on dividing indefinitely, producing unlimited quantities of cells. Not so with adult HSCs derived from bone marrow.

A typical bone-marrow transplant, Moore told me, replaces only one or two percent of a patient's HSCs, and relies heavily on that small handful of cells to divide. The cells' telomeres have already shortened significantly, over years and years of use, and now those same cells are being asked to repopulate entire blood and immune systems. This means more-frequent cell division and, consequently, a faster shortening of telomeres. It is accelerated aging on a cellular level.

In the short term, Moore said, that's no cause for concern. But later in life there may be consequences. For example, a forty- or fifty-year-old who had received a transplant earlier in life might essentially have the immune system of a seventy- or eighty-year-old. (This and other limitations of adult stem cells may be overcome with further research.)

A patient's skin cell used for cloning has telomeres already shortened by years of cell division, but ACT's scientists have demonstrated that a cell's life-span is completely restored through cloning. In a paper published in *Science* in April of 2000, researchers at ACT showed that cloning can restore a senescent cell's telomeres to an embryonic length or greater. As a result, therapeutic cloning can produce cells with their whole "lives" ahead of them, thus providing "youthful" tissue that may in some cases respond better to injury or disease than adult cells would.

"When there's this ethics debate about adult versus embryonic stem cells and cloning," Mike West told me, "I don't think what's properly weighed in the balance is the amazing breakthrough that this is. I mean, the idea that you can take a person of any age—a hundred and twenty years old—and take a skin cell from them and give them back their own cells that are young! Cells of any kind, with any kind of genetic modification! That's such an incredible gift to mankind! For the U.S. Congress to spend two hours and debate this and say, 'Oh, we'll make all this illegal,' to me is unbelievable. They don't understand." He shook his head. "We've never been able to do anything like this before."

Malcolm Moore's main concern is that Congress will shut the door on this research before its full benefits are known—if they indeed exist. "Basically," he told me, "my plea is, don't close down an avenue of research that might be of value in the future in the treatment of human disease. Time, science, and medical practice will be the ultimate proofs of whether these strategies are going to benefit mankind."

Bob Lanza put things more enthusiastically. "I'd stake my life on it," he said. "If this research is allowed to proceed, by the time we grow old, this will be a routine thing." He pounded the table we were sitting at, for emphasis. "You'll just go and get a skin cell removed at the doctor's office, and they'll give you back a new organ or some new tissue—a new liver, a new kidney—and you'll be fixed. And it's not science fiction. This is very, very real."

**BREACHING THE ZONA PELLUCIDA**

On January 29, the night of the State of the Union address and a week after Jose Cibelli and I had fruitlessly traveled to the fertility clinic outside Boston, we again found ourselves sitting at the Starbucks, waiting for the results of another retrieval attempt. "I'm just hoping we get enough eggs," Cibelli said. "About ten. At least ten." A few minutes later his cell phone rang. The procedure was finished. Cibelli hung up and told me, "She didn't say how many."

Inside the clinic Cibelli waved at the embryologist, who was seated at a microscope on the other side of a glass wall. She was wearing a surgical blue-paper hat and gown, and was scanning a dish of fluid retrieved from the egg donor's ovaries, trying to locate eggs. She shook her head sadly at Cibelli and held up just two fingers. "Part of the game," he said, sinking into a chair. He leaned his head back against the wall and tapped his feet nervously. The embryologist continued her search.

In human embryology timing is everything. By the time an egg is collected, it has already started to age; it will lose its viability in the lab within a few hours. The older the egg, the harder fusing it with a skin cell becomes, and the shorter the likely development of any embryo it forms. Since the cloning procedure itself can take several hours, Cibelli had started asking the clinic for "younger" eggs, collected closer to the time of a donor's last hormone injection. Go in too soon, however, and an egg is too immature to be retrieved. It won't yet have entered the fluid-filled space of its ovarian follicle and will stay behind when the surgical team collects the fluid. This day's egg retrieval had been an experiment—collection had been attempted three hours earlier than usual.
"Well, I'm all done doing experiments," the embryologist said with good-natured exasperation, removing a white mask from over her nose and mouth as she came to talk to Cibelli. She and her team had taken fluid from more than a dozen follicles, but had found only two mature eggs. They'd gone in too early.

Two eggs weren't much to work with. Mice are the only animals with which scientists have reported doing therapeutic cloning from start to finish—and so far the numbers are pretty grim. A group at Rockefeller University, in New York, made 1,016 cloning attempts but got only 398 blastocysts, which yielded only thirty-five stem-cell lines. That's one stem-cell line for every twenty-nine eggs. For a team at the Whitehead Institute for Biomedical Research, in Massachusetts, the process was even more inefficient. They started with 202 eggs and produced only one cloned stem-cell line. A team at Monash University, in Australia, consumed 926 eggs to produce a stem-cell line. To get one from just two eggs would require a minor miracle.

If it were up to Cibelli, he would be doing cloning procedures every week, lining up two or three donors for each collection day in case one dropped out or an egg collection failed. ACT had no money in the bank, however, and it was unclear when he was going to be able to schedule the next donor. "And the logistics," Cibelli said to me in frustration. "You have no idea how difficult it is to do this whole thing. We need to find an alternative to human eggs." Still, he was trying to remain optimistic. "I keep thinking about Bob Edwards," he said, referring to the physician who created the first test-tube baby. "He got Louise Brown with only one embryo. He only got one embryo that day."

Cibelli winced. "Two!" he said.

When we arrived back at ACT that night, the only sound was the whir of a vacuum cleaner as the cleaning crew finished up in a hallway. The technician, whom I'll call Kate, was waiting for us in the lab. She was wearing a baseball cap and a white lab coat over jeans with rolled-up cuffs. Cibelli handed her a small vial containing the two eggs; each was going to get its full share of attention. "We can name them," Cibelli said jokingly. Kate moved the eggs to a drop of culture medium at the bottom of a clear plastic dish, and then covered the drop with a layer of oil, to maintain the pH of the medium and prevent evaporation. She examined the eggs through the microscope. "They look good," she said. She flipped on a video monitor so that we could see what she saw.

Magnified many times over, a human egg is perfectly round, and as luminous and mesmerizing as the moon. This one glowed slightly golden and slightly grainy in the light from the microscope. Surrounding the egg is a thick capsule called the zona pellucida—the closest thing a human egg has to a shell. Unlike a chicken-egg shell, for instance, the zona is flexible, and not attached to the egg itself. Instead the egg floats free within it on a thin cushion of fluid. In two dimensions on the video screen, the zona played moon ring to the egg's glowing moon. Although this is among the largest cells in a human body, it is still smaller than a grain of sand.

Kate's first step was to remove each egg's chromosomes. To anchor the first egg in place during the procedure, she had gently applied suction to it with a blunt glass tube called a holding pipette, which we could see on the left-hand side of the video screen. It was about as wide as the egg itself and was firmly suctioned onto the zona. Using a high-tech joystick mounted at the right of her microscope, she moved a much thinner glass tool (officially known as a micropipette, but called a "needle" by ACT's scientists) toward the egg in minuscule increments. The needle is hollow and somewhat like a drinking straw—by changing the vacuum pressure at its end, one can draw things up into it or spit them back out.

The zona of a human egg is rubbery and resilient. Kate would use a machine called a piezo device to make the glass needle vibrate at a high frequency, so that it could tunnel through the zona. Moments earlier she had practiced a few times on a cow egg, withdrawing the needle and spitting out the plug of zona with each pass.

"I suppose while my luck is good I should give it a shot," she said nervously. "Lights, please." Cibelli flipped off the overhead lights so that she could see the field under the microscope more clearly. The rest of us watched the monitor. Keeping the lights low also protects the eggs—the culture medium responds badly to fluorescents and can change in a way that starts to damage the cells it contains.

To make it easier to locate the egg's chromosomes, Kate had soaked each egg in a dye that binds to DNA and shows up blue under ultraviolet light. She stepped briefly on what looked like a small sewing-machine pedal on the floor, and a UV light popped on under the microscope. On the monitor the egg's chromosomes winked into view, standing out like a blue neon sign in a diner's window. They were fat and compact, lined up in "metaphase II"—the state in which an egg sits patiently and waits for the entry of a sperm cell.
West's line of thinking is fully consistent with the conclusions laid out by the NIH Human Embryo Research Panel in 1994. "If the then—they're wrong. It is just cells. It is a kind of raw material for life: the cellular life out of which human life arises."

...memory, nothing of that. But it is an individualized human in a very early stage, and I advocate we don't touch that. But before the beginnings of a human individual sketched out. At that point, according to West, "There is no brain, no sensation, no pain, no genotypes (with each eye a different color, perhaps, or mottled, two-tone skin). Not until the appearance of the primitive streak are twins. Remarkably, two embryos can also fuse into one, eventually resulting in a single person whose body is a patchwork of two entire human beings."

Positions like Senator Brownback's frustrate Mike West. "I'm just very disappointed," he said to me. "I'm sad, because even the critics admit that millions of human beings and their fate in the hospital may be contingent on this research." As a young man, West was an evangelical Christian and a creationist. He protested outside abortion clinics. But swayed by the scientific evidence for evolution, he eventually abandoned the biblical view of creation. Science now dictates his view of the earliest human embryos as well. "You can be as pro-life as you can get," he told me, "but you can't say that making and destroying a pre-implantation embryo is the destruction of a human. Because it isn't. If it was a human life, I wouldn't touch it. Absolutely not." He went on, "A human individual does not begin at conception. It begins at primitive-streak formation."

The "primitive streak" appears after fourteen days of embryonic development in utero. It's like an arrow drawn on the embryo, one that delineates head and tail, front and back. Until then how many individuals, if any, that tiny ball of tissue will produce is entirely unclear. During the first two weeks of development one embryo can still split into two, a process that produces identical twins. Remarkably, two embryos can also fuse into one, eventually resulting in a single person whose body is a patchwork of two genotypes (with each eye a different color, perhaps, or mottled, two-tone skin). Not until the appearance of the primitive streak are the beginnings of a human individual sketched out. At that point, according to West, "There is no brain, no sensation, no pain, no memory, nothing of that. But it is an individualized human in a very early stage, and I advocate we don't touch that. But before then—they're wrong. It is just cells. It is a kind of raw material for life: the cellular life out of which human life arises."

West's line of thinking is fully consistent with the conclusions laid out by the NIH Human Embryo Research Panel in 1994. "If the President and members of Congress really understood what these little balls of cells were," West went on, "they would have a completely different view."

Adrienne Ross has a blunter assessment. "To me," she told me, "it's like, how dare they tell me that I cannot save my son's life? It's as simple as that. You know, if you want to practice your religion, practice your religion. But not when it interferes with other people's lives." She continued, "They're telling me, 'Let your child die, because my religious belief is more important than your child's life.' They can make their choices for their own embryos and they can make their choices for their own children. But they have no right to stop me from saving my son's life."
A SHOT IN THE DARK

In the cloning lab Kate had added several of Trevor Ross's skin cells to the droplet of medium that contained the egg she had just worked on. The cells floated in the solution, a hundredth the size of the egg itself. She drew a promising-looking cell up into the needle, slipped it through the tiny window already drilled in the egg's zona, and deposited it between the egg and the zona. She nudged the zona with the needle, trying to push the egg and the skin cell into contact, but apparently without luck. Kate frowned. "Let me get a better angle," she said, rotating the egg a little, after which she could see that the cells were touching ever so slightly.

Contact was essential, because the plan was to fuse the two cells with a pulse of electricity. Electricity also helps to "activate" the egg—a process, normally performed by sperm, that kick-starts embryonic development. ACT had tried fusing human cells only once before this—and all the eggs had died. Cibelli was apprehensive. "Fusion is kind of a shot in the dark," he told me. "There's nothing you can do with your hands, like going in mechanically and taking the chromosomes out. Here you have to rely on physics."

Before the fusion attempt, Kate repeated the entire extraction procedure with the other egg. Everything went smoothly, and this time she was able to tuck a skin cell securely between the egg and its zona, with lots of contact. "Yeah! Nice!" she exclaimed, giving a thumbs-up and looking at Cibelli. "See? See?" she said.

She turned the operation over to Cibelli. "Okay," she said, beginning an incantation: "Please fuse. Please fuse. Please fuse." She ran both hands over her face. "Who'd think two eggs could be so stressful?"

Cibelli set up at a second microscope—a much simpler one, designed to provide basic illumination from below. On the microscope platform he placed a fusion chamber—a round, shallow plastic dish with two wires lined up along the bottom, separated by a gap of only half a millimeter. He would soon place the eggs, one at a time, between these two wires. He rolled up his sleeves and attached a black lead to one electrode and a red lead to the other, completing the circuit. Then he did a test on the electrical-pulse generator that had been wheeled up beside him on a stainless-steel cart. "Let's play it safe," he said and set the generator for a pulse of ninety volts. Kate asked, "What do you think about being a little bit on the high side for this one, and the second one we drop it down to eighty?" Cibelli agreed and then placed the first of the two eggs in the fusion chamber. Under the microscope the egg looked good—round, with uniform cytoplasm and a healthy space between it and its zona.

If for some reason the egg and the skin cell didn't fuse, there was always plan B: isolating the skin cell's nucleus—the crucial packet containing its DNA—and injecting it directly into the egg. Another member of the cloning team, an expert in injection, was standing by in case this became necessary. But Cibelli was hoping not to have to resort to injection. Isolating a nucleus requires strong handling. "I'm always concerned that will be detrimental," Cibelli said. "We're not sure which method is going to be the one that is going to pay off. Too many things to try, and too few eggs!"

Using a tiny glass rod shaped like a miniature fencing foil, with a bulbous tip that can prod without piercing, Cibelli positioned the egg between the two electrodes at the bottom of the dish. His goal was to line it up so that the wires would send maximum current directly through the two cells, pushing them toward each other and confusing their membranes enough to make them fuse. Too little current and the cells wouldn't fuse; too much and the egg would be "fried," so to speak. With cow eggs the parameters had been well worked out, but with human cells it wasn't clear how much current was best.

If all went well with the cloning procedure, the nucleus of the reconstructed egg would have enlarged dramatically by the next morning. The genes that made the skin cell a skin cell would be silenced; others that had been laid away unneeded would be unpacked; and the genes that initiate early embryonic development would be activated. The process is not well understood, however, and frequently goes awry—which is one reason for the oft-cited fact that it took 277 cloning attempts to produce just one Dolly.

Cibelli flipped the switch, and a mechanical beep sounded as the machine sent a pulse of electricity through the cells. Everybody waited as Cibelli looked through his microscope. There was no camera mounted on this microscope, so only he could see what was going on. "How'd it do?" Kate asked.

"The cell is running away from the egg," he said.

"What?!" she said. "It's not supposed to do that."

Quickly they gave the second egg its pulse of electricity, so that they could then examine both closely.
"I don't see the zona," Cibelli said, peering at one egg. Kate took a look through the microscope. Each egg's zona had disappeared. This had never happened before. "They had a zona before," she said. "Where'd it go?"

"I don't think we got fusion," Cibelli said to Kate. They took a few minutes to load both eggs up again with DNA-binding dye, and then checked them with UV light under the other microscope. "There's no DNA, for sure," Cibelli said. "There's nothing there. There's no DNA."

We all stared at the eggs, which now glowed implacably on the video monitor. Without a zona, the eggs were completely unusable. Twenty-two thousand dollars and three months of waiting had apparently come to naught. The team couldn't try fusion again, because without a zona there was nothing to hold a skin cell in contact with an egg. They couldn't try injection either, because the technique requires anchoring an egg in one place with the holding pipette while a skin-cell nucleus is inserted. The zona's resilience makes it easy to grab with the pipette, but the egg inside is much more delicate. A holding pipette might well simply suck up the egg, destroying it in the process.

The team conferred briefly and came up with a last-ditch plan to save the eggs: using zonas from the cow eggs left over in the cow-cloning lab next door. Within half an hour Kate had vacuumed the eggs out of four or five cow zonas using a much bigger needle. The plan at this point was to suck the human eggs up into this needle and transfer them into empty cow zonas. "Well, if it works, it works," she said, "and if it doesn't, we're going to kill them."

She tried pulling one of the eggs up into the needle, with no luck—its outer membrane ruptured, and cytoplasm rushed through the tear. Kate groaned. "It lysed. Shoot." Looking at Cibelli apprehensively, she asked, "What do you think? Should I try the other one?" He nodded.

With the second egg she proceeded more slowly. As suction drew it into the needle, the egg elongated and distorted beyond all recognition. "It isn't going to like this at all," Kate said. When the egg had inched all the way into the tube, she moved it over to the empty cow zona and began extruding it. As the egg exited the tube, it began to resume its normal round shape.

"Oh, I don't know, Jose, I think this doesn't look good," Kate said.

"Keep going, you can do it," Cibelli replied.

The egg was almost all the way out of the tube, almost safe in the zona, when it suddenly burst. Cytoplasm flooded the microscope field. Everybody in the room let out an anguished yell.

"You tried," Cibelli said to Kate. "Okay, party's over."

It was midnight, and the dispirited team began breaking down the equipment. "We'll have more eggs," Cibelli said, to nobody in particular. "Hopefully, anyway."

This past January, as ACT's scientists were preparing to work with Trevor Ross's skin cells, a newly created presidential advisory group known as the Council on Bioethics met for the first time. President Bush had created the panel to advise him on controversial matters such as stem-cell research and cloning. "You can help be the conscience of the country," the President told his new advisers, adding that they would "help people ... come to grips with how medicine and science interface [with] the dignity of life, and the notion that life is—you know, that there is a Creator."

Bush's remarks set off alarm bells in the scientific community. So did the composition of the council. Expressing a widely held view, a prominent bioethicist, Arthur Caplan, wrote in an editorial that the new bioethics council was "stacked" with members likely to support the President's opposition to cloning research of any kind. More generally, he argued that the council "will rely on religious rather than secular principles to navigate its course."

At this writing the fate of therapeutic-cloning research remains uncertain. A complete ban in the United States is a distinct possibility. At the end of March the President signaled his ongoing opposition to human embryo research of almost any kind by describing Elias Zerhouni, his highly respected new nominee to head the National Institutes of Health, as a man who "shares my view that human life is precious and should not be exploited or destroyed for the benefits of others." And the Bush Administration even appeared to have international aspirations for its anti-cloning agenda: in February a U.S. delegate to the United Nations proposed a "global and comprehensive" ban on all human cloning research.
That proposal met with firm opposition, however, from other countries. In large part this was because therapeutic-cloning research like that being done at ACT is already under way elsewhere around the world. Britain's House of Lords, for instance, has given the go-ahead for therapeutic-cloning research to proceed, with government oversight and funding. And researchers in China claim that they have used therapeutic-cloning techniques to create human blastocysts, and that they have isolated stem cells from embryos created using human cells and rabbit eggs.

In the United States the broad consensus in the scientific community is that therapeutic-cloning research merits significant exploration, and that real progress is likely only with government funding and support. "Such research," Harold Varmus, the former NIH director, wrote last year in The New York Times, "is vital not just to biotechnology companies and their investors, but to the nation as a whole. By structuring our system so that only those with private funds or a commercial motive do this pioneering work, we curb our full capacity to expand our scientific understanding." To put it another way: as long as a federal-funding ban remains in place, the organizations most likely to move forward with therapeutic-cloning research will be companies like ACT—which, despite generally noble intentions, are bedeviled by the need to raise money, generate buzz, and please investors.

Last summer, in recognition of the importance of government support (but with considerable reluctance), Bush announced a small exception to the federal-funding ban: he authorized federal funds for work with a limited number of human embryonic-stem-cell lines already in existence. But he quickly went on to point out that the government would not fund experiments involving the further destruction of embryos. Cells later obtained from embryos—which would include, obviously, cloned embryos—would remain off limits to federally funded scientists. And Congress may, of course, end up banning cloning research altogether.

What is clear is that the potential fruits of therapeutic-cloning research will not come soon enough for Trevor Ross. In February, doctors detected the first signs of childhood cerebral onset of ALD. All hopes of developing an experimental cure for Trevor were dashed; time had run out. The Rosses immediately scheduled a more traditional cord-blood transplant, fully aware of the risks and of the odds of failure. *