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Stem Cells

THE HOPE AND THE HYPE

The debate is so politically loaded that it's tough to tell who's being straight about the real areas of progress and how breakthroughs can be achieved. TIME sorts it out

BY NANCY GIBBS

Illustration for TIME by Leigh Wells

WHEN THERE'S NOTHING else to prescribe, hope works like a drug. A quadriplegic patient tells herself it's not a matter of if they find a cure but when. Who's to say whether salvation is still 10 or 15 years away? After all, researchers have been injecting stem cells into paralyzed rats and watching their spinal cords mend. "Stem cells have already cured paralysis in animals," declared Christopher Reeve in a commercial he filmed a week before he died.

But what is the correct dose of hope when the diseases are dreadful and the prospects of cure distant? Last month, when President George W. Bush vetoed the bill that would have expanded funding for human embryonic-stem-cell (ESC) research, doctors got calls from patients with Parkinson's disease saying they weren't sure they could hang on for another year or two. The doctors could only reply that in the best-case scenario, cures are at least a decade away, that hope is no substitute for evidence, that stem-cell science is still in its infancy.

It is the nature of science to mix hope with hedging. It is the nature of politics to overpromise and mop up later. But the politics of stem-cell science is different. Opponents of ESC research—starting with Bush—argue that you can't destroy life in order to save it; supporters argue that an eight-cell embryo doesn't count as a human life in the first place—not when compared with the life it could help save. Opponents say the promise of embryo research has been oversold, and they point

DR. YORGOS NIKAS—PHOTO RESEARCHERS

to the cures that have been derived from adult stem cells from bone marrow and umbilical cords; supporters retort that adult stem cells are still of limited use, and to fully realize their potential we would need to know more about how they operate—which we can learn only from studying leftover fertility-clinic embryos that would otherwise be thrown away.

Back and forth it goes, the politics driving the science, the science pushing back. Stem-cell research has joined global warming and evolution science as fields in which the very facts are put to a vote, a public spectacle in which data wrestle dogma. Scientists who are having surprising success with adult stem cells find their progress being used by activists to argue that embryo research is not just immoral but also unnecessary. But to those in the field, the only answer is to press ahead on all fronts. "There are camps for adult stem cells and embryonic stem cells," says Douglas Melton, a co-director of the Harvard Stem Cell Institute. "But these camps only exist in the political arena. There is no disagreement among scientists over the need to aggressively pursue both in order to solve important medical problems."

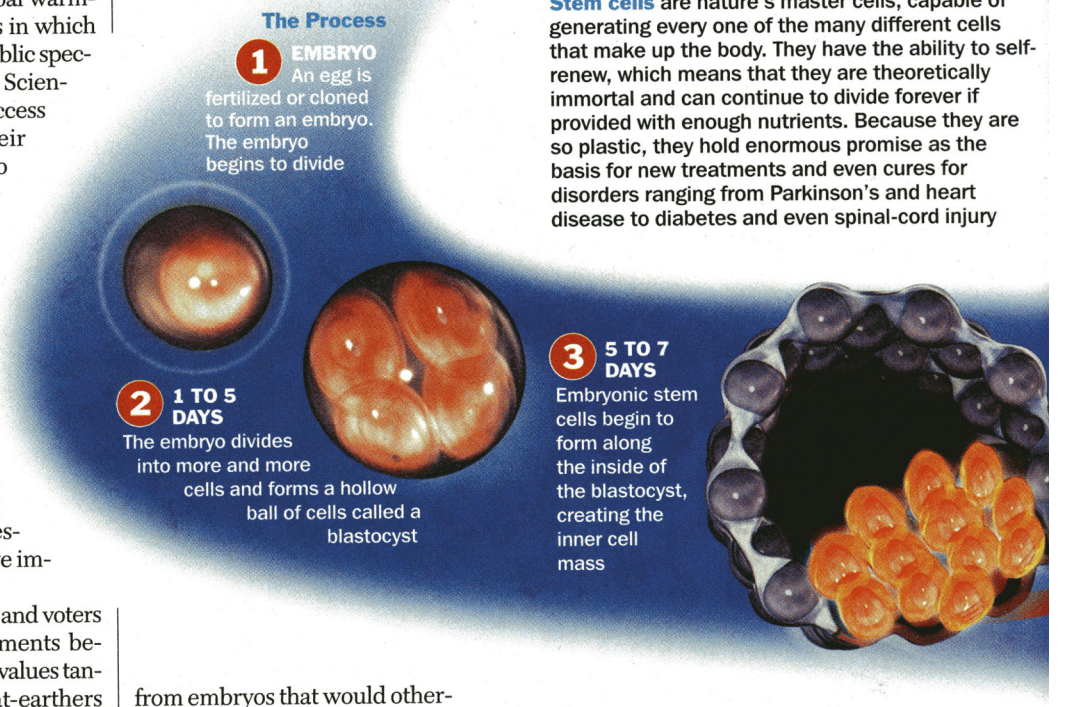
Trapped in all this are patients and voters who struggle to weigh the arguments because the science is dense and the values tangled. Somewhere between the flat-earthers who would gladly stop progress and the swashbucklers who disdain limits are people who approve of stem-cell research in general but get uneasy as we approach the ethical frontiers. Adult-stem-cell research is morally fine but clinically limiting, since only embryonic cells possess the power to replicate indefinitely and grow into any of more than 200 types of tissue. Extracting knowledge from embryos that would otherwise be wasted is one thing, but scientists admit that moving forward would require a much larger supply of fresh, healthy embryos than fertility clinics could ever provide. And once you start asking people about creating embryos for the purpose of experimenting on them, the support starts to slow down.

So where do things stand, five years after Bush provided the first federal funding but radically limited how it could be used?

Making Sense of STEM CELLS

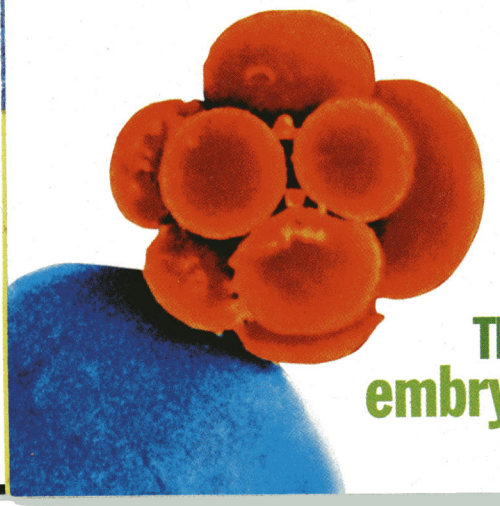
WHAT THEY ARE

Stem cells are nature's master cells, capable of generating every one of the many different cells that make up the body. They have the ability to self-renew, which means that they are theoretically immortal and can continue to divide forever if provided with enough nutrients. Because they are so plastic, they hold enormous promise as the basis for new treatments and even cures for disorders ranging from Parkinson's and heart disease to diabetes and even spinal-cord injury



HOW RED TAPE SLOWED THE SCIENCE

IN A PRIME-TIME SPEECH FROM HIS TEXAS ranch in August 2001, Bush announced that federal money could go to researchers working on ESC lines that scientists had already developed but no new lines could be created using federal funds. "There is at least one bright line," he declared. The speech was a political and scientific landmark. It gave Democrats that rare gift: a wedge issue that split Republicans and united Democrats, who declared themselves the party of progress. Five years later, with midterms looming, they hope to leverage the issue as evidence that they represent the reality-based community, running against the theocrats. States from Connecticut to California have tried to step in with enough funding to keep the labs going and slow the exodus of U.S. talent to countries like Singapore, Britain and Taiwan. Meanwhile, private biotech firms and research universities with other sources of funding are free to



◀ THE EMBRYO

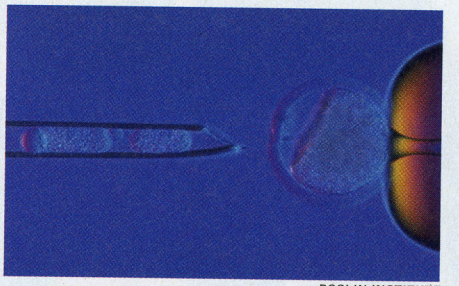
The most versatile stem cells come from embryos, meaning they are also the most controversial

WHERE THEY COME FROM

LEFTOVER OR DEAD-END IVF EMBRYOS

Why they are useful More than 400,000 embryos created during in vitro fertilization lie frozen in clinic tanks in the U.S. Many of them will be discarded, so the embryonic stem cells that exist inside them could be salvaged

Drawbacks The freezing process may make it harder to extract stem cells. Some of the embryos were the weakest ones created by infertile couples and may not yield high-quality stem cells

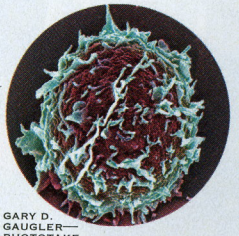


ROSLIN INSTITUTE

◀ NUCLEAR-TRANSFER EMBRYOS

Why they are useful These embryos are created using the technique that created Dolly, the cloned sheep. Stem cells can be custom-made by inserting a patient's skin cell into a hollowed human egg. Any resulting therapies would not run the risk of immune rejection

Drawbacks The process has not yet been successfully completed with human cells, and it requires an enormous amount of fresh human eggs, which are difficult to obtain



GARY D. GAUGLER—PHOTOTAKE

◀ ADULT STEM CELLS

Why they are useful They exist in many major tissues, including the blood, skin and brain. They can be coaxed to produce more cells of a specific lineage and do not have to be extracted from embryos

Drawbacks They can generate only a limited number of cell types, and they are difficult to grow in culture

UMBILICAL-CORD CELLS ▶

Why they are useful Although they are primarily made up of blood stem cells, they also contain stem cells that can turn into bone, cartilage, heart muscle and brain and liver tissue. Like adult stem cells, they are harvested without the need for embryos

Drawbacks An umbilical cord is not very long and doesn't hold enough cells to treat an adult

COLIN CUTHBERT—PHOTO RESEARCHERS

4 STEM LINE
The cells are scraped away and grown on a layer of feeder cells and culture medium

5 TISSUE PRODUCTION
Groups of stem cells are nurtured under specialized conditions, with different recipes of nutrients and growth factors that direct the cells to become any of the body's more than 200 various tissues

Pancreatic islet cells
Could provide a cure for diabetes

Muscle cells
Could repair or replace a damaged heart

Nerve cells
Could be used to treat Parkinson's, spinal-cord injuries and strokes

TIME Graphic

create and destroy as many embryos as they like, because they operate outside the regulations that follow public funds.

For scientists who choose to work with the approved "presidential" lines, the funding comes wrapped in frustration. Today there are only 21 viable lines, which limits genetic diversity. They are old, so they don't grow very well, and were cultured using methods that are outdated. What's more, the chromosomes undergo subtle changes over time, compromising the cells' ability to remain "normal." Back in the late '90s, when the lines were created, "we didn't know much about growing stem cells," says Kevin Eggan, principal faculty member at the Harvard Stem Cell Institute. "They can't do what the newer cell lines can do." Curt Civin, a cancer researcher at Johns Hopkins, has spent the past several years trying to differentiate the presidential lines into blood cells that could be used to treat leukemias and other blood-based cancers. But the age and quality of the cells have been a constant hindrance. "We want to study normal cells," he says. "We're working with Version 1.0. I'd like Version 3.3."

The presidential lines, scientists say, are wasting money as well as time. Larry Goldstein's lab at the University of California at

JEFF MILLER—UNIVERSITY OF WISCONSIN

San Diego is a life-size game of connect the dots. Each machine, cell dish, chemical and pretty much every major tool bears a colored dot, signaling to lab workers whether they can use the item for experiments that the government won't pay for. Goldstein's team is working on a cancer experiment that relies on a $200,000 piece of equipment. They can use either an approved cell line that will yield a less reliable result or a freshly created line that would require the purchase of another machine with private funds. "It's a ball and chain," Goldstein says. "It's goofy. Imagine if your kitchen was a mixture like that, where you can't use those pots with that soup."

Congress tried to address the problem with its bill to allow funding for research on any leftover embryos donated by infertility patients. But even if Bush hadn't vetoed the bill, it wouldn't have solved the supply problems. One study estimated that at best, a couple hundred cell lines might be derived from leftover IVF embryos, which tend to be weaker than those implanted in patients. The very fact that they come from infertile couples may mean they are not typical, and the process of freezing and thawing is hard on delicate cells.

SOLVING A PROBLEM CREATED NEW ONES

IN THE WAKE OF BUSH'S ORIGINAL ORDER, Harvard decided to use private funding to develop about 100 new cell lines from fertility-clinic embryos, which it shares with researchers around the world. Scientists, desperate for variety, snap them up. "Not all embryonic-stem-cell lines are created equal," says Dr. Arnold Kriegstein, who runs the Institute for Regeneration Medicine at the University of California, San Francisco. "Some are more readily driven down a certain lineage, such as heart cells, while others more easily become nerve. We don't understand how it happens, but it does mean we need diversity."

At the same time, Harvard has opened another battleground in the search for cells. After exhaustive ethical review, its researchers announced this summer that they would develop new cell lines through somatic cell nuclear transfer, or therapeutic cloning. In this process, a cell from a patient with diabetes, for instance, is inserted into an unfertilized egg whose nucleus has been removed; then it is prodded into growing in a petri dish for a few days until its stem cells can be harvested. Unlike fertility-clinic embryos, these cells would match the patient's DNA, so the body would be less likely to reject a transplant derived from them. Even more exciting for researchers, however, is that this technique can yield embryos that serve as the perfect disease in a dish, revealing how a disease unfolds from the very first hours.

▲ THE PROCESS

Stem cells can be fou embryos, some adul cells and even in t umbilical cords of newb

The long-term promise is boundless, but the immediate barriers are high. The only people who claim to have succeeded in creating human-stem-cell lines through nuclear transfer were the South Korean researchers who turned out to be frauds. It will take much trial and error to master the process, but where do you get the human eggs needed for each attempt, particularly since researchers find it ethically inappropriate to reimburse donors for anything but expenses? And even if the technique for cloning embryos could be perfected, would Congress allow it to go on?

THE HUNT FOR NEW SOLUTIONS

TO GET AROUND POLITICAL ROADBLOCKS, scientists are searching for another source of cells that is less ethically troublesome, ideally one that involves no embryo destruction at all. One approach is "altered nuclear transfer," in which a gene, known as CDX2, would be removed before the cell is fused with the egg. That would ensure that the embryo lives only long enough to produce stem cells and then dies. That strategy, promoted by Dr. William Hurlbut, a member of the President's Council on Bioethics, has its critic Dr. Robert Lanza of biotech Advanced Cell Technology consid unethical to deliberately create a cr human embryo "not for a scienti medical reason, but purely to addres ligious issue." The most exciting ne sibility doesn't go near embryos at a