





A technician with embryonic stem cells, top left, which grow rapidly under the right conditions

A D U L T C E L L Bone-marrow cells, top right, can generate blood and immune cells

CORD BLOOD

Umbilical-cord cells, in pouch, above right, can produce blood, heart, brain, and liver cells in culture

Shinya Yamanaka of Kyoto University reported tantalizing success in taking an adult skin cell, exposing it to four growth factors in a petri dish and transforming it into an embryo-like entity that could produce stem cells—potentially sidestepping the entire debate over means and ends.

Even if scientists discover an ideal source of healthy cell lines, there is still much to learn about how to coax them into turning into the desired kind of tissue. Parkinson's patients suffering from tremors caused by damaged nerves could benefit

from replacement neurons, while diabetics who can't produce insulin could control their blood sugar with new pancreatic islet cells. But so far, no human ESCS have been differentiated reliably enough that they could be safely transplanted into people, although animal studies with human cells are under way. Not surprisingly, the groups closest to human trials are in the biotech industry, which operates without government funds. Geron claims it is close to filing for permission to conduct the first human trials relying on ESC-based therapy. It is using stem cells to create oligodendroglial progenitor cells, which produce neurons and provide myelin insulation for the long fingers that extend out from the body of a nerve cell. Lanza's group is also close to filing for FDA permission to begin clinical trials on three cell-based therapies: one for macular degeneration, one for

repairing heart muscle and another for regenerating damaged skin. Not to be outdone, the academic groups are just a few steps behind. Lorenz Studer at Memorial Sloan-Kettering Cancer Center in New York City has been able to differentiate ESCs into just about every cell type affected by Parkinson's disease and has transplanted them into rats and improved their mobility. Next, he plans to inject the cells into monkeys.

## THE RISKS ON THE NEW FRONTIER

BUT THE CLOSER SCIENTISTS COME TO HUman trials, the more concerned the FDA will be with ensuring patient safety. The government will look at how the cells were grown and whether there would be risk of contamination from animal products used in the process. Regulators want data on how the cells will behave in the human body. Stem cells have shown a dismaying talent for turning into tumors. Will they migrate into unwanted areas? No one knows. You can't find out for sure until you test in humans, but it's hard to test in humans until you can be reasonably sure you won't harm them in the process.

When human trials finally begin, there's no method for precisely determining whether the transplanted stem cells are functioning correctly. "If we transplanted cells to regenerate a pancreas," says Owen Witte, director of UCLA's In-

stitute for Stem Cell Biology and Medicine, "we can measure in your blood if you're producing insulin, but we can't see whether the cells have grown or evaluate whether they might grow into a tumor." So scientists are seeking to develop marking systems that let them trace a transplant's performance.

## THE PROMISE AND PITFALLS OF ADULT CELLS

EVEN AS SCIENTISTS PRESS AHEAD WITH embryo research, exciting news has come from the least controversial sources: the stem cells in umbilical-cord blood and placentas, and even in fully formed adult organs. While not as flexible as embryonic cells, cord and placental cells have proved more valuable than scientists initially hoped. Although about 90% of cordblood stem cells are precursors for blood and immune cells, the remaining 10% give rise to liver, heart-muscle and brain cells and more. Over the past five years, cord-blood transplants have become an increasingly popular alternative to bonemarrow transplants for blood disorders, particularly when a bone-marrow match can't be found.

If you want to lean out over the edges of science and marvel at what is now possible, visit Dr. Joanne Kurtzberg's program at Duke University Medical Center. Children with blood diseases that were almost certainly fatal a decade ago have got cord-blood transplants that essentially cure them. Now she and her team are taking a more targeted approach by attempting to differentiate cord-blood cells to address heart, brain and liver defects. "I think cord-blood cells have a lot of promise for tissue repair and regeneration," says Kurtzberg. "But I think it will take 10 to 20 years."

Less plastic than cord-blood cells are adult stem cells, which until recently researchers thought couldn't do much more than regenerate cell types that reflected the stem cells' origin—blood and immune cells from bone marrow, for example. Even so,

some scientists believe adult stem cells may prove to be a powerful source of therapies. "In some cases, you may not want to go all the way back to embryonic stem cells," says Kurtzberg. "You may want something more specific or less likely to stray. You wouldn't want to put a cell in the brain and find out later that it turned into bone."

Researchers in Thailand have taken stem cells from the blood of cardiac patients, grown the cells in a lab and reinjected them into patients' hearts, where they set about repairing damage. Two UCLA researchers last week published a study demonstrating that they could transform adult stem cells from fat tissue into smooth-muscle cells, which assist in the function of numerous organs. Welcome as the advances are, the subject of adult stem cells is highly political and invites a conflation of real hopes and false ones. "There are papers that have claimed broad uses for certain adult stem cells, and some people say that is sufficient cause to not work on embryonic stem cells," Witte says. "Many of those claims were overblown."

Even the true believers among scientists, however, dispute eager politicians who have called for a Manhattan Project approach to research. "I hate to say it, but biology is more complicated than splitting the atom," Witte says. "The physicists on the Manhattan Project knew what they needed to accomplish and how to measure it. In biology, we're codeveloping our measurement tools and our outcome tools at the same time." Indeed, a massive centralized effort controlled by the Federal Government could do more harm than good. The key is to have the broadest cross section of scientists possible working across the field. When it comes to such an impossibly complicated matter as stem cells, the best role for legislators and Presidents may be neither to steer the science nor to stall it but to stand aside and let it breathe.

-Reported by Alice Park/New York and Dan Cray/Los Angeles

WTHE CELLS

It takes only a week for embryonic stem cells to blanket the inside of a rapidly dividing blastocyst









## ITICS OF SCIENCE

Democrats smell a political winner in stem cells, but both parties are holding their fire. Will the issue count in November?

BY KAREN TUMULTY WASHINGTON

HE POLITICS OF STEM-CELL REsearch, just like the science of it, is turning out to be far more complicated than either side would like you to think. From the press releases, fund-raising appeals and victory cries that were going up in the hours after President George W. Bush used his veto for the first time, it may have looked as though the Democrats had finally found their gold-

en issue—and a social one at that. "With one stroke of his pen," declared Democratic chairman Howard Dean, "President Bush has once again denied hope to millions of Americans and their families who suffer from diabetes, spinal-cord injuries and Alzheimer's." Added Massachusetts Congressman Ed Markey: "This will be remembered as a Luddite moment in American history."

Democrats were right about one thing. The issue has put Republicans in an uncomfortable spot. White House press secBUZZSAW
Bush got a nasty reception when he visited Denver after the veto

retary Tony Snow apologized last week for saying that Bush considers stem-cell research "murder," explaining that his earlier comment was "overstating the President's position." That rectification came after White House chief of staff Josh Bolten endured an inquisition on *Meet the Press*, in which host Tim Russert demanded to know whether the President's stance against destroying embryos applied not just to federal funding of stem-cell research but also to shutting down the entire field of in vitro fertilization. The answer was a sort-of no.

But so far at least, stem-cell research hasn't rewritten the electoral equation the way many Democrats had hoped it would. The most telling indicator, as always, is how candidates and interest groups are spending their money. A week after the veto, cam-

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