



## Stem-Cell Politics

Susan Okie, M.D.

In Missouri this election season, former Republican Senator John Danforth, an Episcopal priest and abortion opponent, is citing the New Testament in support of a state constitutional amendment

protecting the legality of human embryonic stem-cell research. "I find nothing in the Bible that tells me that cells in a lab dish are people," said Danforth, who lost a brother to amyotrophic lateral sclerosis and believes that the research will lead to new treatments for diseases. "What I do find in the Gospels is an emphasis on healing — relieving people of their suffering."

In Wisconsin, where human embryonic stem cells were first isolated, the reelection campaign of Democratic Governor Jim Doyle has run television advertisements attacking Doyle's opponent, Republican Congressman Mark Green, for voting against a bill that would have increased the

number of stem-cell lines eligible for federal funding. In one ad, the mother of a child with type 1 diabetes says, "When a Washington politician like Mark Green says he's going to outlaw stem-cell research, I say, 'Tell it to my daughter.'"

And in California, Republican Governor Arnold Schwarzenegger responded to President George W. Bush's July veto of that bill by issuing a loan of \$150 million from the state budget to his state's cash-strapped stem-cell research initiative. With its long-term funding tied up by litigation, the California Institute for Regenerative Medicine (CIRM) had been unable to award research grants; now, it is expected to announce

the first ones in about 6 months. Ironically, Bush's veto "brought us to life," CIRM's president, Zach Hall, said.

The President's veto has also brought human embryonic stem-cell research to life as a political issue for many candidates for federal and state offices around the country. Politicians from both major parties are trying to use such research as a "wedge issue" to woo voters. Most Democrats and some moderate Republicans support the research, whereas many socially conservative Republicans oppose it. "I quite literally had a phone call from a candidate for sheriff" seeking information about the issue, said Sean Tipton, president of the Coalition for the Advancement of Medical Research, an alliance of medical groups that support the research. "I think one of the dynamics . . . is that anti-choice voters have shown that they will vote on this issue and

this issue only. And the pro-science, pro-patient community has not shown that to be true.”

One physician in Congress, Representative Joe Schwarz of Michigan, believes that his sup-



Congressman Joe Schwarz, M.D.

port of human embryonic stem-cell research played a role in his loss in an August primary. Schwarz, a moderate Republican from a very conservative district, had voted for the bill that was vetoed by the President, and he lost to a more conservative challenger. “That was one of the cards my opponent played,” he said, adding that he plans to resume practicing otolaryngology and to lend his support to a bipartisan Michigan initiative promoting stem-cell research.

The Bush administration’s policy prohibits federal funding for research using any human embryonic stem-cell lines except those established before August 9, 2001. Only about 21 qualifying cell lines are readily available, and since 2001, approximately \$90 million in federal grants has been provided for

## Single-Cell Storm

Susan Okie, M.D.

Scientists at Advanced Cell Technology, a California company, reported in August that a single cell taken from an eight-cell human embryo can sometimes be coaxed to produce embryonic stem cells, suggesting that such “biopsies” might be a way to generate new stem-cell lines while preserving embryos.

The report, published online by the journal *Nature*,<sup>1</sup> stirred up considerable controversy, in part because both the journal’s initial press release and a podcast interview with senior author Robert Lanza gave the impression that two new lines had been created without destroying any embryos. “What we have done, for the first time, is to actually create human embryonic stem cells without destroying the embryo itself,” Lanza said in the podcast.<sup>2</sup> On the contrary, all 16 donated embryos used in the study were destroyed during the experiments, a fact that was stated, although not emphasized, in the article. A total of 91 cells (called blastomeres) were individually removed from the early-stage embryos and were cultured, in most cases in dishes with other blastomeres. Two of the blastomeres gave rise to embryonic stem-cell lines. The results — together with unpublished work by the authors — suggest, in principle, that single-cell biopsies (which are done on some embryos in IVF clinics for pre-

implantation genetic diagnosis) could be used to derive stem cells without destroying embryos.

*Nature* issued clarifications of its press release shortly after its online publication and again 2 days later, citing “internal communications problems.” Meanwhile, the findings were prominently reported in the national media as a possible solution to the Bush administration’s opposition to the use of federal funds for research on new stem-cell lines. A White House spokeswoman was quoted in news reports, however, as saying that the new technique would not resolve the President’s ethical concerns about the use of embryos in research. Later the same week, Richard Doerflinger of the U.S. Conference of Catholic Bishops, a prominent critic of such research, e-mailed reporters, charging that the study had been misrepresented. “This experiment left no embryos alive and solves no ethical problems,” Doerflinger wrote.

At a hearing of the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies in early September, Lanza received a tongue-lashing from Senator Arlen Specter (R-PA), a strong supporter of stem-cell research. “It’s a big black eye if scientists are making false and inaccurate representations,” Specter told Lanza.

Lanza maintained that he had been quoted out of context by interviewers and said he had been shocked by the critical response. “Our paper was 100% correct,” he said. “It’s very clear that there’s a lot of politics going on here.”

Advanced Cell Technology has had financial troubles, but its stock price experienced a bump after the *Nature* publication, and company officials are clearly hoping that cell lines made with the use of the technique will become eligible for federal research funding. However, James Battey, Jr., chairman of the NIH Stem Cell Task Force, said he doubted that the new method will silence the concerns of some critics. For example, he said it is not certain that removing a cell from an eight-cell embryo does no harm, even though hundreds of apparently healthy infants have been born from embryos that underwent the procedure for genetic testing. It is also unknown whether a single human blastomere can develop into an embryo, as is possible in animals. “My guess is, absent complete reassurance on these issues, there will be individuals who will find this protocol morally and ethically problematic,” Battey predicted.

Dr. Okie is a contributing editor of the *Journal*.

1. Klimanskaya I, Chung Y, Becker S, Lu SJ, Lanza R. Human embryonic stem cell lines derived from single blastomeres. *Nature* (Web only). (Accessed September 28, 2006, at <http://www.nature.com/nature/journal/vaop/ncurrent/abs/nature05142.html>)

2. Abbott A. “Ethical” stem-cell paper under attack. *Nature* 2006;443:12.

such research. Experts say the limitations have hampered progress and have probably discouraged many researchers from entering the politically fraught field. A recent survey of the scientific literature on human embryonic stem-cell research showed that in 2004, articles by authors from other countries outnumbered those by authors from the United States.<sup>1</sup>

The Castle–DeGette bill, passed by Congress last summer, would have allowed the National Institutes of Health (NIH) to fund research on additional stem-cell lines developed from excess embryos donated by couples who had undergone in vitro fertilization (IVF) procedures. Although the bill passed, there were insufficient votes to override the President’s veto, which Bush announced at a press conference surrounded by children who had been “adopted” as embryos. “This bill would support the taking of innocent human life in the hope of finding medical benefits for others,” Bush said. “It crosses a moral boundary that our decent society needs to respect.”

Polls suggest that most Americans do not share that view. In a survey of a nationally representative sample of adults that was conducted in July by the Pew Research Center for the People and the Press, 56% of the respondents said it was more important to conduct stem-cell research that might lead to cures than to avoid destroying human embryos, and only 32% said that preserving the potential life of embryos should be the priority. Annual Pew polls show that public support for embryonic stem-cell research increased by 13 percentage points

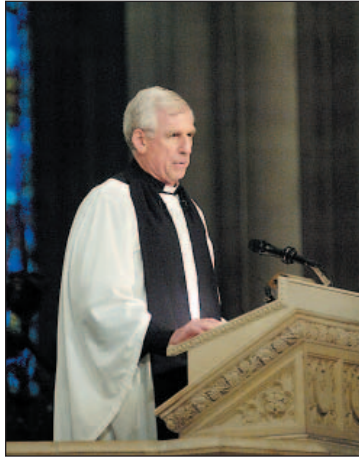
between 2002 and 2004 and has since remained stable. Most people who oppose this research on religious grounds do so because they believe that an embryo is a person from the moment of fertilization.

Those who favor the use of excess IVF embryos for research point out that these embryos are routinely discarded. “To say that embryonic stem-cell research is the taking of innocent human lives without applying the same standard to IVF clinics — I just don’t understand how one can make that line in the sand,” said biochemist and Nobel laureate Thomas Cech, president of the Howard Hughes Medical Institute (HHMI). The board of HHMI decided about 5 years ago to begin funding such research after considering a request from Douglas Melton, an investigator from Harvard University who wanted to derive new stem-cell lines from human embryos. Of more than 300 scientists, including Melton, whose laboratories are supported by HHMI, 8 are currently studying human embryonic stem cells and 26 others have indicated that they plan to do so. Their small numbers probably reflect wariness about political controversy and uncertain funding, rather than doubts about the promise of the field, according to Cech. “It’s considered to be an extremely risky career move to move into an area that could become criminalized,” he said.

In fiscal year 2005, the NIH spent \$40 million on human embryonic stem-cell research and \$198 million for research on more differentiated types of human stem cells (sometimes called “adult” stem cells), chiefly hematopoietic

stem cells, said James Battey, Jr., director of the National Institute on Deafness and Other Communication Disorders and chairman of the NIH Stem Cell Task Force. Battey noted that since the mid-1990s, Congress has included in its annual bills for NIH appropriations a prohibition against NIH funding of research in which human embryos are created or destroyed for scientific purposes. The currently approved stem-cell lines were created without government funding, but after the Bush policy was announced, the NIH awarded infrastructure grants to allow the approved lines to be characterized and made available. Battey said a major scientific argument for developing additional stem-cell lines is that the approved lines have proved not to be biologically equivalent. For example, some can be induced more readily than others to differentiate into a specific type of cell, such as a dopamine-secreting neuron. With additional lines, “functional diversity may yield a cell line more suitable for a given biomedical research application,” Battey said. To date, he added, the Food and Drug Administration has not approved any trials involving the use of human embryonic stem cells or cells derived from them in human subjects.

With the NIH offering limited support, foundations and wealthy individuals have stepped in to fill the gap, and several states — including California, Connecticut, Maryland, Massachusetts, New Jersey, and Illinois — have appropriated money for stem-cell research initiatives, chiefly to compete for scientific and entrepreneurial talent and investment. “This is new to everybody at the state level, and the question is,



Former Senator John Danforth

how sustainable will this be and to what level [of funding]?” said researcher John Gearhart, director of the Stem Cell Biology program at the Institute for Cell Engineering, Johns Hopkins School of Medicine. Gearhart supported a bill passed this year in Maryland that will provide \$15 million for embryonic stem-cell research next year. In states where such research is a political issue, “I would certainly hope that knowledgeable and prominent members of the scientific community would come in and help . . . people to understand” the scientific considerations, Gearhart said. “I’m not saying that they should become lobbyists . . . but I’m certainly considering endorsing candidates who are pro-stem-cell research.”

Both Battey and Cech said they worry that, as the issue becomes increasingly politicized, advocates of stem-cell research are promising the public quick cures for diseases, raising expectations that may not be fulfilled. “Everything gets polarized, and it has to be either black or white, no shades of gray allowed,” Cech said. “People get pushed into making outrageous statements on both

sides. . . . Ultimately, it could come back to haunt the scientific community if the research under a future administration is allowed to go forward and people very reasonably say, ‘Where are the cures?’”

In Missouri, where the constitutional amendment that former Senator Danforth supports is on the ballot, each side has used emotionally loaded language to argue its case. Donn Rubin, chairman of the optimistically named Missouri Coalition for Lifesaving Cures, which is leading the push for the amendment, said it would ensure that any research allowed under federal law would also be permitted in Missouri, and it would ban human reproductive cloning (which Rubin defined as initiating a pregnancy with “anything other than the natural product of fertilization”). The initiative is a response to efforts by state legislators to ban somatic-cell nuclear transfer (SCNT), the process of inserting the nucleus from an adult cell into an enucleated egg and inducing the resulting cell to divide, forming a blastocyst from which embryonic stem cells can be obtained. SCNT has been accomplished in animals but not, so far, in humans. The amendment’s opponents, including the group Missouri Right to Life and Raymond Burke, the Catholic Archbishop of St. Louis, consider SCNT to be cloning — and as morally objectionable as abortion. At a recent rally, one speaker accused the amendment’s proponents of seeking constitutional protection “to clone and to kill.”<sup>2</sup>

Although Missouri is a conservative state, the amendment is backed by dozens of patient groups, medical organizations,

academic institutions, and business groups. The campaign to pass it is financed largely by Jim and Virginia Stowers, founders of the Stowers Institute for Medical Research in Kansas City, which hopes to become a powerhouse of stem-cell research. Rubin, who heads a pro-science coalition in St. Louis, maintains that the quality of science, medical care, and the biotechnology industry in Missouri are at stake. "If our state were to pass laws that threaten to jail scientists merely for . . . seeking cures, it would have a devastating effect on our ability to continue to attract the best and the brightest," he said.

Danforth, who has just published a book about the influence of religion on politics in the United States, said he sees a moral distinction between abortion and embryonic stem-cell research. The early-stage embryos from which stem cells are derived "have not been implanted in a uterus. They cannot become walking, talking, breathing human beings," he said. In Danforth's view, linking stem-cell research to the hope of cures is both justified and politically necessary in order to pass the amendment. "What we're saying is researchers think this

is very promising," he said. "The point is to find cures. The clearer the connection between research and results that you can make politically, the better off you are."

In California, the political debate over stem-cell research is largely over, and the state-funded scientific enterprise is poised to begin. In approving the loan to CIRM, Schwarzenegger sought to gain political capital in his race for reelection against Democratic state treasurer Phil Angelides, a longtime supporter of the stem-cell initiative. CIRM recently issued requests for proposals for seed grants, designed to attract new investigators with funding of up to \$200,000 per year for 2 years, and for comprehensive grants, providing up to \$400,000 per year for 4 years to scientists with a record of accomplishment in human embryonic stem-cell research or a closely related field. "We are expecting an onslaught," said CIRM's Hall, who hopes to announce the grant recipients by March. CIRM also plans to fund 15 California facilities that will provide laboratory space and technical support for culturing human embryonic stem cells, permitting researchers to do projects with nonapproved stem-cell lines.

Last April, CIRM won an important victory when an Alameda County Superior Court judge rejected lawsuits brought by taxpayer and religious groups challenging the organization's legality. The decision has been appealed, and the case may reach the California Supreme Court, but Hall hopes it will be resolved by the end of 2007. Meanwhile, at research institutions around the state, the mood is upbeat. Hall listed eight established stem-cell investigators who have moved to California in the past 2 years or are preparing to do so, including one from Australia and others from Harvard University, Johns Hopkins School of Medicine, Washington University in St. Louis, the University of Michigan, and the Hospital for Sick Children in Toronto. "Everybody's ready to go," said Hall. "People are excited. The phone is ringing off the hook here."

Dr. Okie is a contributing editor of the *Journal*.

1. Owen-Smith J, McCormick J. An international gap in human ES cell research. *Nat Biotechnol* 2006;24:391-2.

2. Mannies J. Varied groups are joining fight against Amendment 2. *St. Louis Post-Dispatch*. September 7, 2006:D3.

## America's New Refugees — Seeking Affordable Surgery Offshore

Arnold Milstein, M.D., M.P.H., and Mark Smith, M.D., M.B.A.

The mainstream media have begun to highlight the plight of some new refugees: seriously ill Americans who receive treatment at advanced private hospitals in low-income countries. These patients are not "medical tourists" seeking low-cost aesthetic enhance-

ment. They are middle-income Americans evading impoverishment by expensive, medically necessary operations, as health care services are increasingly included in international economic trade.<sup>1</sup>

At a recent Senate hearing, two stories were recounted that illus-

trated the physical and financial perils driving patients to pursue care abroad.<sup>2</sup> In the first story, Howard Staab, a self-employed, uninsured, middle-aged carpenter from urban North Carolina who considered health insurance premiums unaffordable, had an