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'Less Morally Problematic Alternatives'

Toward a Stem Cell Solution

In 1999, not long after human embryonic stem cells were first isolated, the National Bioethics Advisory Commission became the first American public body to take up the issue of stem cell ethics. All the commission's members had been appointed by President Clinton and shared his generally liberal views about abortion and embryo research. But the commission also took account of the serious ethical concerns many Americans have about the destruction of embryos for scientific experimentation. Their report, entitled "Ethical Issues in Human Stem Cell Research," concluded that "the derivation of stem cells from embryos remaining following infertility treatments is justifiable only if no less morally problematic alternatives are available for advancing the research."

At the time, there were no such "less morally problematic alternatives"—no ways, that is, of getting the advantages scientists seek from embryonic stem cells without harming human embryos. So in practice, the commission's position was understood as a simple approval of embryo-destructive research, and this became the position of the Clinton administration and then of the American left more generally. Motivated by the humanitarian desire to seek help for those who suffer with disease, they put aside egalitarian concerns about the destruction of nascent human lives in research. The state of stem cell science led them to conclude they had to choose one deeply-held American ideal over the other.

But things have changed, and the forgotten last clause of the commission's conclusion has now become

relevant: over the last two years, researchers have been pursuing precisely that less morally problematic alternative. They have done so on several tracks, and with considerable success so far. Indeed, the emergence of alternative sources of embryonic-like cells has been the great unnoticed stem cell story of the past few years. It has been overshadowed by the simpler and more flashy political story—the one that depicts the left and right in their familiar corners and leaves no room for middle ground. But now middle ground is precisely what is becoming possible.

Two years ago, in the spring of 2005, the President's Council on Bioethics (the Bush administration successor to Clinton's commission) published a report entitled *Alternative Sources of Pluripotent Stem Cells*. It laid out four possible avenues toward producing cells with the abilities of embryonic stem cells but without requiring the destruction of embryos. At the time, all four were essentially speculative. But in the two years since, publications in prominent peer-reviewed scientific journals have demonstrated progress in all four techniques, as well as several more.

The most scientifically promising and ethically appealing of the alternatives considered by the bioethics council involves the reprogramming of normal adult cells to function like embryonic stem cells, but without the need for embryos. And in early June 2007, three separate publications demonstrating great progress toward this goal made front-page news.

The key paper came from a team at M.I.T. led by prominent stem-cell scientist Rudolf Jaenisch. Working with mouse cells, Jaenisch and his colleagues introduced just a few critical chemical factors into normal adult skin cells and produced cells that appeared to pass all the critical tests of so-called "pluripotency"—the ability to be transformed into a large variety of cell types, which is what scientists so value about embryonic stem cells. "Our results show that the biological potency and epigenetic state of in-vitro-reprogrammed induced pluripotent cells are indistinguishable from those of embryonic stem cells," the M.I.T. team reported in *Nature* magazine. Their findings, they assert, "establish that somatic cells can be reprogrammed to a pluripotent state that is similar, if not identical, to that of normal embryonic stem cells." In other words, a regular adult cell, like one of your skin cells, could be turned into the equivalent or near-equivalent of an embryonic stem cell—without destroying any embryos. Two other studies published simultaneously reported similar results.

These techniques are still being perfected, to be sure, and the studies published this spring were all conducted using mice. But they mark the latest significant step on what could well be the road away from the ethical dilemmas of the stem cell debate, and toward a means of advancing the research without harming human embryos.

For now, however, the U.S. Congress does not seem very interested in that potential way forward. Just days after

these latest papers were published, Congress sent President Bush a bill that would fund embryonic stem cell research. The bill—almost identical to the one Bush vetoed in 2006—would have overturned the president's funding policy, and used federal taxpayer dollars to provide an ongoing incentive for the destruction of human embryos. It would say to American scientists: "If you destroy a human embryo, then you will become eligible for taxpayer funds."

As expected, President Bush again vetoed the bill, admonishing Congress that "compelling American taxpayers to support the deliberate destruction of human embryos would be a grave mistake." But as he did so, the president also moved to advance the exploration of the emerging alternative stem cell techniques.

In an executive order entitled "Expanding Approved Stem Cell Lines in Ethically Responsible Ways," President Bush instructed his administration to support alternative sources of pluripotent stem cells. The order formally acknowledges the changing nature of the debate, by changing the very name of the National Institute of Health's (NIH) registry of stem-cell lines eligible for funding from the "human embryonic stem cell registry" to the "human pluripotent stem cell registry." This modest change points to an enormous transformation in our understanding of stem cell science, and to the avenues for ethical scientific progress it makes possible. Under its original name—which referred to the source of particular stem cells rather than to their abilities—the registry could include only the defined set of embryonic stem cell lines that existed before the president announced his policy on August 9, 2001. But newly reconceived under this order, the NIH registry will now include all human stem cell lines with the abilities researchers have prized in embryonic stem cells, provided their development does not require the creation or destruction of embryos. The registry will therefore grow as new and ethically uncontroversial stem cell techniques march forward.

The executive order then instructs NIH to establish new channels for funding that effort, and to encourage scientists to apply. The order marks a crucial turning point in the way the government understands the contours of stem cell science, and defines its role in supporting that science. It shows that the Bush administration, unlike Congress, has begun to catch up with cutting-edge stem cell research and moved past the dispute over so-called "leftover" IVF embryos—a dispute that is no longer of much relevance to the future of the field.

None of this means stem cells will or will not bring hoped-for cures. And none of it means practical applications for pluripotent cells are just around the corner. But this spring's developments do suggest the stem cell debate is at a significant crossroads. Years from now, in retrospect, this period could well be seen as the beginning of the end of this divisive but important debate.

The two premises of the dispute—our desire to advance promising medical research and our desire to respect and protect every human life—seem increasingly likely to reinforce each other, not oppose each other. And with the proper encouragement and aid, America's scientists may well chart a course around the ethical (and thereby the political) controversy.

In some respects, this has all been a long circular path, returning to the hope expressed in 1999 by the Clinton administration's bioethics commission—the hope that alternatives to the destruction of embryos might be found, so that stem cell science might proceed without controversy. That hope clearly still informs the Bush administration's approach to federal funding of stem cell research. But the leaders of Congress have hung a narrower and more political hope on the stem cell debate, and so seem oddly uninterested in the latest scientific developments.

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