

LEGITIMIZING NEW KNOWLEDGE: AMERICAN DEBATES ABOUT ADULT AND EMBRYONIC STEM CELLS, 1998-2004

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I. The Public Role of Science

The outcome of the 2016 presidential election in the United States raised the issue of the role of science in American society. With an eye on the administration's dismissal of research that could affect its policy agenda, researchers, librarians, and activist groups such as Data Refuge sought to find ways to secure data related to issues such as climate change stored on government servers at the National Oceanic and Atmospheric Association (NOAA), the Environmental Protection Agency (EPA), or NASA.¹ In July 2017, the Center for Science and Democracy reported that while "political interference in science is not new," under President Donald J. Trump "these threats to the federal scientific enterprise have escalated markedly."² Meantime, research workers and their supporters took to the streets on April 22, 2017 in "Science Marches" in Washington DC and elsewhere, drawing hundreds of thousands of protesters. Some researchers were ambivalent about such well-intentioned protest lest it "turn scientists into another group caught up in the culture wars and further drive the wedge between scientists and a certain segment of the American electorate."³ The administration's policy and public responses in protest against it are part of a perhaps unprecedented politicization of science in the United States.

These recent developments prompt the historical question of how public legitimacy for science has evolved in the United States over time. Science has long played a cultural role well beyond challenging conceptions of nature or facilitating technological applications. In the United States during the cold war, science was invoked as a model of rationality akin to democracy. When sociologist of science Joseph Ben-David arrived in the United States after World War II, he believed the country to have replaced Britain as a model society. Such a society he expected to be "a scientific society."⁴ This rhymed with the new role science had helped bestow on the federal state during World War II, when nuclear technology boosted American global influence and power. After private foundations had provided the support to implement research-based science in a top tier of

1 "Activists Rush to Save Government Data—If They Can Find It," *New York Times*, March 6, 2017.

2 "Trump Creates 'Hostile Environment for Federal Agency Scientists, Report Says," *Washington Post*, July 27, 2017.

3 See Robert S. Young's opinion piece, "A Scientists' March on Washington Is a Bad Idea," *New York Times*, January, 31, 2017.

4 Gad Freudenthal, "General Introduction," *Scientific Growth: Essays on the Social Organization and Ethos of Science* (Berkeley, 1991), 12-13.

private American universities before 1940, the cold war provided the political and cultural framework for an unprecedented expansion of federal support for research. In the 1950s and 60s, physics became the poster child of science in the context of a growing federal defense establishment and the evolving space program.

In the wake of the politics of détente, in the 1970s momentum began to shift from physics to biology as the state's most relevant research field.⁵ This shift in attention to the field of biology occurred in the context of public controversies about the risks of using new technologies to alter the DNA of living organisms (recombinant DNA or rDNA).⁶ This mid-seventies debate about genetic engineering broadened the scope of public attention to developments in science to include risks for individuals and for the environment.⁷ After Congress, in 1980, allowed universities to patent results of research that the federal government had funded, genetic engineering kicked off what came to be called the "biotech boom." Patents derived from biological research became an important source of revenue and reshaped academia's relations with industry as universities turned themselves into hubs for technology development and investment.

In this brief overview, I will focus on aspects of the debate on human embryonic stem cells between 1998 and 2004 as a key development for the public legitimacy of science in the United States. During this controversy, developmental biology came to represent the legitimacy of a modernist vision associated with science at large. The political history and the outcome of the debate, I would like to suggest, provide important insights into the peculiar role that science has come to play in the United States.

Many countries discussed the use of human embryonic stem cells (hES cells) after 1998 but the political and regulatory response differed widely. Hence it serves as a good example for a discussion of the challenges that follow from the scientific profession's ongoing work of questioning the cognitive basis of worldviews.⁸ The debate involved several related topics, all of which came together to challenge the public's notions about the role of science. The successful isolation of hES cells was an important success for the field of developmental biology, which seeks to understand the processes that generate an organism along a trajectory from embryo to adult. The cells also were hailed by patient advocacy groups for their promise of medical advances but the opposition to this research placed them into the context of debates about abortion and the status of the embryo. The

5 Jon Agar, *Science in the 20th Century and Beyond* (Cambridge, 2012), 508.

6 Susan Wright, *Molecular Politics: Developing American and British Regulatory Policy for Genetic Engineering, 1972-1982* (Chicago and London, 1994).

7 Joachim Radkau, "Hiroshima und Asilomar: Die Inszenierung des Diskurses über die Gentechnik vor dem Hintergrund der Kernenergie-Kontroverse," *Geschichte und Gesellschaft* 14 (1988): 329-63.

8 For my use of the term "profession," see Peter Münte and Ulrich Oevermann, "Die Institutionalisierung Der Erfahrungswissenschaften und die Professionalisierung der Forschungspraxis im 17. Jahrhundert. Eine Fallstudie zur Gründung der Royal Society," in *Wissen und Soziale Konstruktion*, ed. Claus Zittel (Berlin, 2002), 165-230.

first successful cloning of a mammal two years earlier (Dolly, a female domestic sheep) had also raised important questions for biologists and the public. It prompted an international debate about the feasibility and the ethics of cloning that carried over into the discussion about stem cells. The range of practical political options that were available to the American public were restricted by the country's specific regulatory tradition, of which at least some discussants were not fully aware. Overall, the debate about human embryonic stem cells stands out because it provided the occasion for a striking politicization of science. In 2001, stem cells were front-page news and expected to define the legacy of incoming President George W. Bush.

I will provide some context about the political history of this debate. In keeping with our current focus on the history of knowledge at the GHI Washington, however, I will concentrate on the new knowledge and on what was at stake for its proponents. The political debate had an impact on the field of developmental biology. Researchers wore two hats: They were the ones explaining to journalists and to the public at large what they had learned while they continued to test this knowledge. At the same time, their presentation of the nature and potential of hES cells was tied to the political aim of securing public funding for their work. Scientists scored an ambivalent success: While they were able to find supporters for their ongoing work on understanding early human development, the debate about hES cells played a part in fracturing the political public along party lines.⁹

II. From Conceptualizing to Isolating Human Embryonic Stem Cells

Stem cells entered the public arena when James Thomson at the University of Wisconsin and John Gearhart at Johns Hopkins University reported that their teams had isolated embryonic stem cells (hES cells) and that they had been able to preserve in vitro the ability of these cells to grow into different types of human tissue. The concept of the stem cell had evolved since World War II. In 1949, biologist Leon Jacobson, who had been health officer at the Manhattan Project, sought to understand the relative significance of bone marrow and of the spleen in the blood-forming system, which is particularly sensitive to radiation. He found that protecting the spleen of a mouse from lethal radiation allowed the animal to live, and that something in the spleen caused the blood system to reconstitute itself after radiation had wiped it out. When it had become clear that cells were responsible for rebuilding blood, Ernest McCulloch and

⁹ On the broader issue, see *Legitimizing Science: National and Global Publics, 1800-2010*, ed. by Axel Jansen, Andreas Franzmann, Peter Münte (Frankfurt and New York, 2016). The term "fracture" relates to an idea introduced by Daniel T. Rodgers in his *Age of Fracture* (Cambridge, MA, 2010). For an overview of transatlantic stem cell debates, see Thomas Banchoff, *Embryo Politics: Ethics and Policy in Atlantic Democracies* (Ithaca: Cornell University Press, 2011).

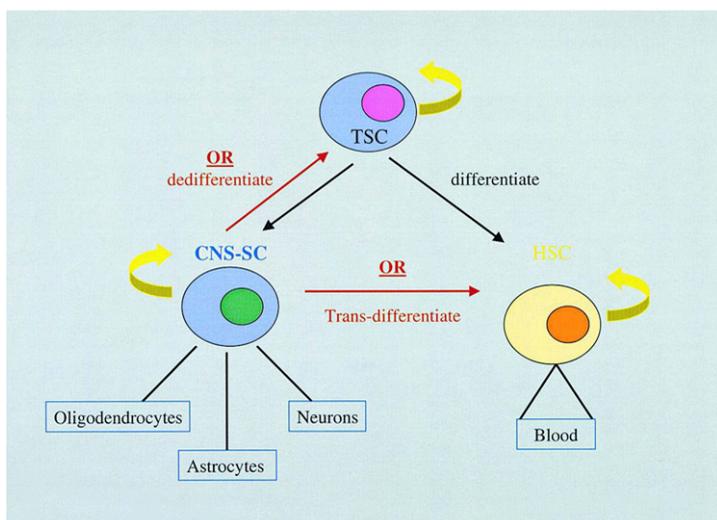


Figure 1. "Possible Sources of Tissue-Specific Stem Cells from another Tissue," from: Irving L. Weissman, "Stem Cells: Units of Development, Units of Regeneration, and Units in Evolution." *Cell* 100, no. 1 (January 7, 2000): 157-68. Used by permission. Weissman wondered whether adult stem cells' plasticity could be explained by either direct transdifferentiation of central nervous system stem cells (CNS-SC) to cells of another lineage (blood) — or by dedifferentiation of such a cell into a cell higher up in the hierarchy (a totipotent stem cell, TSC) and then a differentiation of a TSC into a blood cell. The difference was significant because transdifferentiation would have called into question the (hierarchical) stem cell model as such.

basis of such work, in 1969 E. Donnall Thomas performed the first bone marrow transplant on a leukemia patient, who had previously been exposed to radiation to kill cancer cells. The question remained whether transplanting bone marrow could be avoided if blood-forming cells could be located and put to use instead. But conceptualizing such cells and finding them were two different matters.

By 1981 Martin Evans at the University of Cambridge and Gail Martin at the University of California, San Francisco, were able to isolate from mice and preserve in vitro what Martin called "embryonic stem cells." "Embryonic" stem cells were considered "pluripotent" because they could transdifferentiate into cells of all different cell lineages in the body. This separated them from lineage-specific stem cells that could create more specific cells only, such as blood cells (instead of, say, nerve cells). By 1991, blood-forming stem cells in mice and in humans had been identified in Irving Weissman's lab at Stanford.¹¹

10 Jos Domen, Amy J. Wagers, and Irving L. Weissman, *Regenerative Medicine* (Bethesda, MD, 2006), 19, http://stemcells.nih.gov/info/Regenerative_Medicine/Pages/2006Chapter2.aspx.

11 E. Donnall Thomas, "A History of Haemopoietic Cell Transplantation," *British Journal of Haematology* 105, no. 2 (May 1, 1999): 330-39; A. J. Becker,

E. A. McCulloch, and J. E. Till, "Cytological Demonstration of the Clonal Nature of Spleen Colonies Derived from Transplanted Mouse Marrow Cells," *Nature* 197, no. 4866 (February 2, 1963): 452-54; Domen, Wagers, and Weissman, "Regenerative Medicine"; G. R. Martin, "Isolation of a Pluripotent Cell Line from Early Mouse Embryos Cultured in Medium

Conditioned by Teratocarcinoma Stem Cells.," *Proceedings of the National Academy of Sciences of the United States of America* 78, no. 12 (December 1981): 7634-38. For an overview, see Davor Solter, "From Teratocarcinomas to Embryonic Stem Cells and Beyond: A History of Embryonic Stem Cell Research," *Nature Reviews. Genetics* 7, no. 4 (April 2006): 319-27.

James Till in 1963 inferred that certain cells could both self-renew and give rise to most if not all other blood cells. Stem cells came to be defined by their ability to choose, in the case of blood-forming stem cells, "between self-renewal (remain a stem cell after cell division) or differentiation (start the path towards becoming a mature hematopoietic cell)."¹⁰ On the

By the early nineties, biologists had established a hierarchical model of cells, with embryonic stem cells at the top and more differentiated stem cells below. They had been able to identify such cells in different model organisms and they had isolated human *blood-forming* stem cells. But they had not isolated *human embryonic* stem cells, which became a perhaps obvious challenge in order to verify the overall model and to make such cells available for potential therapies.

Well before national publics would discuss such matters, therefore, researchers who considered taking on such work had to take positions on the ethical questions involved. Isolating hES cells involved human fetal tissue and this touched on the contentious status of the embryo. When he set out to isolate hES cells, James Thomson worked with fertilized human eggs discarded by parents who had given consent for their use in research.¹² After he retrieved the desired hES cells from the eggs, the eggs expired. Thomson had decided that he considered the knowledge and therapies to be gleaned from these discarded eggs to be more important than preserving them. But Thomson and Gearhart knew that their work would spark strong opposition. During the 1990s, so-called “Christian patriots” targeted and even assassinated abortion clinic staff.¹³ With reference to his research at Johns Hopkins University, Gearhart pointed out to the *Washington Post* in 1996 that there was “going to have to be a real educational process on how to represent this material to the public.” His work was considered “so sensitive that security officials have been apprised of the routes he takes between home and work, lest antiabortion activists or others try to harm him.”¹⁴

In the United States, a peculiar regulatory tradition set the stage for the public debate about stem cells. While other countries such as the United Kingdom had long implemented a regulatory regime for research on human embryos (including fetal tissue and fertilized eggs) that could respond to research developments and regulate by force of law, the United States had no such regulation in place. Here, the status of embryos remained unresolved. Regulation was facilitated, not through law, but through Congress allowing or preventing the tax-funded National Institutes of Health (NIH) from funding certain types of research. This kept the matter in the public arena. In 1995, Congress passed an appropriation bill rider, the so-called Dickey-Wicker Amendment, which prohibited the NIH from funding any “research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death.”¹⁵

12 Katherine Esposito, “James Thomson: The Embryonic Man,” *Isthmus*, April 7, 2011, <https://isthmus.com/daily/article.php%3Farticle%3D33010>.

13 Herbert Gottweis, “The Endless hESC Controversy in the United States: History, Context, and Prospects,” *Cell Stem Cell* 7, no. 5 (November 5, 2010): 556.

14 *Washington Post*, July 26, 1996.

15 Gottweis, “Endless hESC Controversy,” 557.

Because of such restrictions, Thomson and Gearhart had relied on private funds for their work. Since the 1980s, private capital had begun to play a significant role in biological research. When the idea of isolating hES cells first came up in the early 1990s, Roger Pederson at the University of California, San Francisco was approached by the biotech company Geron about doing such work. But Pederson declined because he hoped that, given the recent election of William J. Clinton, the regulatory context would change and that the president would work with Congress to change restrictions imposed on NIH funding. “I think this area of investigation is something that is so at the headwaters that it’s not appropriate for private investors to control the headwaters of the river,” he told Geron. Isolating human ES cells, he argued, would be “something that could benefit all the people and therefore it should be developed by the people, by the federal government.”¹⁶ After Congress passed the Dickey-Wicker Amendment, however, Pederson decided to put Geron in touch with Thomson and Gearhart, who considered doing such work.

When Thomson and Gearhart were ready to announce the successful isolation of human embryonic stem cells to the public in 1998, the NIH was keen on using the momentum to convince Congress that it should be allowed to support such research. The agency put itself on track to open that route by going through the procedure to establish official guidelines for their use by NIH grant recipients, which threw the controversial issue of fetal tissue research back into the court of public debate. This time, however, the agency could counter its critics with the prospect of medical therapies and saving lives. Publication of draft guidelines in August 2000 prompted thousands of responses from the public as stem cells (along with cloning) came to dominate national news. “I think we cannot walk away from the potential to save lives and improve lives, to help people literally get up and walk, to do all kinds of things we could never have imagined,” President Clinton argued in support of the NIH proposal to fund stem cell research, “as long as we meet rigorous, ethical standards” such as the ones the NIH promised to provide.¹⁷ But when the 2000 presidential election put Republican George W. Bush in the White House, the matter remained unresolved as both sides struggled to convince the incoming president to accept or reject NIH support for research using hES cells. By the time George W. Bush made up his mind in 2001, the NIH had put opponents of such work on the defensive. In response, these opponents sought to turn to science to keep their footing. Conservative Christians, led by the Catholic Church,

16 Stephen S. Hall, *Merchants of Immortality: Chasing the Dream of Human Life Extension* (Boston, 2003), 98, 122.

17 *New York Times*, August 24, 2000.

decided to attack hES research by pointing to what it considered viable scientific alternatives.

Such alternatives were highlighted by opponents of hES research such as Republican Senator Sam Brownback who called the use of such cells “illegal, immoral and unnecessary.” Work done on “adult” stem cells, some researchers claimed, were as useful as hES cells.¹⁸ Adult stem cells are more differentiated cells that function as stem cells of a particular cell lineage and can be derived from grown human bodies instead of embryos. This made them attractive to anyone looking for alternatives to hES cells. In 1999, Richard Doerflinger of the Conference of Catholic Bishops explained that scientists had no need for hES cells because “new research showed that a different kind of stem cell isolated from a patient’s own body would provide the therapeutic benefits imputed to embryonic stem cells.”¹⁹ Such views were echoed by journalist Nicholas Wade in the *New York Times* who explained that “recent experiments have shown that the blood-making stem cells can also be coaxed to make muscle cells and even nerve cells.”²⁰ In the ensuing controversy, one strand of research within developmental biology was pitted against another. By hitching their wagon to one particular position in the evolving scientific debate, opponents of embryonic stem cell research had accepted the authority of science. They were thus exposed to developments within the research field that would undermine their claim. And for the field of developmental biology, the political significance of competing theoretical claims also had an important effect because researchers had to balance their interest in advancing their particular claim against their colleagues with their joint interest in preserving the integrity of their field against outside interference.

III. Adult Stem Cells as Political Ammunition

Before Thomson and Gearhart published their work on embryonic stem cells, few researchers paid attention to papers claiming that adult cells were more flexible than had been thought. Blood-forming stem cells, for example, were supposed to act as stem cells for the blood system and give rise to cells within their lineage, not to cells of another type, such as nerve or fat cells. The idea that adult stem cells were more versatile than expected derived from the other major event in the public history of biomedicine of that period, the cloning of Dolly the sheep in 1996. Cloning had been achieved by taking the

18 *New York Times*, August 24, 2000.

19 *Washington Post*, May 23, 1999, A01.

20 Nicholas Wade, “New Rules on Use of Human Embryos in Cell Research”, *New York Times*, Aug. 24, 2000.

nucleus out of an adult cell, implanting it in an egg from which the original nucleus had been removed, and by implanting this egg (with the new nucleus) in a uterus. Hence, the nucleus of an adult instead of an embryonic cell had given rise to a female domestic sheep. For developmental biologists, the transfer raised the question of how the egg had done the trick of “reprogramming” the nucleus that had come from an adult cell. They figured that cells generally received from their environment important clues about how to develop.

In 1998 and 1999 researchers began to publish papers in which they claimed that adult cells were much more flexible than previously thought. While established theory held that cell development was irreversible, two Italian teams suggested that the commitment of cells to a particular developmental fate could be changed. A Milan-based team suggested in *Science* that blood stem cells in mice could recreate muscle tissue, i.e. that they could create not just blood cells but also cells of another cell type.²¹ A few months later, another group reported that in mice, neural stem cells engrafted (joined) into the blood-forming system, if that system previously had been erased through radiation.²² Taken together, these papers indicated that stem cells in the adult body could potentially be harnessed for therapy. To the editors of *Science*, this was the next big thing. Representing the “promise of youth,” both papers in 1999 together were identified as “Breakthrough of the Year.”²³ As developments within the field were picked up by the media while Americans (and incoming President George W. Bush) tried to make up their minds about the relevance of research using hES cells, more and more researchers joined the adult-stem-cell camp.

In a January 2000 review essay in the journal *Cell*, Elaine Fuchs and Julia Segre pointed out that in the preceding year, “some spectacular fireworks have exploded many long-standing dogmas in the stem cell world.”²⁴ They explained that even though adult stem cells formerly were thought to be dedicated to one cell lineage, recent work had shown that they were more flexible. But Fuchs and Segre offered few insights into how the transdifferentiation potential of such adult stem cells could be explained, let alone controlled. They conceded that while an understanding of growth factors perhaps responsible for such transformations was evolving, the system was “hopelessly complex.” But they felt certain that perceptions of what stem cells “look like and where to find them ... [had been] revolutionized.” Even though

21 The group had transplanted genetically marked cells taken from the bone marrow into mice where these cells repaired degenerated muscles. This seemed to prove that bone-marrow-derived cells could evolve into muscle cells, indicating that these cells were more flexible than assumed in the conventional model. Giuliana Ferrari et al., “Muscle Regeneration by Bone Marrow-Derived Myogenic Progenitors,” *Science* 279, no. 5356 (March 6, 1998): 1528–30.

22 Christopher R. R. Bjornson et al., “Turning Brain into Blood: A Hematopoietic Fate Adopted by Adult Neural Stem Cells in Vivo,” *Science* 283, no. 5401 (January 22, 1999): 534–37.

23 Gretchen Vogel, “Capturing the Promise of Youth,” *Science* 286, no. 5448 (December 17, 1999): 2238–39, doi:10.1126/science.286.5448.2238. For a general account of the adult-stem-cell debate of 2000 and 2001, see Stephen S. Hall, *Merchants of Immortality: Chasing the Dream of Human Life Extension* (Boston, 2005), ch. 13.

24 Elaine Fuchs and Julia A Segre, “Stem Cells: A New Lease on Life,” *Cell* 100, no. 1 (January 7, 2000): 143–55.

they could not explain what came to be called “transdifferentiation,” they went on to promote adult stem cells as an alternative to human embryonic stem cells. The latter had “come under serious ethical scrutiny, with no clear resolution in sight. Adult stem cells offered an alternative. If “the plasticity [i.e. ability to transform into cells of another lineage] of [adult, somatic] stem cells is truly greater than previously imagined,” they wrote,

then it may be feasible in the future to reroute easily procurable [adult] stem cells to stem cells such as neuronal or pancreatic that are more difficult to obtain. While such notions may still border on the unlikely and perhaps even preposterous, the newly discovered versatility of at least some somatic stem cell types is provocative and may have enormous ramifications for stem cell therapeutics in the future.²⁵

The momentum would eventually peak in 2002 when Minnesota-based researcher Catherine Verfaillie made a splash by claiming to have discovered the “ultimate stem cell.” Suggesting that this cell had all the capabilities of human embryonic stem cells to “turn into every single tissue in the body,” the *New Scientist* pointed out that this “might turn out to be the most important cell ever discovered.”²⁶ In response, Senator Sam Brownback and Leon Kass of the President’s Council on Bioethics praised the work as genuine and important because it showed the promise of adult stem cells.²⁷ The news seemed too good to be true: A super-adult-stem-cell resolving the ethical dilemmas posed by hES cells. But Verfaillie’s paper had not been published in a peer-reviewed journal²⁸ and it was immediately attacked from many sides. One senior biologist later remembered that he wondered about how likely it was that these results would stand up to scrutiny, given that seventeen researchers were listed as authors.²⁹

Even though (or because) such papers were celebrated by editors of prestigious academic journals, developmental biology had a problem. At a time when the NIH was trying to convince the public and the federal government that it should be allowed to pay for research on human embryonic stem cells, such papers provided welcome ammunition for those opposing it. “Opponents of using embryonic stem cells are quite likely to cite Dr. Verfaillie’s findings,” the *New York Times* observed, “to support their argument that cell therapy can be

25 Ibid., 153.

26 Sylvia Pagán Westphal Boston, “Ultimate Stem Cell Discovered,” *New Scientist*, January 23, 2002, <https://www.newscientist.com/article/dn1826-ultimate-stem-cell-discovered/>.

27 Hall, *Merchants of Immortality*, 242.

28 Ibid., 397 n. 242.

29 Author’s interview with Rudolf Jaenisch, 2012.

based on adult stem cells alone.”³⁰ In an important strategic reorientation, American anti-abortion groups began to lean on adult stem cells as the perfect argument against human embryonic stem cells. If indeed stem cells were about the regeneration of tissue, anti-abortion advocates argued, why not use adult cells that could be taken from the patient’s body? In the spring of 1999, Sam Brownback began to argue that research using human embryonic stem cells was unnecessary. “Destructive embryo research,” he declared, was less promising than research on adult stem cells. “We should focus our attention on legitimate research,” he wrote in a letter to the *Washington Post*, criticizing that paper’s more liberal stance.³¹ Brownback’s reasoning rhymed with advice emerging from the Vatican: “The progress and results obtained in the field of adult stem cells (ASC),” the *Pontifical Academy for Life* suggested in August 2000, “show not only their great plasticity but also their many possible uses, in all likelihood no different from those of embryonic stem cells.”³²

By endorsing this position, however, the Catholic Church and spokesmen of the religious right came to share its fate. The endorsement reflected an urge not to stand in the way of promising medical therapy, and to endorse biomedical research where it aligned with religious values. As it turned out, religious endorsement and active support for one side in the emerging scientific debate challenged the research field to retain its balance in two ways: First, by preserving its research standards at a time when editorial choices by publications such as *Science* and *Nature* seemed to respond to public debate; and second, by preserving all promising research options, including research on embryonic stem cells, at a time when that option was questioned from within science itself.

30 “Scientists Make 2 Stem Cell Advances,” *New York Times*, June 21, 2002.

31 *Washington Post*, Oct. 23, 1999.

32 Pontifical Academy for Life, “Declaration on the Production and the Scientific and Therapeutic Use of Human Embryonic Stem Cells,” August 24, 2000, http://www.vatican.va/roman_curia/pontifical_academies/acdlife/documents/rc_pa_acdlife_doc_20000824_cellule-staminali_en.html#_ednref9.

In the ensuing debate, the NIH and prominent researchers in the field of developmental biology took the stance that while adult stem cell plasticity was not proven, all options should be investigated, including research on human embryonic stem cells. Stanford-based biologist Irving Weissman emerged as a vocal critic of adult stem cells. He had been instrumental in developing the stem-cell concept during the previous decades. He had identified the first blood-forming stem cell in mice in 1988 and then in humans four years later. In response to claims about the plasticity of adult stem cells, he co-authored an editorial with Nobel laureate David Baltimore in April 2001. Determined to stem the tide against hES research, they insisted that groups involved in the policy-making process had to make a

decision on the basis of available facts, among them the reality that “published accounts suggesting adult stem cell pluripotency [i.e. the ability to give rise to cells of various lineages] have not successfully established that one type can produce a cell of another tissue type.” While adult stem cells might indeed prove to be valuable in the future, such value had not been shown. Accordingly they called adult cell plasticity “simply a hope, and it would be foolish to abandon the surer path for the unproven one.”³³

As the debate on NIH guidelines intensified during the summer and the *New York Times* reported on the topic every single day during the month of July, researchers had begun to fight back. In June 2001 Secretary of Health and Human Services, Tommy G. Thompson circulated a report by the NIH concluding that stem cells derived from embryos, despite immune-reaction issues, were “more promising for developing cures for a range of debilitating diseases than stem cells from the bones and organs of adults.”³⁴ Based on a review of literature and on interviews with researchers, the study “affirms the scientific consensus” that all “avenues of research should be exhaustively investigated, including both adult and embryonic sources of tissue.”³⁵ At an event held by the National Academy of Sciences in the summer of 2001 Irving Weissman strongly rejected adult-cell alternatives as “a delaying tactic when the need [for therapies] is urgent.”³⁶ But efforts to unshackle NIH funding for this type of fetal tissue research and the implicit claim for a new legitimacy for embryo research were bound to run into problems as long as the relative advantage of hES cells over adult stem cells could not be spelled out on the basis of evidence-based clarifications. Weissman attacked claims about the malleability of adult stem cells on two levels, in papers he published in peer-reviewed journals and by taking a stance in the wider public, pointing out that adult stem cell plasticity was all but certain. Weissman could not yet show that adult stem cells were less powerful, as claimed by some of his colleagues. But he and other proponents of such work were nevertheless able to convince enough conservatives to force a compromise on the incoming president.

By 2001 there was considerable public buzz about adult stem cells. The *Wall Street Journal* in April quoted a spokesman for the American Life League who pointed out that due to their coverage in the national media, adult stem cells had become “the keystone in our public relations battle” against embryonic stem cells. A paper by a UCLA plastic surgeon who claimed to have turned readily available fat

33 Irving L. Weissman and David Baltimore, “Editorial: Disappearing Stem Cells, Disappearing Science,” *Science*, New Series, 292, no. 5517 (April 27, 2001): 601.

34 David E. Sanger, “Bush Leans Against Support for Stem-Cell Research, Aides Say,” *New York Times*, June 22, 2001.

35 Robert Pear, “U.S. Study Hails Stem Cell’s Promise: It Says those from Human Embryos Have a Special Worth,” *New York Times*, June 27, 2001, <http://search.proquest.com/docview/91877176/abstract/75A12D9D35BD40DFPQ/75?accountid=9851#>.

36 William Safire, “Stem Cell Hard Sell: Bush’s Most Fateful Decision,” *New York Times*, July 5, 2001.

cells into bone and muscle cells was reported by all three TV nightly network newscasts.³⁷ As journalists struggled to make sense of the details, many science writers touted the virtues of the adult-stem-cell alternative.³⁸ Developmental biologist Austin Smith complained that transdifferentiation by adult cells was “picked up by politicians and lobbying groups” and that it turned out to be “quite difficult to argue against [them] because they will just list all these published [scientific] papers.”³⁹

In the meantime, President Bush and his advisors were moving towards a decision. Conservatives insisted that the president deliver on campaign promises to the pro-life camp. The president of the Southern Baptist Convention’s Ethics and Religious Liberty Commission, Richard Land, argued that not following through on the stem cell issue would be “the cultural equivalent of going back on the [President H. W. Bush’s] no-new-taxes pledge” (which had helped Bush win the 1988 presidential election before it came to haunt him after a budget compromise two years later).⁴⁰ But proponents of embryonic-stem-cell research were able to muster new support in Congress. During the summer some members of Congress defected the anti-abortion camp and came out in support of research on hES cells, among them Republican Senators Orrin G. Hatch and Bill Frist.⁴¹ In July, Nancy Reagan joined the supporters.⁴² That month, a bipartisan group of 61 senators signed a letter written by Senator John Kerry to President Bush, asking him to permit use of federal funds for human embryonic stem cell research.⁴³

A compromise emerged when scientists signaled that they would be content with a limited number of hES cell lines instead of all-out NIH support. Weissman in late June told the *New York Times* that a “finite number [of hES cell lines] would be sufficient.” He added that if “we had 10 to 15 cell lines, no one would complain.”⁴⁴ A decision seemed imminent when Bush went to visit Pope John Paul II on July 23. The administration wanted the stem cell issue off the table prior to that trip so as not to appear to align with the Vatican on the issue. Bush announced a compromise solution in his first television address as president of the United States on August 9, 2001: The NIH would fund research on human embryonic stem cell lines that had

37 Antonio Regalado, “Advances in Stem Cells, Cloning Renew Controversy. Scientists Say Embryo Research Is Needed Despite Fat Finding,” *Wall Street Journal* (Eastern Edition), April 27, 2001. Also see Denise Grady, “Fat Is Good Source of Stem Cells, a Study Says,” *The New York Times*, April 10, 2001. The articles refer to Patricia A. Zuk et al., “Multilineage Cells from Human Adipose Tissue: Implications for Cell-Based Therapies,” *Tissue Engineering* 7, no. 2 (April 1, 2001): 211–28.

38 Stephen S. Hall, “Adult Stem Cells,” *Technology Review*, November 2001. Hall would later present a more nuanced account of the debate in Hall, *Merchants of Immortality*.

39 William A. Wells, “Is Transdifferentiation in Trouble?,” *The Journal of Cell Biology* 157, no. 1 (April 1, 2002): 15.

40 *New York Times*, July 21, 2001.

41 *New York Times*, July 19, 2001.

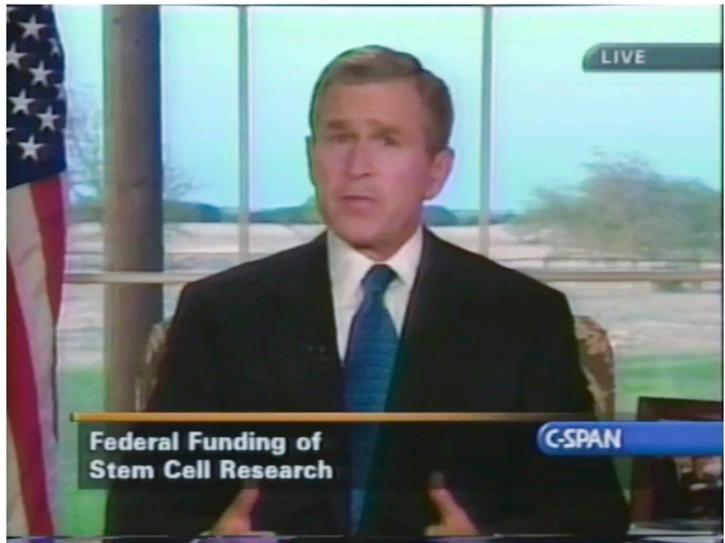
42 “From Nancy Reagan, a Nod toward Embryonic

Stem Cell Research,” *New York Times*, July 13, 2001.

43 *New York Times*, July 21, 2001.

44 David E. Sanger, “Bush Leans Against Support for Stem-Cell Research, Aides Say,” *New York Times*, June 22, 2001.

already been isolated, but not on new embryonic stem cell lines derived from fertilized eggs after the day of his announcement. While some liberals considered Bush's decision a scandal, it was in fact a lenient solution, allowing the NIH to fund research, albeit only on some embryonic stem cell lines. A senior scientist familiar with the 1990 German *Embryonenschutzgesetz*



pointed out that in addition to not prohibiting such work by law (which was in line with the American regulatory tradition), the decision provided research with options by allowing some NIH funding.⁴⁵ Such funding provided public endorsement and legitimacy for work with hES cells. For opponents of hES research, however, the Bush decision was not yet a total defeat. Some conservatives had bolted over the issue of stem cells, which suggested that the biomedical community had provided effective public leadership on behalf of science. But religious conservatives would continue to exert pressure through the viable alternative of adult stem cell research until 2002, when developmental biologists disproved their claims.

That year, Weissman published a paper in *Science* in which his team refuted the key claim that adult stem cells of one lineage were sufficiently flexible to give rise to cells of another type. Weissman had questioned such plasticity in earlier publications. In 2000, he had asserted that in cases where adult cell plasticity seemed to have been observed “I propose that neither dedifferentiation nor transdifferentiation occurred ..., but rather that stem cells ... in unexpected places are responsible.” At that time, Weissman had challenged his opponents to show that when they reported that blood-forming stem cells made muscle cells, it was indeed blood-forming stem cells that did the job, not muscle-forming stem cells. Fuchs and Segre had emphasized potential medical

Figure 2. U.S. President George W. Bush announced his decision on stem cell research during prime time on August 9, 2001. www.c-span.org

⁴⁵ Author's interview with Rudolf Jaenisch, 2012.

46 Amy J. Wagers et al., “Little Evidence for Developmental Plasticity of Adult Hematopoietic Stem Cells,” *Science* 297, no. 5590 (September 27, 2002): 2256–59. The paper had been submitted in June 2002. Another article had tested and questioned transdifferentiation: Raymond F. Castro et al., “Failure of Bone Marrow Cells to Transdifferentiate into Neural Cells in Vivo,” *Science* 297, no. 5585 (August 23, 2002): 1299. Neil D. Theise, “Stem Cell Research: Elephants in the Room,” *Mayo Clinic Proceedings* 78, no. 8 (August 1, 2003): 1008. When challenged by transdifferentiation proponents (in a letter to the editors of *Science*) to provide an “adequate description of the methodologies used” so as to make sure that the same markers were used to identify the cells, Weissman’s group pointed out that their experiments had not been “designed to replicate precisely the work of other investigators, but to clarify and extend their observations by reestablishing, through the transplantation of single ... isolated ... HSC” whether the production of cell types other than blood-cells was part of their common function. Some transdifferentiation proponents remained unconvinced, arguing that Weissman’s group should have reproduced their experiment, not improve on it.

47 Neil D. Theise, “Stem Cell Plasticity: Recapping the Decade, Mapping the Future,” *Experimental Hematology* 38, no. 7 (July 1, 2010): 533.

48 Helen Pearson, “Stem Cells: Articles of Faith Adulterated,” *Nature* 420, no. 6917 (December 19, 2002): 734–35.

applications for adult stem cells while Weissman had discussed the broader significance of the stem cell concept for the “evolution of development” and the field of biology. Two years later, Weissman had directed experiments on adult cells himself. He made sure that he knew what he was looking at by inserting into the host organism only one single adult blood-forming stem cell. When his team looked at what this adult cell did, they found “little evidence” that it contributed to anything other than what it was supposed to do: make blood cells.⁴⁶ For the time being, Weissman’s paper had the effect of discrediting the idea of adult stem cell plasticity. One of his opponents later complained that the “prestige of the journal in which it appeared, let alone the prestige of the laboratory from which it emerged,” guaranteed that Weissman’s paper would have “a central and enduring role in all discussions of the entire field.”⁴⁷ In December 2002, *Science* reported that adult stem cell studies, “particularly those by newcomers to the field” had come under increased attack.⁴⁸

IV. Rallying California behind Embryonic Stem Cell Science

Within the field of developmental biology, one may surmise that adult stem cells may not have received as much attention after 1998 had they not been an important instrument in political debate. But the promise of adult stem cells threatened to limit NIH funding for hES research and so researchers such as Irving Weissman began to address adult-stem-cell claims head-on. In doing so, they demanded that their field retain all research options instead of limiting them. But their involvement had effects that transcended future opportunities for their research field. Because these researchers had provided effective arguments in a political fight about policy, their perspective acquired a political value for Democrats in their political efforts to confront President George W. Bush. The leverage provided by this topic became all the more relevant in the wake of 9/11 and the difficulties involved in criticizing a president when America was “under attack.” In the context of an increasingly unpopular war in Afghanistan and in Iraq, stem cell research offered a progressive alternative for (and to) national policy. In 2004, presidential candidate John Kerry waved the banner of scientific progress in the face of George W. Bush, whose 2001 compromise on hES cells Democrats declared too restrictive. Democrats used the promise of stem cell research as a symbol to claim scientific modernism for their party, and to deny it to their political opponents. At their national

convention, they were able to present Ronald Reagan's son Ron Reagan who explained in his televised speech that Americans had to choose between "reason and ignorance, between true compassion and mere ideology" and that they should cast a vote for the Democratic Party and embryonic stem cell research.⁴⁹ Such claims had important effects at a time when the American political landscape was shifting. No federal law existed to ban research using human embryonic stem cells. Bush was reelected to the White House in 2004 and continued to prevent the NIH from funding such work. But others remained free to do so. While some American states restricted work on stem cells by law, others endorsed an opportunity to outflank Washington.⁵⁰

In 2004, the State of California passed Proposition 71, a ballot measure dedicated to human embryonic stem cell research. "It's the first time I know of that a state has said that the federal government has neglected its opportunity to lead in this area of research," Irving Weissman argued, "so it is the right of the states to take over where the federal government left off."⁵¹ Real estate developer Robert Klein, father to a son with type 1 diabetes, initiated and helped fund a multimillion dollar campaign for Proposition 71. This state referendum created the California Institute of Regenerative Medicine (CIRM) which was funded by a three billion dollar bond issue over ten years and shielded from state lawmakers through elaborate constitutional anchors. CIRM outflanked the NIH to become the largest funder of stem cell research in the world. It allowed researchers to work with human embryonic stem cell lines other than the ones the NIH allowed for after the 2001 Bush decision. At the time of the California referendum in 2004, the U.S. was bogged down in costly and unsuccessful wars in Iraq and Afghanistan. Klein and his supporters — the medical profession, patient-advocacy groups, and journalists — in a well-organized public campaign used biomedicine as a means to reinvigorate ambitions for preserving the state's leadership in science and technology, and as a popular progressive movement against George W. Bush in Washington and against the state's political establishment in Sacramento (even if Democrats controlled the State Legislature while Republican Arnold Schwarzenegger was Governor). The pro-stem-cell line-up included well-known actors Michael J. Fox, who suffers from Parkinson's, and Christopher Reeves, who had suffered a severe spinal cord injury. While key advisers such as Weissman helped design CIRM as an agency that would oversee the development of findings from research to therapy and clinical testing

49 "Ron Reagan, Remarks to the 2004 Democratic National Convention—July 27, 2004," July 27, 2004, <http://www.presidential-rhetoric.com/campaign/dncspeeches/reagan.html>.

50 Geoffrey Lomax, "Rejuvenated Federalism: State-Based Stem Cell Research Policy," in Benjamin J. Capps and Alastair V. Campbell, *Contested Cells: Global Perspectives on the Stem Cell Debate* (London, 2010), 369.

51 Daniel S. Levine, "Irv Weissman: A Researcher Becomes a Warrior," *San Francisco Business Times* 18, no. 43 (May 28, 2004): S12.

(for companies a costly “valley of death”), campaign managers overlaid the promise of therapies for major diseases.⁵²

Not surprisingly, therapies would be slow in the making. In 2012, one researcher explained that there was “quite a bit of pressure” on the stem cell research community in California, given that development of a drug, if successful at all, usually costs a billion dollars and takes fifteen years. But CIRM’s funding system was geared towards therapies. “They want you to develop a drug and get it into trials,” which required adjustment by academics focused on basic research.⁵³ In 2018, CIRM funds 48 clinical trials, including one on the use of stem cells to treat blindness from age-related macular degeneration, which appeared promising, but no marketable therapy has emerged thus far.⁵⁴ CIRM is “always looking for a blockbuster success that may never come,” the *Los Angeles Times* observed in 2015.⁵⁵ If such a blockbuster drug were to materialize from CIRM grants, however, Proposition 71 would secure for the State of California income from patents, royalties, and licenses.⁵⁶ While the federal government had retained the option for research on human embryonic stem cell research, therefore, a California stem cell coalition in 2004 successfully emphasized federal hesitations and created a new symbol for scientific progress around which to rally their state. Other states, such as Missouri, New York, and Massachusetts, have also responded to the stem cell hype. By 2007, all American states together spent over 500 million dollars a year on stem cell research.⁵⁷ These developments attest to major shifts in the relationship between the states and the federal government since 1980, and in the shifting and increasingly polarized role of science in America.

Adult stem cells would stage a comeback after 2006 when Shinya Yamanaka showed how adult cells could be reprogrammed into

52 Eileen Burgin, “Human Embryonic Stem Cell Research and Proposition 71: Reflections on California’s Response to Federal Policy,” *Politics and the Life Sciences* 29, no. 2 (September 1, 2010): 73–95.

53 Author’s interview with stem cell researcher, October 2012.

54 See CIRM website, <https://www.cirm.ca.gov/clinical-trials>.

55 “Ten years in, California’s stem cell program is getting a reboot,” *Los Angeles Times*, January 3, 2015, <http://www.latimes.com/business/hiltzik/la-fi-hiltzik-20150104-column.html>.

56 Full Text of Proposition 71, voterguide.sos.ca.gov/past/2004/general/propositions/prop71text.pdf.

57 James W. Fossett, “Federalism by Necessity:

State and Private Support for Human Embryonic Stem Cell Research,” Rockefeller Institute Policy Brief (Albany, New York: The Nelson A. Rockefeller Institute of Government, August 9, 2007), http://www.rockinst.org/pdf/health_care/2007-08-09-federalism_by_necessity_state_and_private_support_for_human_embryonic_stem_cell_research.pdf.

pluripotent stem cells (iPS cells), which could then give rise to cells of a different lineage.⁵⁸ This confirmed critics' earlier hesitations to endorse the idea of "transdifferentiation" while it showed that cells indeed could be nudged to create cells of a different cell lineage if they were first pushed back to an earlier (pluripotent) state. Supporters of former President George W. Bush claimed that such work had become possible because of their insistence on finding alternatives to hES cells. By that time, however, the prospect of translating such work into therapy seemed remote as the public had learned to be wary of inflated promises. Even though Yamanaka suggested that his work had initially been prompted by concerns about using human embryonic stem cells, it provided little relief to the Catholic Church, one of the key opponents of research using hES. In a 2007 publication by the *Pontifical Academy of Sciences*, Cardinal Lehmann in his essay on "Bioethik und Menschenrechte" (bioethics and human rights) did not refer to adult stem cells.⁵⁹ And in her introductory essay to the same volume, biologist Nicole le Douarin left no doubt that results of studies on adult stem cells, which had been "reported in the flurry of scientific literature ... during the past few years[,] failed to be confirmed by other research groups."⁶⁰

V. Conclusion

The stem cell debates in the United States between 1998 and 2004 were remarkable for many reasons. While other countries, such as the United Kingdom or Germany, relied on a regulatory framework in dealing with new knowledge and with the options it opened up for research and for medicine, the United States had no such legal system in place. When the NIH wanted the federal government to endorse the research and to fund it, a decision had to be made by Congress and the president, which put the matter into the public arena. In this article, I have focused on the debate's impact on the field of developmental biology and on how the field struggled to preserve its coherence at a time when some of its ideas were used in an attempt to limit research options. During this debate, proponents of adult stem cell plasticity unwittingly provided ammunition for political opponents of research on human embryonic stem cells. While no one at the time knew whether adult stem cells really did what some claimed they could do, prominent researchers in the field advocated that all stem cell research, including research on hES cells, should retain public funding through the NIH. In this way, they pursued (national) public endorsement and support for the knowledge they had established

58 Unlike earlier ideas associated with adult stem cell plasticity, instead of a "transdifferentiation" of adult cells from one cell lineage straight to another, what could be achieved was a "dedifferentiation" of adult cells to an earlier stage, which then opened up to them a different lineage pathway. For his overall assessment of research developments in view of his own contribution, see Shinya Yamanaka, "Induced Pluripotent Stem Cells: Past, Present, and Future," *Cell Stem Cell* 10, no. 6 (June 14, 2012): 678-84.

59 Karl Lehmann, "Bioethik und Menschenrechte: Reflexionen über die Gefährdung und die Würde des Menschlichen Embryo," in *Stem Cell Technology and Other Innovative Therapies*, Scripta Varia 111 (Vatican City, 2007), 14-31, <http://www.casinapioiv.va/content/dam/accademia/pdf/sv111/sv111-lehmannde.pdf>.

60 Nicole M. Le Douarin, "Introduction," in *Stem Cell Technology and Other Innovative Therapies*, Scripta Varia 111 (Vatican City, 2007), 8, <http://www.casinapioiv.va/content/dam/accademia/pdf/sv111/sv111-lehmannde.pdf>.

and for the knowledge they hoped to gain. Other influential groups, such as patient advocacy groups, strongly supported such demands. Even though the medical promise of stem cell research was frequently exaggerated, it allowed its advocates to recruit conservatives such as Nancy Reagan to their campaign. For the Democratic Party, this provided political leverage to attack conservative world views centered on the abortion issue. But in 2004, Democrats were unable to unseat George W. Bush, who returned to the White House. The campaign for science that human embryonic stem cells had come to represent was endorsed in particular states instead of at the national level, a pattern that continues to play out today.

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