Point/Counterpoint

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TECHNOLOGICAL ADVANCEMENT, ETHICS, AND DEMOCRACY: WHAT CAN BE LEARNED FROM STEM CELL RESEARCH?

Potential therapies associated with stem cell research have captured the imagination of the public. The idea that some types of serious health problems could be corrected by growing our own cells anew is compelling. Nonetheless, the seminal research in this area relied upon extraction of cells from human embryos. The source of these pluripotent cells, in itself, raised ethical objections tied to the sanctity of life that have impacted government regulation and funding of research in this area. Further, the advent of human embryonic stem cell research at times presented scientists with uncomfortable ethical choices in the pursuit of often very fundamental scientific research. Scientists have since developed methods of reprogramming cells from adults into induced pluripotent stem cells so that they can also be differentiated for alternative purposes in the body, but questions remain about permissible sources and uses of these cells. Of course, all of this research comes at a considerable cost that should be weighed against both current and realistic future advances of the technology.

Thus, stem cell science lies at the intersection of the advancement of technology, societal concepts of ethical behavior, and the role of government. In this Point/Counterpoint, I have invited two leading groups of authors to discuss the complex issues related to stem cell research, as well as what might generally be learned from them by addressing the following questions:

1. Should federal funding for human embryonic stem cell research be expanded, diminished, or halted altogether?
   a. What specific advances in science (scientific knowledge?) and medicine have resulted from federal investments in human embryonic stem cell science?
   b. How have ethical, legal, and regulatory issues associated with federal funding for stem cell research influenced the character and trajectory of the field?
   c. How do (should?) new methods to induce pluripotency in human cells alter the calculus for thinking about federal funding for human embryonic stem cell research?

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2. What lessons should science policymakers (scholars?) draw from the case of human embryonic stem cell research?

One group of authors participating in the Point/Counterpoint is composed of Jason Owen-Smith (University of Michigan, Barger Leadership Institute Professor of Organizational Studies and Associate Professor of Sociology and Organizational Studies), Christopher Thomas Scott (Stanford University Center for Biomedical Ethics, National Core for Neuroethics, The University of British Columbia), and Jennifer McCormick (Mayo Clinic, Assistant Professor, General Internal Medicine and Health Care Policy Research). The other group of authors is composed of J. Benjamin Hurlbut (Arizona State University, School of Life Sciences, Assistant Professor) and Jason Scott Robert (Arizona State University, Franca Oreffice Dean's Distinguished Professor in the Life Sciences, and the Lincoln Associate Professor of Ethics in Biotechnology and Medicine).

STEM CELLS, SCIENCE, AND PUBLIC REASONING

J. Benjamin Hurlbut and Jason Scott Robert

INTRODUCTION

These are interesting days in the scientific, social, and political debates about human embryonic stem cell research. Pluripotent stem cells—cells that can, in principle, give rise to the body's full range of cell types—were previously derivable only from human embryos that were destroyed in the process. Now, a variety of somatic cell types can be reprogrammed to a pluripotent state. Meanwhile, long-standing promises about the therapeutic potential of pluripotent stem cells are inching toward realization, as several early-phase clinical studies are underway. At the same time, despite presidential declarations in favor of expanding human embryonic stem cell research, the regulatory environment is as complex as ever. Scientifically, clinically, socially, and politically, the stem cell debates are far from over.

So, should federal funding for human embryonic stem cell research be expanded, diminished, or halted altogether? The only honest, actionable answer in our complex civil society is *maybe*. There are better, more fundamental questions that require answers beforehand: What good is (stem cell) science, what good is public funding of (stem cell) science, and what is it that makes them good (or not)? These are more apt questions, more adequate to science in a democratic society. Answering them is a prerequisite to being able to answer questions about whether public funding should be expanded.

To date, embryonic stem cell science has not directly produced any major advances in clinical medicine. It has produced no new therapeutics that have passed Food and Drug Administration review; two experimental cell therapies are at the earliest stages of human trials. Induced pluripotent stem cell-based platforms have helped identify and test drugs with potential to treat several rare diseases (Lee et al., 2009; Jin et al., 2011; Yazawa et al., 2011; Ebert et al., 2008). Some cell-based

platforms for toxicity screening have been developed using hPSCs. But no one has been cured, no medical breakthroughs have been achieved, the foundations of the medical *status quo* have not been shaken. What does this tell us? Very little.

For a field this young—and this fundamental—asking what specific clinical outcomes it has produced is the wrong question. There is little doubt that much will be learned through the study of human embryonic stem cells (hESCs); indeed much already has been. Whether and how research will be translated into clinical applications is uncertain (Saha & Hurlbut, 2011; Fox, 2011). The challenges associated with translating hESCs from a research platform into a therapeutic tool should not be underestimated (Crystal, 2009; Maienschein et al., 2008).

But this is in no way unique to hESC science. Technological outcomes are notoriously hard to predict, particularly in the biomedical sciences. The notion that basic discoveries at the bench have—or can be predicted to have—particular applications at the bedside is a phantasm (Maienschein et al., 2008). The pipeline is a pipe dream. Furthermore, the linkage between scientific discovery and health outcomes is not as straightforward as is widely believed (Crow, 2011).

Pluripotent stem cell science holds great promise precisely because so much remains unknown about the mechanisms of human development—and pluripotent stem cells can be a powerful tool for interrogating the biological unknown (Robert, Maienschein, & Laubichler, 2006). Given the flexibility of PSCs, they can serve as a platform for studying development, for modeling human disease "in a dish," for predicting the toxicological effects of chemicals on humans, including in experimentally inaccessible domains such as human fetal development, and for much more (Saha & Jaenisch, 2009; Rubin & Haston, 2011). In short, these cells are powerful tools for asking scientific questions. What will come of this research area? Who can say? But it is safe to say that much of it will be scientifically interesting, and there is ample reason to believe that it will be useful.

Yet there is a deeper lesson here. As a society, we have tended not only to ask what this research has produced, but what it *will* produce. We have tended to ask scientists to make concrete predictions about the future. How long until hESC research, if funded, produces cures for juvenile diabetes? How long until someone with paraplegia will walk again? There has been criticism of scientists for "overpromising" about the potential of hESC research, and untenable promises have indeed been made. As any young researcher who has been questioned by patients about how much longer they must wait for cures can attest, excessive expectations have been created.

These expectations are excessive too in that they ask scientists to defuse moral disagreement in the present by offering scientific certainty about the future. While numerous researchers have (over)confidently predicted the future, this has often been at the public's (or its representatives') behest. For instance, in a 1999 Senate hearing—early in the life of this controversy—Senator Arlen Spector repeatedly asked testifying scientists to predict the timeframe from public investment to cures for specific diseases. "People in Congress like to have figures. . . . . Let me press you on the question . . . this business of advocacy is a very tough issue . . . If you talk in terms of being close, and what the dollars will do, then you start to create an impetus for it" (Stem Cell Research, 1999, p. 113.) By the end of the hearing, he had his numbers.

This sort of exchange has been repeated again and again, though with progressively less provocation required. One need only look to the days leading up to the vote on California's 2004 ballot initiative for $3 billion in hESC research funding to see how scientific prognostication was called upon to shape democratic politics (Hurlbut, 2010).

The problem here is not merely that overly optimistic predictions were made (Dresser, 2010), but that politics demanded them. In our characteristically American

predilection for cost-benefit analysis as a mode to resolve democratic disagreement, we sought to resolve moral and political controversy by weighing future outcomes against each other—as if they could be known in advance. But it is a profound expression of hubris to think that we can predict the future with sufficient accuracy that we can reduce a challenging moral (democratic) disagreement to an issue of technical (un)certainty, with competing (future) goods weighed against each other (Jasanoff, 2003; Wynne, 2001).

THE COMPLEX TRAJECTORY OF HUMAN PLURIPOTENT STEM CELL RESEARCH

Ethical, legal, and regulatory issues associated with federal funding for human embryonic stem cell research in the United States have influenced the character and trajectory of the field in profound ways. Scientists assuming the role of prognosticators is but one example. This research domain and the controversy surrounding it came into existence at the same moment. It would be remarkable—and concerning—if the field had not been affected by democratic disagreement over whether the research deserves public support. Some scholars have noted that the "policy uncertainty" engendered by presidential proclamations in 2001 and 2009, and the Sherley v. Sebelius lawsuit, have profoundly impacted stem cell biologists' ability to conduct their research (Levine, 2011). Clearly, these relatively sudden policy shifts have made it difficult for researchers to seek funding and plan research projects, let alone careers. (Nevertheless, it should be noted that numerous researchers had—and continue to have—substantial support from nonfederal sources such as the Howard Hughes Medical Institute, and that substantial sums of NIH dollars did flow to research on approved lines under the Bush administration.) However, the observation that the policy environment has had a "chilling effect" on research is not sufficient grounds for criticizing funding limitations as such. Human subjects research protections have a definitive chilling effect on lots of forms of research; that is precisely their purpose. They are intended to prevent (well-intentioned) researchers from violating ethical norms that they may not themselves recognize or agree with.

The appropriate response to policy uncertainty is not to liberalize policy, but to attend to political uncertainty—to uncertainty about the questions that need addressing, and the forms of deliberation, restraint, and deference that are appropriate to public reason in a democracy. While the outcomes of such deliberation are (rightly) hard to predict, taking public disagreement seriously will engender far less uncertainty than a kind of political tug-of-war, in which the democratic discomfort that engenders policy uncertainty is a hurdle to be strategically overcome. Policy uncertainty really comes down to uncertainty over how long a tenuous and poorly achieved settlement will hold before the balance of power shifts. This is no way to build a robust research enterprise; about that there is no question (Sahlman, 2010). But the solution is not to wish away the underlying political uncertainty; it is to address it head on as a democratic (rather than scientific) community.

Such an approach brings its own challenges. The advent of hESC research has raised difficult questions. It has forced the problem of how the state, in undertaking a public project, should make moral sense of developing life. This in turn has raised important questions about how we think—and talk about—the relationship between science and the state. One important consequence of the fact that policy debate around hESC research has been about funding is that discourse has tended toward a rhetoric of public investment—and return on investment. This framing has invited the sort of prognostication and cost-benefit balancing discourse described above. Democratic disagreement, values pluralism, and restraint in the face of moral uncertainty were less conceptually tangible than predicted therapeutic outcomes, and less amenable to inclusion in a calculus of return-on-investment. Instead, we saw

bizarre—and rather tenuous—balancing of predicted research outcomes against alternative allocations of scare public dollars; for instance, between California's stem cell initiative and Medicaid (Hurlbut, 2010). Asking only about the (predicted) instrumental utility of research distracts from the deeper question of what makes for scientific projects that reflect the values, needs, and aspirations of the society in which they are undertaken. These are questions about science itself and about the social contract with science—about how society's aspirations can and should be reflected in the forms of science it supports and upon which it relies (Jasaonoff, 2005).

The significance of this reliance on science has been unusually evident in the hESC controversy, and not merely because great expectations have been placed on this research domain. It has also been evident in society's struggle to find the right ways—and the right terms—in which to reason together about such a morally and technically complex sphere. Society's reliance on science has not been limited to questions of what specific scientific information was relevant to policymaking. It has embraced larger questions of the right relations between scientific and democratic institutions, most importantly, for the ways democracy relies on science to help it to reason well.

It is here that we see one of the main consequences for the hESC scientific community. This dependency was particularly evident in debates over the terminology that should be employed in public deliberation. Some actors, invoking scientific expertise, argued that public debate was confused by ambiguous terms—terms that though clear to an expert meant something else to the layperson. These scientists advocated purging public discourse of these terms to thereby cleanse the debate of these concepts' value-laden valences. They offered alternative terms, for instance substituting *nuclear transplantation to produce stem cells* for *therapeutic cloning*. These interventions were made not merely in the name of good science, but in the name of good politics (Hurlbut, 2010). As the International Society for Stem Cell Research (ISSCR) put it in a statement on nomenclature change in 2004, "the aim of this terminology change is to provide accurate, standardized terminology that will facilitate frank scientific, ethical and public debate on stem cells and their potential for medicine" (ISSCR, 2004).

These debates over terminology have largely been seen as conflicts over whose language properly represents the natural facts. But they are better understood as efforts to define the role that science should play in shaping and guiding public deliberation, and in assessing (and policing) the quality of public debate in a morally and technically complex domain. These attempted interventions represent an overextension—and overtaxing—of expertise, one that sought to reform politics in the name of scientific truth-to-nature. But democracy done well depends on explicit engagement with value-laden imaginations of the world, social and natural alike. It is for precisely this reason that such overextension had a corrosive effect on the relations between science and democracy.

INDUCING PLURIPOTENCY, CHANGING THE GAME?

Some commentators have maintained that debates about human pluripotent stem cell research are completely changed—even made irrelevant—by the advent in 2007 of reprogramming techniques to induce pluripotency in human somatic cells. One plausible, and popular, response to this development has been that the technique resolves the ethical problems with human pluripotent stem cell research. That is, the creation of iPS cells, unlike the creation of hES cells, does not require either the procurement of human oocytes or the destruction of human embryos, and so two of the major sources of ethical controversy have now been sidestepped. Jose

Cibelli, a prominent stem cell researcher, declared in the wake of the discovery of induced pluripotency, "if their method is as good as the oocyte" in reprogramming somatic cells, "we will be no longer in need of oocytes, and the whole field is going to completely change. People working on ethics will have to find something new to worry about" (Vogel & Holden, 2007, p. 1225). James Thompson, the researcher who first characterized hESCs, predicted that "a decade from now, [the divisive stem cell debate] will be just a funny historical footnote" (Kolata, 2007, p. A1). It would be a great loss if this controversy were reduced to a footnote, for there remains much to worry about. There will be many more ethical challenges in this research domain as work at the nexus of human developmental biology and bioengineering progresses. Equally importantly, however, it would be a loss if the deep moral challenges associated with this controversy were seen to have been definitively resolved—and rendered moot—through a technical achievement. If we as a society decide that one technical course is preferable to another out of deference to public moral concerns, then that is all very well. This, however, would be as much a democratic achievement as well a technical one—and should be appreciated as such. Indeed, we should aspire to precisely such resolution.

Yet the stem cell debates have tended toward the opposite. Over the course of the stem cell controversy, much discussion has been given to the biological equivalency (or lack thereof) between hESCs and so-called alternatives: adult stem cells, cord blood stem cells, multipotent adult progenetor cells, iPSCs, or hESCs differently derived. Assays of equivalency have been extensively debated, as have the relative therapeutic potential of different cell types. Some have argued that ESCs are the "gold standard" and must be preserved as a research tool (CIRM, 2010). Numerous papers purport to reveal aspects of iPSCs that will prove problematic for cell therapies (Bock et al., 2011; Gore, 2011; Lister et al., 2011; Zhao et al., 2011). These discussions have sometimes sought to resolve questions of what forms of research are "necessary" (or "unnecessary") on purely technical grounds.

There is no question that hESCs are useful in the lab, but it is impossible (and disingenuous) to declare that hESCs will be a better therapeutic tool than PSCs derived by other means. There is no way to know this in advance, and the criteria for usefulness will be what specific cell lines can do for us scientifically and therapeutically; the criteria ought not be whether some cells are like or unlike some other cells that have been *predicted* to be therapeutically useful (Apostolou & Hochedlinger, 2011). Furthermore, though some systemic differences do seem to exist between ESCs and iPSCs, there are also substantial differences from one ESC line to the next, and likewise for iPSCs. To put it simply, ESCs $\neq$ iPSC, but then iPSCs $\neq$ iPSCs, and ESCs $\neq$ ESCs (Bock et al., 2011; Gore et al., 2011; Hussein et al., 2011; Lister et al., 2011; Wilmut, Sullivan, & Chambers, 2011**)**. So, how can we figure out which specific cells will be must useful for specific applications? The way we always find things out in science: through experiment.

In short, discussions over the significance of iPSCs for federal funding policy ought not be reduced to technical debate; moral disagreement cannot be reduced to a calculus of biological sameness—nor should it be. Rather, continued moral deliberation should proceed alongside biological assessment. If limitations are placed on funding, it should not be because iPSCs have rendered hESCs scientifically moot, but because, all things considered, moral discomfort with embryo-derived cells warrants restraint in a democratic society, particularly when promising alternative pathways exist. If we can identify alternative scientific routes to our desired destinations, and we can do so through a robust democratic process, then science and democracy have worked well together. For moral concerns are not obviated by technical accomplishments, and neither should they be forgotten where science finds a way to temporarily sidestep them.

LESSONS LEARNED?

Good science is an achievement of a good society, and not the reverse. The ways we reason together as a society, and the policy resolutions we settle on, should reflect this. Facile references to politics "standing in the way of good science"—too common in the hESC controversy—denigrate the foundations of science and democracy alike. Science depends on a space in which it can observe its internal norms and exercise its specialized skills, but in a way that coheres with, rather than contradicts, the norms and aspirations of the democratic societies in which science is embedded. For science itself is but a piece of the larger project of civilization.

For this reason, problems of science policy should be seen not as "scientific decisions based on facts" (Obama, 2009), but as problems for democracy, democracy that includes science as an important social institution and reservoir of expertise for public reasoning. Democratic disagreements cannot be reduced to technical questions and delegated to scientific experts. The normative problems associated with hESC research cannot be resolved through expert predictions of the future, nor can promised future outcomes be weighed against present costs or concerns. To do so ignores the forms of uncertainty—scientific and moral—that are intrinsic to this sort of enterprise. More importantly, however, it shirks a democratic responsibility to face questions that by their nature cannot be definitively resolved by recourse to apparently external epistemic authority. Prediction of the future by a few elites amounts to an appropriation from the democratic polity of the responsibilities of governance; so too does reliance on science to supply the terms of deliberative discourse.

The reflex to seek scientific resolution of political disagreement is by no means specific to the hESC controversy, though there it has tended toward extremes. It traces to a tendency in American political culture to seek escape from politics by invoking the certitude of science to silence the sometimes cacophonous roar of political disagreement. Tough problems are tough and should not be simplified through technocratic tricks, even if it is the pressures of politics that push for simplification. Therefore, policymakers and publics ought not lean on scientific experts to be expert on matters that exceed their competencies. Where we do defer to experts, we should recognize such delegation as an expression of democratic authority. When scientists acquiesce to pressures to resolve problems of politics through scientific expertise, they place unsustainable burdens on science, straining its limits and compromising its ability to serve its important political role.

We should neither buy into the fiction that true resolution can be thereby achieved, nor ought we shirk our responsibilities as a society. The responsibilities of reasoning, deliberating, and finding positions of mutual respect—and, perhaps, precaution—are the weighty tasks for a democratic community. Such challenges of politics are not duties to be delegated, but responsibilities to be owned and welcomed. Scientists can better serve the collective good through expressions of appropriate agnosticism and humility than by accepting the excessive forms of authority that society is prepared to imbue them with, and society can likewise serve science by demanding humility in the face of hubris. Both science and society will be far better-off for such a posture.

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EXPAND AND REGULARIZE FEDERAL FUNDING FOR HUMAN PLURIPOTENT STEM CELL RESEARCH

Jason Owen-Smith, Christopher Thomas Scott, and Jennifer B. McCormick

Human embryonic stem cell (hESC) research has sparked incredible scientific and public excitement, as well as significant controversy. hESCs are pluripotent, which means, in theory, that they can be differentiated into any type of cell found in the human body. Thus, they evoke great enthusiasm about potential clinical applications. They are controversial because the method used to derive hESC lines destroys a

2- to 4-day-old human embryo. Research and discoveries using human pluripotent stem cells (hPSCs) are simultaneously cutting-edge contributions to fundamental understanding and potentially invaluable sources of new treatments for some of our most devastating diseases and injuries.

Stem cell science represents an important case of "use-inspired basic research," a class of scientific work that Donald Stokes (1997) compellingly argued could be used to reframe the increasingly fragile contract between science and society (Guston & Kenniston, 1994). In this case, however, federal funding restrictions, legal challenges, and public controversy continually impose on the field's development. Thus, hESC research also offers a laboratory for examining the effects high-level science policy decisions have on the trajectory of an emerging scientific field. Today, nearly 15 years after the discoveries that made hPSC science feasible, continued federal funding for this research is highly uncertain. We believe that federal funding for hPSC science should be expanded and stabilized through legislation. Explaining why requires that we begin with a simplified, schematic history of the field.

BACKGROUND: POLICY, CONTROVERSY, AND DISCOVERY

In 1998, two research teams led by James Thomson at the University of Wisconsin and John Gearhart at Johns Hopkins published articles reporting the successful derivation and culturing of hESC lines (Shamblott et al., 1998; Thomson et al., 1998). The discovery was heralded as *Science* magazine's 1999 breakthrough of the year, but scientists could not receive federal grants to support their research because a 1996 law, the Dickey-Wicker Amendment, banned the use of federal tax dollars in research that creates, harms, or destroys human embryos. A legal opinion drawing a fundamental distinction between human embryos and stem cells derived from them served as the basis for successful efforts to develop policies to enable the NIH to fund hESC research under President Clinton. Grant review was halted soon after the inauguration of President George W. Bush. Prospects for federal funding of hESC research remained uncertain until August 9, 2001, when he issued an executive order allowing federal funding for research on a small number of cell lines created before that time. Federal money could not be used to derive new lines.

Science progressed despite these restrictions, but controversy continued as it became clear that the small number of viable and fundable cell lines were not appropriate for all scientific or therapeutic purposes (Martin et al., 2005; Rao & Auerbach, 2006; Wang & Sun, 2005) and were very genetically homogenous (Mosher et al., 2010; Laurent et al., 2010). Congress passed bills expanding federal funding for hESC research in 2006 and again in 2007. President Bush vetoed both bills. At the end of 2007, new research reporting that hESC-like cultures—called human induced pluripotent stem cells (hiPSC)—could be made by reprograming adult fibroblast cells obtained from skin biopsies (Takahashi et al., 2007; Yu et al., 2007), increased hopes for cures and for ending the political and ethical controversies surrounding hESCs. In 2008, *Science* announced hiPSC as the breakthrough of the year, and in 2009 Shinya Yamanaka, who is widely credited with the discovery of hiPSCs, received the prestigious Lasker Award for Basic Medical Research. Recently, though, the idea that hiPSCs are medical or ethical panaceas has been subject to skepticism (Devolder, 2010; Kim et al., 2010; Lo et al., 2010; Pera, 2010; Zhao et al., 2011).

Stem cells occupied diametrically opposed positions in the presidential platforms of both the Democratic and Republican parties in 2008. Among President Barak Obama's campaign promises was a pledge to rescind the restrictions placed on hESC research under the Bush administration. In March 2009, President Obama issued an executive order doing just that. A month later, the NIH released draft guidelines for public comment. When the comment period closed in May, they had received

approximately 49,000 responses. Revised guidelines took effect in July 2009.[1] The impact of those new rules has been mixed. Several cell lines that had been eligible for funding were ruled ineligible under new ethical rules and many new cell lines were added to the registry. Newly eligible lines have yet to appear in significant numbers in research, which continues to rely disproportionately on a very small number of legacy cell lines (Scott et al., 2010).

The effects expanded funding might have on research in this field were further obscured in August 2010 when a Washington, D.C. district judge, Royce Lamberth, issued a preliminary injunction to block implementation of the 2009 NIH guidelines and with them all federal funding for hESC research. The suit—brought against the NIH by a pair of adult stem cell researchers and two organizations, the Christian Medical Association and Nightlight Christian Adoptions, as well as two couples seeking to adopt embryos—alleged that the NIH guidelines violated the Dickey-Wicker Amendment. The ruling caused great consternation and uncertainty among stem cell scientists, stopped new funding for hESC research, and raised the specter of a complete ban. A federal appeals court stayed the injunction pending consideration of the Obama administration's appeal. In April 2011, a three-judge appeals panel reversed the district court's ruling in a two-to-one decision.

In July of 2011, Lamberth granted summary judgment to the NIH, a finding that supports the Obama Administration's position that hESC funding can legally be expanded. Nevertheless, the plaintiffs have appealed the case, which could lead to a legal battle that could progress to the Supreme Court. As 2012 opens, despite an executive order to the contrary, hPSC science faces the possibility of a more restrictive federal funding regime than held a decade ago under President Bush.

ARGUMENTS FOR EXPANDED FUNDING

We believe that federal funding for all hPSC research should be expanded.

There are now three methods that have been shown to successfully create pluripotent cells. Those lines can be made using donated frozen embryos scheduled to be discarded from in vitro fertilization (IVF) facilities or by the hiPSC method, which reprograms somatic cells using embryonic transcription factors. A third method of generating pluripotent cells, commonly called somatic cell nuclear transfer (SCNT), involves removing the nucleus from an egg cell and replacing it with a nucleus from a different cell in order to create an hESC line genetically identical to the donor nucleus. SCNT has been successfully used to derive many mammalian pluripotent lines but has met limited success in primate cultures, including human. The first successful creation of a human pluripotent cell line using SCNT techniques is a recent development. Though it was derived with an extra set of chromosomes, a viable cell line was reported in October 2011 (Noggle et al., 2011). The new NIH guidelines disallow lines made by SCNT from the U.S. registry, limiting funding for research pursuing this method to private and state sources.

Given this growing diversity of methods and sources, we invoke hPSC research rather than the more narrow and established case of hESC research. We do so to suggest that funding decisions for the latter are, at least in the near-term, inextricably intertwined with the prospects of new and exciting scientific discoveries in hiPSC and SCNT research and possibly other future methods for creating pluripotent cells (Scott et al., 2011).

When we contend that funding should be expanded, we mean three related things. First, the volume of funding for hPSC research should be increased. Second, the

[1] http://stemcells.nih.gov/policy/2009guidelines.htm, accessed 6/09/2011.

range of cell lines and methods of derivation eligible for funding should be encouraged to grow. Finally, federal funding for hPSC research should be regularized through unambiguous legislation allowing researchers to plan and execute their often technically challenging, uncertain research programs on stable institutional ground.

Our position is based on three observations. First, we note that both the clinical and the scientific potentials of hPSC research are beginning to be realized. Expanded, regularized research support will accelerate those trends. Second, widely accepted ethical standards and effectively implemented institutional rules make the expansion of federal support for hPSC research unproblematic. Third, and finally, the uncertainty, ongoing controversy, challenges, and rule revisions imposed on stem cell scientists may be as damaging to the field as are restrictions.

CLINICAL, SCIENTIFIC, AND INSTITUTIONAL DEVELOPMENT

Recent years have seen significant advances toward therapies as the Food and Drug Administration (FDA) has approved hESC-based clinical trials for patients whom spinal cord injuries have rendered paraplegic;[2] for Stargardt's macular dystrophy, a disease that causes progressive blindness in children; and for age-related macular degeneration.[3] More progress is likely in the future as several new hESC lines that carry markers for diseases such as hemophilia, Charcot-Marie-Tooth disease—a hereditary neurodegenerative disorder—spinal muscular atrophy, and Duchene muscular dystrophy have been developed and approved for federal funding.

The process of creating "disease-specific" stem cells from human embryos relies on preimplantation genetic diagnoses (PGDs) and thus requires that scientists be able to identify and take advantage of opportunities presented by PGD that lead IVF clinics to forgo implanting an embryo with particular disease markers. Deriving disease-specific iPS cell lines is much more easily done and such lines offer new opportunities to model diseases ranging from Parkinson's to type 1 diabetes and Down syndrome (Park et al., 2008; Zhu et al., 2011).

All five of the disease-specific hESC lines on the NIH registry and many of the disease-specific iPS lines currently in use were developed by academic researchers. We believe that the development of these cell lines and their (possible) eligibility for federal funding represent an essential step toward the realization of some of the goals of regenerative and personalized medicine. We thus recommend both that more support be directed toward research using existing as well as new, genetically diverse, and potentially clinically useful lines. Moreover, the trend toward increasing numbers of available lines should be encouraged to continue.

Both the volume and the visibility of more basic, published hPSC research have increased dramatically in the last decade. The first full year in which any federal funding for hESC research was available was 2002, and the year after saw publication of 32 hESC papers worldwide. In 2010, we identified 574 hPSC publications, a rate of growth of well over an order of magnitude (Scott et al., 2011). The United States does the largest share of this research (approximately 41 percent in 2008) (Loser et al., 2010). The discovery and very rapid development of hiPSC technology relied on scientific skills and protocols developed for hESC research. The impressive speed of development of this new technology may also have been driven by researchers' efforts to conduct hPSC research without restrictions (Scott & Pera, 2008).

[2] http://www.geron.com/media/pressview.aspx?id=1235, accessed 6/22/2011.
[3] http://www.advancedcell.com/news-and-media/press-releases/advanced-cell-technology-receives-fda-clearance-for-clinical-trials-using-embryonic-stem-cells-to-tre/, accessed 6/22/2011.

Among other important discoveries has been the derivation of functional cells from hESC lines similar to those found in the human heart (cardiomyocytes), liver (hepatocyte), and central nervous system (CNS) (oligodendrocytes) (Binah et al., 2007; Zhang et al., 2009). These cells, like the hPSCs that spawned them, are important tools for use-inspired basic research. The great therapeutic possibilities that come with being able to model diseases and test potential interventions *in vitro* are matched by the possibility of fundamental discoveries about human development.

In addition to notable scientific and therapeutic developments, the institutional infrastructure to support ethical, expanded funding in the United States has grown significantly in the last few years. The National Academy of Sciences' 2005 guidelines for hESC research have been widely adopted, revised to include other pluripotent cells, and become normative standards for the ethical use of human stem cells. The International Society of Stem Cell Research has promulgated guidelines that address the clinical use of stem cells and begin to establish rules for regulatory harmonization among countries conducting hPSC research. The establishment of local oversight mechanisms governed by stem cell research oversight (SCRO) committees brings local scientific, ethical, regulatory, and community expertise to bear on the deliberative process of approving stem cell research protocols.

The NIH stem cell registry process appears to be working effectively to insure that cell lines eligible for federal funding meet strict ethical guidelines. While we disagreed with the institute's initial decision to retroactively apply contemporary ethical standards to cell lines derived in accordance with policies in place at the time of their creation (Taylor, 2009), the result of the NIH's uniform application of those new standards has been to develop a registry that we believe can be expanded. The creation of that infrastructure, however, has not been without cost. Prior inconsistencies in the NIH guidelines preempted lines made from earlier stages of the embryo. Requiring that foreign and domestic lines derived prior to July 7, 2009 must provide "protections at least equivalent" to the new rules means that some potentially useful lines are ineligible for federal funding.[4]

In applying today's tighter ethical standards to established cell lines, the NIH was forced to make several very difficult, but we now believe correct decisions. In June of 2010, the NIH rejected 47 new hESC lines submitted to the new federal registry by Reproductive Genetics Incorporated (RGI), a private fertility clinic specializing in PGD. Forty-two of the rejected lines carried mutations for specific diseases including hereditary breast cancer, cystic fibrosis, sickle cell anemia, and Huntington's disease. The committee advising the Director ruled that RGI's application " . . . did not meet the high ethical standards that are appropriate for federal funding of human embryonic stem cell research," (Waldman 2010 p. 852), a decision that several high profile stem cell scientists characterized as "detrimental to the research community" (Waldman, 2010, p. 852).

The most widely used Bush-era stem cell line, Wisconsin's H09, was almost rendered ineligible as well, sparking a scramble to locate, identify, and translate into English the original consent documents signed more than a decade before at an Israeli fertility clinic.[5] Though the Obama guidelines removed several lines that were approved under Bush, the approach to these and other eligibility decisions has resulted in a situation where we believe there is general agreement about the ethical standards employed in the derivation of cell lines supportable with federal funds.

[4] http://stemcells.nih.gov/policy/2009guidelines.htm, National Institutes of Health Guidelines on Human Stem Cell Research. Accessed 11/14/2011.
[5] http://www.wicell.org/index.php?option=com_content&task=view&id=385&Itemid=170, accessed 6/22/2011.

The infrastructure that is now in place will support more effective and ethically defensible pursuit of expanded hESC research.

An earlier decision further illustrates the care with which the pedigree of newly approved cell lines is being scrutinized. In December 2009, the NIH limited the use of 27 cell lines derived by the Harvard Stem Cell Institute to research focused on type 1 diabetes in accordance with explicit language in the relevant informed consent documents. The HUES lines, as they are known, were among the first derived with private funds during the Bush years, and had been widely distributed. Several were becoming prominent in published literature and were expected to be approved for federal funding in the wake of Obama's executive order. Much research using these lines was outside the realm of type 1 diabetes.

The story of one Harvard line in particular, HUES9, is emblematic of the challenges shifting rules, and uncertain legal and administrative standards imposed on hPSC research. Immediately following the Obama executive order, HUES9 was the most commonly used nonfederally approved cell line (Scott et al., 2010). For reasons no one entirely understands, different cell lines sometimes manifest distinct characteristics in culture. HUES9 is well known among scientists for its ability to easily differentiate into CNS cells, a property that prompted scientists working on neuronal cells with nonfederal research support, from, for instance, the California Institute for Regenerative Medicine (CIRM), to begin projects using HUES9 for CNS research.

We have been interviewing both established and junior stem cell scientists for a year as part of an ongoing project studying the effects policy changes have on scientific decisionmaking. One junior researcher working with HUES9 described her reaction to the Obama executive order and subsequent NIH decision about her cell line in a fashion that encapsulates many of the challenges we associate with the uncertainty caused by fluid and sometimes inconsistent application of policy. While the senior investigators we have interviewed are often quite forthright in their evaluations of recent and past policy decisions, younger investigators tend to couch their reactions in terms very specific to their own ongoing projects. In this case, the ways in which policy implementation can impact entire lines of research and nascent careers are on clear display.

> The day the Obama Executive Order came out, it was huge excitement. . . . In my lab we have a lot of federal money and I thought "Finally! I can use this money," because the things that we do are very expensive. Then, the whole NIH review came around and [HUES9] got taken back off the list. For my purposes it got taken back off the list. This was a horrible time for me because I invested so much. I told my boss "I'm not going to do that again with another line."[6]

Several features stand out in this account. A new line of research was begun during the Bush years using CIRM funding. After months of work with HUES9, the research began to pay off with a set of high-profile papers. Just as this student was poised to graduate, the Obama policy offered hope that she could expand this promising research using federal funds at the next stage of her career. Her hopes were dashed when the NIH review panel limited funding for this particular cell line to diabetes research. She is now considering leaving the field entirely. Here, we have graphic evidence of the impacts, not of restrictive policies, but of difficult to predict efforts to expand research support (Levine, 2011).

In sum, we take the last several years of hPSC research to be a story of scientific success, despite challenges, of growing clinical impact, and of important institutional developments that provide the basis for expanded funding while emphasizing

[6] Interview conducted June, 2010 by Jason Owen-Smith.

the need for stable, unambiguous policies for a field that remains under legal threat. The question remains where hPSC science and therapies would be if researchers and institutions had the benefit of a decade of federal funding and consistent regulatory policy. Invoking Stokes (1997) once again, stem cell researchers overwhelmingly select their questions and methods based on the potential relevance to real-world problems. Though curiosity-driven research has long been a feature of early human development and cell biology, use-inspired basic research finds a high degree of affinity with applied approaches, a union that is important to the common good.

We believe that now is the right time to expand federal funding for hPSC research in hopes of accelerating scientific discoveries that may more quickly move toward the clinic. Accomplishing these goals requires that we think of expansion in several related ways. First, more funding for researchers in the United States will speed rates of discovery and may incentivize talented young scientists to continue working in this field. Second, a wider range of eligible hPSC lines, and particularly of disease specific ES cell lines, will increase the likelihood that fundamental discoveries can move quickly to the bedside. Steps must be taken to allow support for approaches to develop disease specific cell lines.

Third, both the level and the character of support for hPSC research should be made as stable as possible. While we believe various stakeholders have set the institutional groundwork necessary to support a broader range of better funded hPSC research, scientists' reactions to some of the more difficult decisions that were taken in the course of implementing the Obama administration's policy suggest the challenges that uncertain, changeable federal funding create. A legal decision that curtailed or banned federal support for hPSC will have direct negative consequences in that it would undermine (at least in the United States) much of the progress we describe above.

The specter of legal and policy risks above and beyond the usual run of scientific and professional uncertainties is also having telling indirect consequences. Worries about the stability and availability of funding lead investigators to be conservative in their choice of cell lines. They thus underutilize newly approved materials, rendering past institutional victories less effective (Scott, McCormick, & Owen-Smith, 2009, 2010). As our brief discussion of HUES9 suggests, uncertainty brought on by political and legal forces beyond the control of researchers at the bench makes this field and particularly work with newer, untried materials more challenging for young investigators who may choose other areas of study. In short, expanding funding for now via administrative fiat is not enough. Legislation that replaces the Dickey-Wicker Amendment with a law that clearly and unequivocally assures more stable federal support for hPSC research is necessary. Such legislative steps will allow American hPSC scientists the freedom of motion and access to resources essential to accelerating both basic and translational discovery using all manner of technically feasible, ethically supportable methods to develop hPSC lines.

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GOOD GOVERNANCE CONNECTS SCIENCE AND SOCIETY

J. Benjamin Hurlbut and Jason Scott Robert

Owen-Smith et al. answer the question about expanding funding for human pluripotent stem cell (hPSC) research decisively and emphatically. They conclude that the U.S. federal government should expand funding in volume and scope, and stabilize it through regularity. If the clear goal of policy should be to increase present and future activity within the hPSC research domain over the long term, the solutions are simple—and their recommendations are on target. This, however, is the right solution to the wrong problem.

Owen-Smith et al.'s recommendations imply that the sole challenge for policymakers is neutralizing "legal and policy risks," but these so-called risks are themselves symptoms of as yet unresolved democratic disagreement. This disagreement must

be taken seriously, regardless of what policies one prefers. Ignoring disagreement will not make it go away—quite the reverse. Policymaking that proceeds in spite of disagreement will guarantee that controversy and instability persist. Indeed, such a course is likely to further mutate disagreement into intractable and corrosive ideological polarization. Instead, policymaking must acknowledge the stem cell arena as involving genuine moral challenge that demands collective deliberation, mutual respect, and prudence.

The rationale for Owen-Smith et al.'s recommendations appears to be that hPSC research is a self-evident public benefit: the "use-inspired" (Stokes, 1997) orientation of hPSC research will engender innovation that will serve the "common good." However, this assessment privileges innovation as such over other considerations, most notably that modalities of innovation should themselves comport with—or be an expression of—public values and aspirations.

Yet, we agree that thinking of hPSC research as use-inspired is a step in the right direction. This is because the phrase acknowledges that this research domain is embedded in—and should ideally be an expression of—concerns, values, and aspirations that transcend the research itself. The contention that "basic" science can be (and frequently is) undertaken in "applied" contexts, though not particularly new, is an important observation because it encourages us to appreciate the ways in which scientific projects are embedded in and undergirded by a larger social world. Use-inspired research is research that is supposed to be good for something other than itself, research that is supposed to address problems that are defined and experienced elsewhere. A variety of scholars have observed that these sorts of research goals shape the dynamics of science itself: what norms are employed, what uncertainties tolerated, what forms of accountability are demanded, and what kinds of answers are expected. They note that the insulated nature of basic research (or "normal science") cannot exist in these domains (if it ever existed at all), because here research is subject to a different set of expectations, norms, and criteria of credibility (e.g., Funtowicz & Ravetz, 1994; Jasanoff, 1994; Nowotny, Scott, & Gibbons, 2001).

Given that science increasingly aspires toward application; that scientists have become and have been encouraged to become more reflexive—and proactive—about the implications, aspirations, and social embeddedness of their work; and that publics are increasingly aware of the ways science affects their values, interests, and forms of life, governance approaches are ill served by re-inscribing a boundary between science and society. This applies in both directions: to the impact of science (and technology) on society, and of society—with its values, preferences, and ideas of the common good—on science. Therefore, insofar as science is use inspired, it should be explicitly recognized that inspiration is necessarily drawn from well beyond the limits of science.

Some progress can be made by re-thinking stem cell science in these terms. First, it becomes clear that it is a fool's errand to try to disentangle *science* from *society*, particularly in this case. Scientific projects, forms of discourse, and even biological categorizations within stem cell science have been co-produced (Jasanoff, 2004) alongside public moral disagreement, regulatory mutations, and shifting imaginations of the public good. This is not a failure of science (or politics), but a function of its use-inspired social embeddedness. Second, recognizing this can enhance our approaches to governance—our strategies for seeking solutions on a policy level. If we begin not by seeking to purify science of politics, but instead by exploring the kinds of interpenetration that might engender socially (and scientifically) robust approaches to governance, we will have made progress.

With this in mind, we highlight two premises of Owen-Smith et al.'s essay that we find particularly problematic.

First, we should not mistake the categorizations of research—or research objects—that are employed in public debate and policymaking as matters for

science alone. They do precisely this in lumping all forms and sources of cells under the heading of "PSC research." The question of whether it makes sense to distinguish between different categories of PSCs or derivation techniques for PSCs cannot be resolved by looking to the biological assay du jour. Neither should these categories be constructed on the basis of (predicted) technological application. Social preferences and moral concerns are equally relevant to making sense of what something "is" for purposes of public deliberation and policymaking. When nuanced technical distinctions—for instance between human embryonic stem cell (hESC) and hiPSC epigenetics—become public preoccupations (Pollack, 2011), it is because the science is inseparably linked and irrevocably imbued with matters of public concern. This is a function, not a failure, of use-inspired research.

Wrapped in the mantel of human aspirations, there is no pure "nature" to carve up at the joints. Therefore, constructing categories—whether in scientific, regulatory, or political settings—cannot be apolitical or normatively neutral. Adhering to the fiction that they are, or aspiring to make them so, is counterproductive. Instead the categories that traverse from laboratory to legislature should be appreciated to be of a mixture of epistemic, legal, and normative ingredients; they should be constructed transparently and inclusively such that the discourse of public reasoning is genuinely shared and categories are workable across domains. Efforts to do otherwise suggest certainty where there is uncertainty, and thereby guarantee that instability will persist even where categories—and the rules that are applied to them—appear secure.

A second, related, critique applies to Owen-Smith et al.'s assertion that "widely accepted ethical standards and effectively implemented institutional rules make the expansion of federal support for hPSC research unproblematic." This is a truly remarkable claim. It is correct that more elaborate and standardized approaches to governance have emerged in the last several years, in particular with the National Academies guidelines and the creation of Embryonic Stem Cell Research Oversight (ESCRO) committees, but these institutional developments in no way reflect—and should not be mistaken for—a resolution of broader controversy. Rather, ESCROs in effect assume responsibility for resolving broader political disagreement by appearing to perform the deliberative work requisite to achieve ethically secure ground. This model of governance effectively privatizes democratic politics by claiming that its institutions have the competency to do the work of public reasoning behind closed doors (Jasanoff, 2011).

Beyond the obvious problems of democratic accountability here, this privatizing move is particularly significant because it further shifts responsibility for defining categories of concern out of the public sphere. This is especially problematic because, given the fluidity and complexity of the field that these structures are supposed to govern, their operations cannot be easily constrained by fixed rules and definitions. Pretending that they can be, and in a way that is unproblematic, will inevitably cause downstream problems. Even in their short lifespan, ESCROs have had to redefine their scope and mandate as the advent of induced PSCs complicated the previously clear connection between pluripotency and the need for (and focus of) ethics review. In assuming authority to redefine their own role, ESCROs simultaneously extended it. Indeed, the recently resolved Sherley vs. Sebelius case was also an outgrowth of ontological ambiguities that did not exist—and were not anticipated—when Dickey-Wicker was drafted, namely the notion that "research" involving human embryonic materials might take place independent of (or temporally far removed from) manipulation of human embryos. Note that the UK's Human Fertilization and Embryology Authority, often held up as a model regulatory structure, has faced similar moments where its ostensibly stable natural categories were rendered problematic by novel biological constructions, for instance with somatic

cell nuclear transfer (Testa, 2011), and "admixed" embryos. This is the nature of the beast.

These episodes of instability trace to uncertainty over how to handle perturbations to existing categories, categories that—though apparently natural—turn out be stitched together by both ontological and normative (or, scientific and social) strands. These moments of perturbation have been resolved by drawing on very different political cultural dispositions in different national settings (Jasanoff, 2005, 2011; Hurlbut, 2010; Metzler, 2011; Testa, 2011), thus revealing just how profoundly national context informs how such problems are understood and resolved. Yet, problems of this sort can be anticipated easily enough, and steps can be taken. The appropriate approach to governance should not be to pretend all is settled and what remains is the straightforward task of rule making. Yet, American regulatory approaches—official and unofficial—in hESC research reflect an effort to stabilize governance structures without doing the hard work of seeking underlying clarity about what good governance entails.

Therefore, no matter how standardized, extensive or "effectively implemented" institutional rules may be, they simply cannot render federal support for research unproblematic in the face of underlying democratic disagreement. Neither can they legitimately claim to represent relevant disagreement by flying the proceduralist flag of pluralist deliberation, nor by invoking the univocal authority of scientific knowledge.

Of course policy, like science, must move forward, even where controversy persists. But there are better and worse ways to proceed. If the goal is to mitigate legal and policy risk, acknowledging and anticipating that scientific, regulatory, and political environments are subject to change, and finding settlements that are respectful rather than neglectful (or inflammatory) of democratic disagreement will prove most prudent in the long run. In a domain as unsettled as this, resolutions will necessarily be tentative, partial, and subject to revision. Science will not proceed utterly unrestrained—nor should it. Indeed, if science is to be good science—productive, stable, and in the service of the public—it must be coupled with, and inviting of, good politics. If resolutions are achieved through a commitment to reason and transparency, if they invite critical reassessment and revision, if they are open to and respectful of skeptical disagreement, if they acknowledge uncertainty and ignorance, then they will reflect the values—and the forms of humility—that form the bedrocks of science and democracy alike.

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DEMOCRACY *IS* WORKING

Jason Owen-Smith, Christopher Thomas Scott, and Jennifer B. McCormick

As contemporary students of science and science policy, it is hard to gainsay the easy abstractions of Hurlbut and Robert's commentary. "Good science is an achievement of a good society". We also share much common ground on the details. For instance, we endorse the majority of their thoughts with regard to the implications new iPSC technologies have for both science and policy. We are struck by the fact while both we and Hurlbut and Robert acknowledge similar scientific and clinical developments, the recent history of the field leads them to conclude that "The pipeline is a pipe dream" while we view the same developments as evidence of real movement toward admittedly and perhaps damagingly overoptimistic goals. In what follows, however, we choose not to dicker over the relative success or failure of the field because we concur with the idea that a flat cost-benefit analysis of the therapeutic and scientific return on public investments is an injustice to both science and democracy.

If we share so much in common, why do we find ourselves deeply disheartened by Hurlbut and Robert's commentary? One answer is that we cannot find even a provisional answer to either the questions posed at the outset of this point-counterpoint or to the reframed versions of those queries that they proffer. More importantly, however, we think that Hurlbut and Robert share with us a very similar set of concerns about the role of science in a democratic society but they misread the

implications of the human pluripotent stem cell case. Their misreading strikes us as potentially more damaging to the idea of democratic science policymaking than even the overweening scientific experts they seem to believe have cynically captured control of the political debate.

We could not agree more with Hurlbut and Robert's concerns about "policy uncertainty," a key feature of our own thinking. Indeed, the history of uncertain stem cell funding policy is "no way to build a robust research enterprise". Though history has taught us the benefits of thoughtful, rationally driven science policy (the response by the scientific community to recombinant DNA research offers a historical case in point), some types of research are chilled by thoughtless, irrationally driven science policy. We take the response by the political conservatives to climate change and human embryonic stem cell science to be exemplary of this negative case. Both policies created uncertainty, yet one spurred public benefit from a promising field of science; the other threatens to undermine it. The fact that restrictions or uncertainties exist does not represent a *prima facie* reason to liberalize existing policy. We disagree, however, with Hurlbut and Robert's implication that restrictive policies are necessarily a public good, because they prevent narrowly focused researchers from doing bad things. We think blanket restrictions based on generalized fears of violating ethical or moral norms are overly blunt instruments that stand to undermine entire fields of inquiry. This is particularly troubling because we, as a democratic society, have developed mechanisms such as institutional review boards and embryonic stem cell research oversight (SCRO) committees whose purpose is to subject specific research protocols to broad social, ethical, and scientific justifications. In the latter case, community participants and non-scientist SCRO members add a degree of deliberative democracy that we would expect them to applaud.

Hurlbut and Robert contend that questions of stem cell policy should be left to the messy, pluralistic, and value-laden deliberations of a democratic, not a scientific, society. They suggest that the failure of such deliberation and the resulting political uncertainties in this case stem from the unwarranted interventions of scientists who overreach the legitimate bounds of their expertise in corrosive, hubristic, appropriations of the "responsibilities of governance" through simplifying "technocratic tricks".

In stark contrast, we believe that democracy is working in this case, though messily, in fits and starts. Ballot initiatives and legislation in several states have both liberalized and further restricted stem cell research. Congress has twice sent bills expanding stem cell research funding to a Republican president and those bills have twice been vetoed. The new NIH guidelines developed in response to Obama's executive order solicited and responded to more than 49,000 public comments. After much public discussion and an injunction and associated appeals, a federal court case challenging those NIH policies was dismissed only to be pursued at a higher court by the plaintiffs. Public opinion polls such as Gallup consistently show majorities of Americans in favor of easing federal restrictions. Rational, pluralistic, and democratic processes at international, national, state, and local levels developed policies that have been conscientiously applied to ensure the ethical derivation and use of new and existing human embryonic stem cell lines.

Our call to liberalize and regularize funding for stem cell research is predicated on what we perceive to be scientific and clinical momentum as well as on the development of what we take to be a robust institutional infrastructure for ensuring that such research takes place within ethical boundaries acceptable to the majority of citizens. The former we take to be a success of science, while the latter we take to be an outcome of democratic process. This is by no means the idealized and abstract deliberative democracy that Hurlbut and Robert invoke. Would that the realities of contemporary politics did not intervene in the workings of democracy.

While we share the sense that an anti-democratic impulse underpins the current state of federal stem cell policy, we believe it arises not from terminological efforts of scientists and stem cell research supporters, but from a dedicated and well-funded minority whose fervent convictions serve many of cynical ends Hurlbut and Robert attribute to scientific expertise. The political uncertainty that concerns us here is best remedied by legislative action that rescinds the Dickey-Wicker Amendment, itself a quiet and anti-democratic compromise, in favor of open debate about the proper role of federal support in the development of pluripotent stem cell research. Congress should enact laws that would expand and liberalize support for this research, but we recognize that our perspective may not win the day. We are certain, however, that Hurlbut and Robert's call for society to demand humility from scientists as a means to serve science in order to remove anti-democratic expertise from the discussion will only yield the field to interest groups who we believe have time and again proven themselves antithetical to both science and the democratic values that Hurlbut and Robert espouse.

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