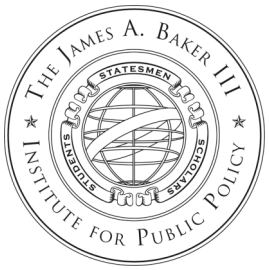

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Human Embryonic Stem Cell Research: Recommendations for the Next Administration

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December 19, 2008

These papers were written by a researcher (or researchers) who participated in a Baker Institute research project. The research and views expressed in these papers are those of the individual researcher(s), and do not necessarily represent the views of the James A. Baker III Institute for Public Policy.

Overview

Stem cell research should be allowed to expand in a responsible, thoughtful and ethical manner and a comprehensive federal stem cell policy should be developed that includes ethical oversight of all such research, regardless of who pays for it and where it is done. This paper seeks to describe and explain recommendations for the next administration in the context of the current state of the science, existing stem cell policy, and public opinion in the United States.

Recommendation 1: Expand federal funding for human embryonic stem cell research.

1.1. Support research on all types of human stem cells, including embryonic, adult, nuclear transfer derived (also known as therapeutic cloning) and induced pluripotent derived.

1.2. Authorize federal funding of human embryonic stem cell research on lines derived according to strict ethical guidelines, regardless of the date the cell lines were derived or created.

1.3. Remove the Dickey Amendment (which severely limits the National Institutes of Health funding of embryonic research) from the Department of Health and Human Services appropriation bills.

Recommendation 2: Create a comprehensive federal stem cell research oversight policy with the National Institutes of Health taking the lead.

2.1. Ban any effort to clone a human being, regardless of the source of funding.

2.2. Create an Embryonic Stem Cell Research Oversight (ESCRO) board within the National Institutes of Health to review controversial research and recommend policy for the agency.

2.3. Continue the President's Council on Bioethics.

Background

Human embryonic stem cell (hESC) research is an emerging field of biomedical research that started in 1998 with the derivation of the first cell line. These cells, created from a five- to six-day-old fertilized egg are called "pluripotent" because they have the potential to replicate themselves for indefinite periods and to produce cells of a more specialized type, such as a muscle or neuron. Scientists are confident that hESCs can potentially advance research in areas as diverse as developmental biology, cancer research, and regenerative medicine. Advocates predict that hESCs will be used to produce tissues or organs to replace damaged ones, to understand and combat diseases, and to test and develop new drugs. Adult stem cells also have medical promise. But, in contrast to adult stem cells, which are specialized to particular tissues or organs, hESCs have the potential to specialize into any cell in the body and therefore have the capability to be utilized in tissues and organs where stem cells are missing or damaged.

Stem cell research has helped scientists begin to see the potential for near term therapies. Biotechnology companies are working on clinical trials for therapies such as repairing spinal cord injuries, where other approaches have made little progress. In addition, hESCs have been hypothesized as a new source of clean, universal blood. Scientists are optimistic that in the future hESCs can be used to better understand and treat debilitating diseases such as juvenile diabetes, Parkinson's disease, and cancer. Furthermore, researchers have used the knowledge gained from research on hESCs to help develop "induced" pluripotent cells (iPS), which are normal cells that have been stimulated and reprogrammed to become embryonic-like again. Induced pluripotent cells could lead to advances in personalized medicine, with the goal of future medical care being tailored to an individual's genome, thus avoiding unintended consequences of drugs and other treatments that work for some, but not for others. While hESC research is starting to break new ground, further studies need to be done to better understand how these cells work and how they can be used before research results can be applied to treatment or therapies.

With this exciting and potentially powerful new area of research also came significant controversy due to concerns about the source of hESCs—a human fertilized egg. Progress in the United States has been severely limited by the lack of federal funding and oversight. In 2001,

President George W. Bush ordered that federal funding would only be permitted for research on hESCs that were created before August 9, 2001. No new hESCs could be created with federal funding, nor could federal funds be used to perform research on hESCs created after August 2001, whatever their source. Based on this policy, only 21 cell lines were available for federally funded research. But this policy only controls federal funding. So, research using state and private funds continues with minimal federal oversight and regulation (only regulations related to clinical uses by the Federal Drug Administration (FDA) apply).

During his administration, President Barack Obama should revisit the 2001 decision that limits federal funding and regulation of hESC research. He should also promote public policy and federal stem cell policy that expands research in a responsible, thoughtful and ethical manner, while laying a foundation for future scientific advances.

Recommendations

Recommendation 1: Expand federal funding for human embryonic stem cell research.

Public support for expanded federal funding of hESC research has increased over the past seven years. Research!America polling in 2006 showed that 60 percent of people polled supported hESC research and 56 percent supported federal funding of the research.[1] Other polls from Gallup, Inc., and Virginia Commonwealth University have seen support of hESC at 60 and 54 percent respectively.[2]

In response to growing public support, the U.S. Congress attempted to expand hESC research by passing the Stem Cell Research Enhancement Act with bipartisan support in 2006 and 2007. The bill, which was vetoed both times by President George W. Bush, would have allowed federal funding of research on hESC lines that were created using leftover *in vitro* fertilized (IVF) eggs regardless of the date of derivation. RAND Corporation estimated that in 2003 there were more than 400,000 such leftover *in vitro* fertilized (IVF) eggs, which are otherwise discarded.

[1] Research!America data is available online at www.researchamerica.org.
[2] Gallup's Pulse of Democracy, Stem Cell Research: http://www.gallup.com/poll/21676/Stem-Cell-Research.aspx; and Virginia Commonwealth University Life Sciences Survey, 2007: http://www.vcu.edu/lifesci/images2/survey2007.pdf

Recommendation 1.1: Support research on all types of human stem cells, including embryonic, adult, nuclear transfer derived (also known as therapeutic cloning), and induced pluripotent derived.

Findings:

- Stem cells can be located in the embryo during the early stages of development (around five or six days after fertilization), in the umbilical cord and placenta, and in several adult organs.
- Embryonic-like stem cells can be created by stimulating normal cells to revert back to an earlier form—known as induced pluripotent stem cells or iPS cells—or by removing the genetic material from an egg and replacing it with the genetic material from a normal cell—known as somatic cell nuclear transfer (SCNT) or therapeutic cloning.
- Induced pluripotent stem cells are not yet a feasible replacement for all hESCs. The process by which iPS cells are created might, in fact, alter the cells so they are not viable for therapeutic research. And without hESCs, we cannot determine if the iPS cells have undergone any potential undesirable changes.
- Each type of stem cell is valuable in different areas of research. For instance hESCs can be an important tool for understanding early human developmental biology, perhaps elucidating issues involved in infertility and birth defects, while iPS or SCNT derived cells could further understanding of the development of specific diseases such as Parkinson's or Alzheimer's.
- Current federal funding only supports umbilical cord, adult, very limited embryonic stem cell research, and research with iPS cells. SCNT derived cells and hESCs created after Aug. 9, 2001, cannot be used in federally funded research.
- In fiscal year 2008, NIH spent $41 million on hESC and an additional $203 million on non-embryonic human stem cell research from its $29.5 billion budget, while California alone predicted it would spend $100 million during the same time.

The United States needs a new progressive stem cell policy that will increase federal support of all human stem cell research. By encouraging research on all types of human stem cells, we will allow the best research to move forward regardless of the cell source. Research on all human stem cell types is also essential to develop future therapies and cures for debilitating diseases and

injuries such as diabetes, spinal cord injuries or Parkinson's, which impact millions of Americans.

Recommendation 1.2: Authorize federal funding for human embryonic stem cell research on lines derived according to strict ethical guidelines, regardless of the date the cell lines were derived or created.

Findings:

- When the Bush administration's policy was announced in 2001, the National Institutes of Health (NIH) declared that there were 60 to 75 lines that met the qualifications for federal funding. Since that announcement, only 21 lines were found to be available for distribution.
- In using these lines, scientists have come across additional problems.
    - All 21 lines were created using mouse cells and reagents to help support growth, which means that the cells could be contaminated with mouse cells or proteins. This could potentially limit their use for medical purposes.
    - Several of the lines have proven difficult to grow.
    - Each line has a propensity to grow into specific cell types, which restricts research.
    - The cell lines lack genetic diversity, which could limit potential treatments for a broad number of patient communities.
    - None of the cell lines are disease-specific, thereby limiting research on genetic diseases.
    - Of the 21 lines, five are suspected to have been obtained without appropriate informed consent.[3]
- To counteract the limited funding situation, some universities, including Harvard and the University of Wisconsin–Madison, were able to obtain private funding for their research. Other researchers were able to convince state legislatures and governments such as California, Illinois, and Connecticut, to fund projects. But many researchers were left

[3] Steiffer, R. "Informed Consent and Federal Funding for Stem Cell Research," Hasting Center Report 38, No. 3 (2008): 40-7.

without readily available funding sources outside of NIH, the major funding source for biomedical research in the United States.

- Over the past seven years, while research on adult stem cells has surged in the United States, hESC research has stagnated compared with other parts of the world.
    - From 2002 to 2004, the fraction of hESC research publications from American researchers decreased from one-third to approximately one-quarter.[4]
    - Recent research from Georgia Institute of Technology confirmed that the United States is underperforming in hESC research.[5] The report found that American researchers produce fewer publications than would be predicted based on other areas of biomedical research.

The next administration should permit NIH to provide funding for: (a) research on hESCs regardless of when they are derived and who derives them, (b) the derivation of new hESC lines, e.g., from discarded embryos from IVF clinics, and (c) SCNT derived stem cell lines. Using these lines, scientists will be able to study genetic diseases more quickly and efficiently, and hopefully even discover new therapeutic techniques that will, in the future, avoid the need for hESC lines.

Recommendation 1.3: Remove the Dickey Amendment (which severely limits the National Institutes of Health funding of embryonic research) from the Department of Health and Human Services (DHHS) appropriation bills.

Findings:

- Starting in 1995, the Dickey Amendment, named after an appropriation rider introduced by Rep. Jay Dickey (R-AZ), has been attached to DHHS appropriation bills each year.
- The amendment bans any federal funding for "the creation of a human embryo or embryos for research" and "research in which a human embryo is destroyed, discarded, or knowingly subjected to risk of injury or death."

[4] University of Michigan, *U.S. falling behind in embryonic stem cell research, study says*, Press Release, April 2006, http://www.umich.edu/news/index.html?Releases/2006/Apr06/r040606b.
[5] Levine, A.D. "Identifying Under- and Overperforming Countries in Research Related to Human Embryonic Stem Cells." Cell Stem Cell 2 (2008): 521-4.

In the future, any federal restriction on the use of human embryos for research should be passed as a bill, signed into law, not as a rider on an annual appropriations bill. This approach would allow for appropriate discussion and informed debate on the subject. It will also stabilize the policy instead of leaving it in its current ambiguous state, where researchers are unsure if the amendment will continue to appear year to year. President Obama should veto any DHHS appropriation bill that contains the Dickey Amendment or similar rider.

Recommendation 2: Create a comprehensive federal stem cell research oversight policy with the National Institutes of Health as the lead.

Recommendation 2.1: Ban any effort to clone a human being, regardless of the source of funding.

Findings:

- Human reproductive cloning is the process of creating a human being that is the exact genetic copy of the donor.
- In contrast, therapeutic cloning (also known as SCNT)—which should not be banned—refers to a process in which the cells are grown *in vitro* (outside the body, in a lab), not *in utero* (in a woman's uterus) to produce an infant.
- Attempts at reproductive cloning for animals have been error-prone and inefficient, resulting in the failure of most clones to develop. Those that do survive have a marked shorter life expectancy.
- Human reproductive cloning has been denounced by both scientists and policymakers around the world. Polling from Research!America found that between 77 percent and 83 percent of Americans oppose human reproductive cloning.[6]
- Fourteen states and over 40 countries have already banned human reproductive cloning.

For these reasons, the United States should ban human reproductive cloning—both in the public and private sectors.

[6] Research!America data is available online at www.researchamerica.org.

Recommendation 2.2: Create an Embryonic Stem Cell Research Oversight (ESCRO) board within the National Institutes of Health to review controversial research and recommend policy for the agency.

Findings:

- Oversight of hESC research during the George W. Bush administration was left to the universities and research institutes as well as private industry.
- In the past, for previous controversial areas of biomedical research, NIH would play a strong leadership role in creating research policy. For example, the Recombinant DNA Advisory Committee (RAC) was created to review proposals involving the use of DNA in research and clinical therapies.
- Since the majority of hESC research was performed without federal funding, NIH was not involved in the oversight. But, the public would support an increase in its role; Research!America polling showed that approximately two-thirds of Americans agree that there should be a uniform federal hESC policy.[7]
- Responding to the demand for guidance by the research community and the lack of a comprehensive research and oversight policy, the National Academies (National Academy of Science, National Academy of Engineering and the Institute of Medicine) filled the vacuum and assumed a leadership role. In 2005, they released the report "Guidelines to Human Embryonic Stem Cell Research" to help steer universities and research institutes on how to provide research oversight on this ethically contentious issue.[8]
- The National Academy guidelines were voluntary, and some state and private funding agencies already had organizations in place with their own oversight procedures. Moreover, there was no mechanism with which to oversee the fulfillment of the guidelines.

The next administration should use the NIH and an ESCRO board within the agency to oversee stem cell research. The ESCRO board (similar to those recommended for universities by the National Academies) should contain representatives with expertise in developmental biology,

[7] Research!America data is available online at www.researchamerica.org.
[8] The National Academies report "Guidelines to Human Embryonic Stem Cell Research: is available online at www.nap.edu.

stem cell research, molecular biology, assisted reproduction, and ethical and legal issues in hESC research. The role of the board should be to review all grant applications involving the derivation of hESC lines and to develop policy options for all aspects of research involving human embryos. Moreover, NIH should work with states that have already implemented human stem cell programs to provide guidance on ethics and research, as well as to help with peer review.

In addition, all hESC lines used in NIH-funded project should be required to comply with informed consent procedures outlined by the National Academies. And any hESCs used in federally funded research should be available in a national or international cell banks so they can be characterized, tested, expanded and available for other researchers to utilize. This would require banks to have clear material transfer agreement procedures to allow for easy access to lines.

Recommendation 2.3: Continue the President's Council on Bioethics (PCB).

Findings:

- The PCB is a group of individuals (up to 18) appointed by the president to give advice on bioethical issues that may emerge as a consequence of advances in biomedical sciences and technology.
- The council and its members serve two-year terms, at which time both are reappointed by the president.
- The PCB was formed by the Bush administration in 2001, but the Clinton administration had a similar bioethics advisory group, the National Bioethics Advisory Commission, which dealt with some of the early issues related to human stem cell research.

President Obama should continue the PCB and select members early in the administration so they can continue the important work of investigating and discussing bioethical issues and providing policy recommendations to the President. In addition, the president should give the council a mandate, along with the necessary financial support, to carry out relevant policy research and formulate recommendations to guide the president and federal agencies on policy issues related to health and biomedical research.

Conclusion

As the United States undergoes a smooth transition from one administration to another, Americans and the global community have a unique opportunity to benefit from a change in the research policies of a traditional leader in biomedical research—especially in areas where current controversial policies have proved to be unpopular with the American public and allowed the United States to fall behind other nations in an important area of medical research. Human embryonic stem cell research was a new and virtually untested area of research in 2001. The George W. Bush administration created a compromise policy to help encourage limited hESC research. Unfortunately, over the past eight years, this compromise—and the complex system of policies and practices that resulted from it—has impeded research and negatively impacted the United States' status as a leader in biomedical research. Many scientists around the country who are interested in human stem cell research have found other means to continue their research, if on a smaller scale, but polls have shown that most Americans understand the need for a uniform and comprehensive stem cell policy that includes research on all stem cell types as well as ethical oversight.