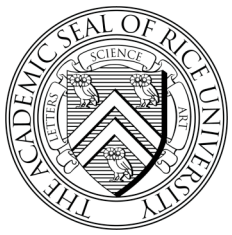

The James A. Baker III Institute for Public Policy
Rice University

Avenues for Advancement

Conference Summary

by

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August 2007

Introduction

Since 2004, the James A. Baker III Institute for Public Policy's Science and Technology Policy Program has hosted a series of conferences on human embryonic stem cell (hESC) research, titled "Stem Cells: Saving Lives or Crossing Lines." The purpose of the series was to examine the complexities of stem cell research policies at the state, national and international levels. The series highlighted research advances including the benefits and risks of possible therapeutic applications of both embryonic and adult stem cell research. It also reviewed the complex array of underlying ethical and policy issues surrounding the use of human embryos in research. Our intention was to raise public awareness of the implications of hESC research and the fact that, for the first time in modern history, the United States could lose its leadership position in biomedical research due to insufficient federal funding and regulation.

On October 24, 2006, the institute's Science and Technology Policy Program hosted the third conference of the series at the Carnegie Institute of Washington in Washington, D.C. This conference, titled "Avenues for Advancement" and the first held in the nation's capital, built on the foundation of previous conferences, which emphasized ethical debates, state initiatives, and the roles of business and the media in implementing stem cell policy. Support for this conference was generously provided by the Richard Lounsbery Foundation, Texas Tech Health Science Center, the University of Texas M.D. Anderson Cancer Center, the University of Texas Health Science Center at Houston, and the University of Texas Medical Branch at Galveston.

The "Avenues for Advancement" conference highlighted models for regulating embryonic research. Representatives from different countries came to review their current regulatory schemes, what they covered, how they were implemented, and what future changes were foreseen. We were honored to have guests from Canada, Italy and the United Kingdom address their country's respective policies. We also had a scholar on embryonic policies review legislation and regulatory schemes in developing countries. In addition to current national policies, we reviewed proposed or voluntary regulatory guidelines from the President's Council on Bioethics (PCB), the National Academies (the National Academy of Science and the Institute of Medicine), the International Society for Stem Cell Research (ISSCR), and the Hinxton Group.

By holding the conference in Washington, we were able to build and expand the influence of the series. Our goal was to introduce to staff from the U.S. Congress, federal agencies, and nongovernmental organizations the issues and lessons we learned in earlier conferences, as well as to address the wealth of new ideas and models for embryonic regulation which the United States could implement. In excess of one hundred participants attended the one-day event to hear more than a dozen distinguished scholar presentations. Keynote speakers included LeRoy Walters, professor of philosophy from Georgetown University and expert on intercultural perspectives on hESC research; Michael Gazzaniga, director of the Sage Center of the Mind at the University of California, Santa Barbara, and member of the PCB; Thomas Zwaka, assistant professor of molecular and cellular biology at Baylor College of Medicine and hESC researcher; and Mark Frankel, director of the Scientific Freedom, Responsibility & Law program at the American Association for the Advancement of Science (AAAS).

Scientific and Political Climate in the United States

To promote thoughtful discussions, the program began with several talks addressing the scientific and political landscape in the United States. Zwaka discussed the current advances in embryonic stem cell research, Walters lectured on social cultures and policies influencing stem cell research, and Frankel updated the audience on policies in the United States, including federal and state advancements.

Zwaka's talk kicked off the conference by reviewing the biology of stem cells, the differences between embryonic and adult stem cells, and the overall direction of current stem cell research. His presentation highlighted historical research progress as well as future goals, such as somatic cell nuclear transfer (also known as therapeutic cloning, which is cloning for biomedical research) and therapeutic advances, in a candid and balanced manner. Overall, he provided the audience with a basic knowledge of hESCs to help audience members follow future speakers as they discussed more specific regulatory issues involved in hESC research.

Walters's presentation described hESC philosophies and regulations in different countries around the world. He surveyed national policies and organized countries into four categories: *restrictive*

(those which prohibit hESC research), *permissive* (those which allow hESC research and therapeutic cloning), *moderate* (those which allow hESC research on leftover *in vitro* fertilization (IVF) eggs, but not therapeutic cloning), and *compromise* (those which use only existing hESC lines for research). He also discussed different religious perspectives on embryonic research: Judaism (generally accepting); Islam (generally accepting); Christianity (diverse opinions, many not accepting); Buddhism (either accepting or not accepting depending on personal motivations); Taoism (not accepting); and Hinduism (generally accepting).

Frankel outlined the existing climate on stem cell policy regulation in the United States. As mentioned in the previous Baker Institute Policy Report, "Lessons Learned: U.S. Embryonic Stem Cell Policies,"[1] the United States does not have one stem cell policy; instead, it has a range of polices. To quote Frankel, "more is not better." Before 2001, the restriction on human embryonic research was a result of the Dickey-Wicker Amendment attached to the Department of Health and Human Services (DHHS) appropriation bill, which funds the National Institutes of Health (NIH) and almost all federal biomedical research. This amendment does not in itself ban hESC research, only the use of federal monies for the destruction of human embryos and consequently the creation of hESC lines using federal funds. In 2001, President George W. Bush further defined the policy to permit federal funding only of research that uses hESC lines created before August 9, 2001 (the date of his speech).

In addition to the federal policy, Frankel pointed out that states have begun moving forward with their own policies. Some states have criminalized hESC research or therapeutic cloning, while others are funding the research using state monies. The majority of states have no legislation specifically addressing the issue. The wide range of policies has created a state of uncertainty and confusion for scientists trying to pursue research in this area by requiring them to keep up with the changing political landscape at the state as well as federal level. Furthermore, supporters use economic arguments to gain support for state programs, leading to a push for short-term goals versus long-term and basic research, potentially doing more harm than good.

International Policies

A large portion of the afternoon compared several different national-level hESC policies. An Italian scholar outlined the policy in Italy, a country that is similar to the United States in that it has restrictions on public funding only. A Canadian and a British representative both discussed policies in their respective countries – two countries which both have very clear regulations. Finally, a postdoctoral fellow from the Centre de Recherché en Droit Public at the University of Montreal reviewed the hESC policies of 24 countries in the developing world.

Maurizo Mori, a professor of philosophy at the University of Turin, summarized Italian policy and how the government has dealt with hESC research. Policy in Italy must respond to pressures from a strong Catholic majority, a conservative public, and the lack of scientific discussion. In 2000, while a governmental commission was assessing hESC research, a law was passed prohibiting federal funding for hESC research. Similar to the United States, it did not outlaw privately funded research. In 2004, a law was developed on assisted reproductive technology, stating that the embryo deserved respect as a citizen, and therefore the destruction or freezing of embryos was forbidden. This legislation did not address the thousands of IVF embryos already frozen. Moreover, the Italian government pushed that the European Union's Seventh Framework Programme (the initiative in the European Union for funding scientific research from 2007 to 2013) not include funding to create hESC lines, although it eventually withdrew its support of this ban after a new government administration came into power in 2006. Mori lamented the lack of discussion by scientists on hESC research or other science policy issues: "In Italy, scientists have a defensive attitude. They prefer not to speak out." This is a consequence of "an antiscientific attitude" that Mori believes is common in Italy and negatively impacts research in the country.

Timothy Caulfield, professor of law at University of Alberta, outlined Canada's hESC policy. Canadian law on embryonic research dates back to a study in 1993 on reproductive research. The study ultimately led to the Assisted Human Reproduction Act, which was introduced in 2002 and proclaimed in 2004. The act regulates research and activities involving human reproductive materials, bans certain activities (therapeutic and reproductive cloning, sex selection, and buying

and selling gametes, which are sperm and egg cells), and allows research utilizing spare IVF embryos. Even with the passage of the act, the ban on therapeutic cloning is still being debated in Canada. Caulfield mentioned that there was limited discussion on therapeutic cloning when the law first was proposed. Instead, the focus of the discussion was on the commoditization that could result from the donation of eggs for research. The recent emphasis on the moral status of the embryo has been a relatively new argument in Canada.

Angela McNab, chief executive of the Human Fertilisation and Embryology Authority (HFEA), reviewed the present regulatory climate in the United Kingdom. As discussed in the previous Baker Institute reports "Stem Cells: Saving Lives or Crossing Lines"[2] and "Lessons Learned: U.S. Embryonic Stem Cell Policies,"[3] the United Kingdom has a liberal hESC policy, allowing therapeutic cloning and hESC research with strict regulation and oversight. The debate over embryonic research in the United Kingdom dates back to the first IVF baby in 1978 and the release of the Warnock Report in 1984, which first set 14 days as the limit for research on embryos. In 1990, the Human Fertilisation and Embryology Act was passed, creating HFEA, a nondepartmental public body with a lay majority that can grant licenses and make policy decisions with regard to reproductive research. The act prohibits reproductive cloning, altering the genome, growing hESCs after 14 days, and implanting of a human embryo into an animal or vice versa. In 2001, the regulation was updated to allow research on spare IVF embryos, embryos created using donated gametes, therapeutic cloning, and parthenogenesis (a procedure where a human egg is activated to develop in the absence of sperm).

Rosario Isasi summarized how developing countries were addressing hESC research. With only 10 percent of the world's biomedical research expenditures directed toward diseases that affect 90 percent of the world's population (commonly known as the 90/10 rule), developing countries are beginning to invest in areas they believe will benefit their population. Furthermore, developing countries are increasingly playing a role in international policy development. For example, Costa Rica, with help from the United States, moved the debate at the United Nations from banning reproductive cloning to successfully banning all forms of cloning.

Isasi's presentation highlighted results from a survey by the International Stem Cell Forum.[4] The survey reviewed legislation from 50 countries with hESC policies. Twenty-four of the countries surveyed were from the developing world as listed by economic level. When examining the survey results, Isasi noted that 23 out of 24 countries in the developing world banned therapeutic cloning (the exception being China). Five countries legally allowed hESC research with lines created from surplus IVF eggs, and an additional four allowed the research through their guidelines (although they do not have a specific law regarding it). Seven countries specifically prohibited the creation of hESC lines. Overall, in the countries prohibiting research, the importation of hESC lines was seldom regulated, and frequently there were not any regulations addressing IVF or the destruction of surplus IVF eggs. Isasi also observed that many of the developing countries have started to liberalize their policies to allow for more research on more lines, but some countries such as Costa Rica still prohibited all hESC research.

Stem Cell Regulation Models

United States Policy and Regulation Guidelines

There were two presentations that specifically dealt with the creation of policy and regulation in the United States. Gazzaniga, the conference opening keynote speaker, assessed the President's Council on Bioethics (PCB) report, "Human Cloning and Human Dignity: An Ethical Inquiry,"[5] and Frances Sharples, director of the Board of Life Sciences at the National Academy of Science, reviewed the National Academies report, "Guidelines for Human Embryonic Stem Cell Research."[6]

Gazzaniga presented the deliberations and arguments of PCB, a diverse group of individuals with different religious backgrounds, scientific training and beliefs appointed by President Bush to address ethical issues arising from biomedical research. The principle issue that the council was asked to address was whether therapeutic cloning should be allowed in the United States. Three positions surfaced during these deliberations. One group posited that since embryos have the potential to become a human being they, therefore, should not be used in research that would potentially hurt or destroy them. The second position held that therapeutic cloning would lead toward a "slippery slope" of morally questionable research, such as research beyond the

prescribed 14 days and the cloning of a human being; as a consequence, research should not be permitted until regulation is set in place. The third group argued that the use and donation of embryos is similar to donating organs from a brain-dead individual and should be treated respectfully, but still allowed. The outcome of the deliberations, which was summarized in the 2002 publication, "Human Cloning and Human Dignity: An Ethical Inquiry," was that seven members of PCB supported therapeutic cloning, three members wanted to ban all cloning, and seven members wanted to wait for regulations to be put into place. Gazzaniga believed it was unfortunate that the official report described this in such a way as to suggest that 10 members did not want to do the research by adding the seven members who wanted a moratorium to the three members asking for a ban.

According to Gazzaniga, the 2005 PCB report "Alternative Sources of Human Pluripotent Stem Cells"[7] highlighted additional ways of doing stem cell research, such as using dead IVF eggs, removing only one cell from an early embryo (at the eight-cell stage), or altering a blastocyst so it could not become a human. However, all were experimental procedures already supported by the National Institutes of Health. In the end Gazzaniga believed the results of the report were merely "science chasing policy."

Sharples discussed the National Academies report, "Guidelines for Human Embryonic Stem Cell Research."[8] While the National Academies are not federal agencies, regulatory or otherwise, many people look to them for guidance on difficult science policy issues. The goal of the 2005 report was to develop hESC research guidelines to be used in the United States regardless of the funding source. These guidelines defined three areas of research: *permissible* research (using existing approved lines); *research which is permissible after review* (creating or using new lines); and *prohibited* research (cloning of a human-being, culturing cells beyond 14 days, using hESC in nonhuman primates, and breeding animals that have implanted hESCs). These guidelines also recommended that each research institution should create an embryonic stem cell research oversight (ESCRO) committee to oversee the research. Furthermore, it recommended that all donations of cells, eggs and sperm should be reviewed; all donors should give consent for research; researchers should not deal with patients directly, and patients should deal with an intermediator with no ties to research; no payments should be given for donations; and donor

information should be kept private. It also suggested the creation of a national oversight committee to discuss guidelines and update them when necessary, which the National Academies organized in 2006.

International Research and Collaborations

Collaborations are an important part of scientific research, but in hESC research this is complicated by the various national policies and guidelines. As part of the conference, representatives from the Hinxton Group and the International Society for Stem Cell Research (ISSCR) presented their guidelines on research and how to improve collaborations across borders.

Debra Mathews, assistant director for science programs at the Phoebe R. Berman Bioethics Institute at Johns Hopkins University and a member of the steering committee for the Hinxton Group, introduced the Hinxton Group and their consensus statements from their February 2006 meeting.[9] The Hinxton Group, an international consortium on stem cells, ethics, and law, is an assembly of 50 ethicists, scientists, lawyers, policy experts, and journal editors from 14 countries that met in Hinxton, England. Their goal was to identify challenges faced by scientists in pursuing international collaborations; to develop basic guidelines for conduct across national boundaries; to encourage oversight and data sharing; and to promote strategies for scientific and ethical integrity. While there is a wide range of variation on how nations deal with hESC research, the Hinxton Group was able to develop a consensus document of 19 statements to help promote better international, ethically sound collaborations. These statements ranged from asking for clear and explicit laws, to promoting submission of hESC lines to stem cell banks, to requiring journal editors to support and promote ethical integrity in hESC research.

Insoo Hyun, assistant professor at Case Western Reserve University and member of the ISSCR task force, presented the ISSCR guidelines, which were available as a draft at the time of the meeting.[10] The task force included scientists, ethicists and lawyers from 14 countries. They were charged with identifying core principles and guidelines for hESC research. Using the National Academies report and the Hinxton Group statements as a guide, ISSCR recommended many of the same ideas, such as banning reproductive cloning, creating institutional review boards

specifically for stem cell research, and requesting that journal editors and funders require senior authors to sign documents affirming ethical research. In addition, ISSCR provided researchers with sample documents for informed consent and material transfer agreements, as well as links to international laws and references to ethical treaties. They also announced their intention to create and maintain a Web site with a list of stem cell lines and documentation on their provenance.

Conference Conclusions

At the Baker Institute's conference "Avenues for Advancement," scholars from around the world came together in Washington, D.C., to discuss different cultures, policies and practices for regulating hESC research. From the presentations, we learned that while many countries have adopted policies, few provide specific regulations and oversight for the research, both in developing and developed countries. Several countries (Italy and the United States, for example) have failed to provide an overarching policy that addresses research funding by public and private sources. Furthermore, the debates about hESC research, the creation of new hESC lines, and therapeutic cloning are still ongoing in countries with clear regulation and policy – as we saw in Canada.

During the conference discussions, it was noted how rare it is to actually ban scientific research. It is even more unusual to attach a criminal punishment in one location, while a short distance away the same research has governmental support. For instance, therapeutic cloning is banned in Canada with criminal and civil penalties, while in Illinois and California there are state grants available for the same research. Caulfield questioned, "Is the criminalization necessary?"

It was also observed that the relationship between policy and science has become confused. Frankel noted, "On one hand we have policy driving the science; on the other we have science driving the policy." While research discoveries in the past 10 years have lead to increased debate on hESC research and therapeutic cloning, scientists are pursuing research in alternative directions, such as parthenogenesis and the use of dead IVF embryos, to find ways around policy

limitations. Several speakers questioned if this was the right way for medical research to proceed.

This conference in Washington was a part of a larger effort by the Baker Institute's Science and Technology Policy Program to promote conversations between policymakers, scientists, ethicists and the general public. It is our hope that the discussions and publications of the conference as well as those from the earlier conferences in the series will contribute to the resolution of current federal- and state-level stalemates concerning oversight and regulation of hESC research. The conference series was sponsored by the Richard Lounsbery Foundation. The Baker Institute's International Stem Cell Policy Program is funded by the State of Qatar and the Emir of Qatar, His Highness Sheikh Hamad Bin Khalifa Al Thani, through the State of Qatar Endowment for International Stem Cell Policy.

Endnotes

[1] Baker Institute Policy Report #33, "Lessons Learned: U.S. Embryonic Stem Cell Policies," is a summary of U.S. federal and state policies. It is available online at www.bakerinstitute.org/Pubs/pr_33.pdf.
[2] The Baker Institute Policy Report #31, "Stem Cells: Saving Lives or Crossing Lines," is a summary of the November 2004 conference with the same title. It is available online at www.bakerinstitute.org/Pubs/study_31.pdf.
[3] Baker Institute Policy Report #33, "Lessons Learned: U.S. Embryonic Stem Cell Policies," is a summary of U.S. federal and state policies. It is available online at www.bakerinstitute.org/Pubs/pr_33.pdf.
[4] A summary of survey results can be found in the article by Isasi, R. and Knoppers, B.M., "Mind the Gap: Policy Approaches to Embryonic Stem Cell and Cloning in 50 Countries," *European Journal of Health Law,* 13:9-26 (2006).
[5]The report, "Human Cloning and Human Dignity: An Ethical Inquiry," can be found online at www.bioethics.gov.
[6] The report, "Guidelines to Human Embryonic Stem Cell Research," can be found online at www.nap.edu.
[7]The report, "Alternative Sources of Human Pluripotent Stem Cells," can be found online at www.bioethics.gov.
[8] The report, "Guidelines to Human Embryonic Stem Cell Research," can be found online at www.nap.edu.
[9] The Hinxton Group consensus statement can be found at www.hinxtongroup.org/au.html.
[10] The ISSCR guidelines can be found at www.isscr.org/guidelines/index.htm.