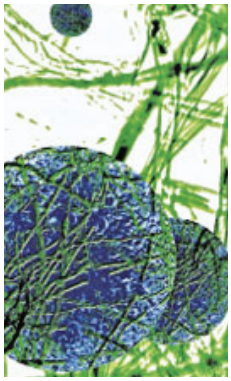

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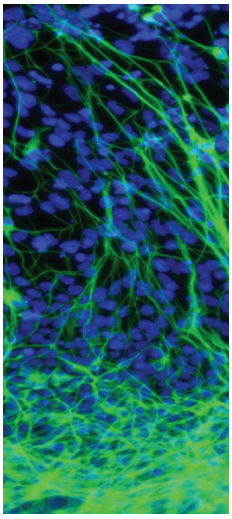

Stem Cell Policy in the Obama Age: Texas, U.S., and U.K. Perspectives

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Stem Cell Policy in the Obama Age: Texas, U.S., and U.K. Perspectives

A September 2009 Conference Report by

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INTRODUCTION

Stem cells—embryonic, cord blood, adult, and induced pluripotent—are viewed as a critical area of research by many in the scientific and medical community. They can be used to improve our basic understanding of cell development and specialization. But many experts are excited about their potential as biomedical tools in regenerative medicine that could one day treat or cure debilitating injuries or diseases such as diabetes, Parkinson's disease, and spinal cord injuries. Indeed, some blood stem cells have been used to develop cures and treatments for blood-borne cancers. While a significant amount of work must be done to better understand and utilize these cells, U.S. policies in the last decade have impeded stem cell research, especially the study of human embryonic stem cells (hESCs).

In March 2009, newly elected President Barack Obama signed an executive order requesting a revision of existing U.S. stem cell policy. The resulting policy permits new federal funding of stem cell research in the United States. The more permissive policy also impacted funding at the state level, with some states decreasing funding (and allowing the federal government to take over), others complementing federal funding, and a few attempting to ban hESC research.

On September 14–15, 2009, the Baker Institute Science and Technology Policy Program hosted a workshop titled "Texas-U.K. Collaboration."[1] The event was the fifth in the institute's International Stem Cell Policy Program conference series "Stem Cells: Saving Lives or Crossing Lines" (see box: The Baker Institute). Part of the workshop, organized by the Texas-UK Collaborative, was devoted to stem cell research to help promote collaborations between Texas and U.K. stem cell researchers. In addition, the institute's Science and Technology Policy Program worked with the UK Science and Innovation team to organize discussions that examined the well-established U.K. stem cell regulatory framework as well as the new U.S. policy and its impacts on the state of Texas.[2]

The Baker Institute International Stem Cell Policy Program

The mission of the Baker Institute International Stem Cell Policy Program is to bring together scientists, ethicists, policymakers, media experts, and community and business leaders to find new ways to engage the general public in a dialogue on international stem cell policies and the ethical use of stem cells for research. It is a part of the Baker Institute Science and Technology Policy Program.

Additional information can be found online at **science.bakerinstitute.org.**

The U.S. and U.K. policies were highlighted in greater detail in a special evening panel discussion with Neal Lane, Ph.D., the institute's senior fellow in science and technology policy; and Lord Naren Patel, M.D., D.Sc., chairman of the UK National Stem Cell Network

[1] Read more about the event "Stem Cells: Saving Lives or Crossing Lines: Texas-U.K. Collaboration" at http://www.bakerinstitute.org/events/txukstemcell09 and http://www.bakerinstitute.org/events/stemcelldinner09.

[2] See the UK Science & Innovation Section at the British Consulate-General, Houston, at http://ukinusa.fco.gov.uk/en/about-us/other-locations/houston/scienceinnovation/.

Steering Committee. The striking contrast between these two regulatory cultures and their view of embryonic and hESC research emphasized the need within the U.S. system to continue to understand and address issues of embryonic research.

STEM CELL RESEARCH AND REGENERATIVE MEDICINE

Chris Mason, Ph.D., a professor of biochemical engineering at University College London, presented an overview of stem cell therapies and regenerative medicine at the workshop. Mason defined regenerative medicine as the replacement or regeneration of cells, tissues, or organs to restore or establish normal function. Mason noted that tissue-engineered products (therapies that employ scaffolds or delivery systems to create functional tissues), cell therapies (therapies that employ cells to repair or regenerate aged or diseased tissues), and regenerative compounds (compounds that trigger endogenous regeneration) all fall under the category of regenerative medicine.[3] The utilization of stem cells could become a major tool in regenerative medicine.

Unlike normal cells such as muscle, nerve, or blood cells, stem cells can replicate indefinitely. They are unspecialized or partially specialized cells, which can give rise to multiple cell types. In humans, embryonic stem cells can be extracted from a five- to six-day-old embryo; other types of stem cells are found in the umbilical cord and placenta and in several adult organs. Furthermore, stem cells can be produced in a lab by triggering a normal cell (such as a skin cell) to return to an earlier developmental stage; such cells are called induced pluripotent stem (iPS) cells and are similar to hESCs (see Figure 1: Pathways to Pluripotent Cells).

"Stem Cells are both health and wealth."
– Chris Mason

In addition, scientists have attempted to create hESCs through a technique called somatic cell nuclear transfer (SCNT), sometimes referred to as therapeutic cloning. SCNT involves removing the nucleus (or DNA) from an unfertilized egg, replacing it with the nucleus from a normal cell (such as a skin cell), and activating the egg to divide. While this technique has not been successfully used to produce hESCs, it has been used to clone animals, a sheep named Dolly being the most famous.[4]

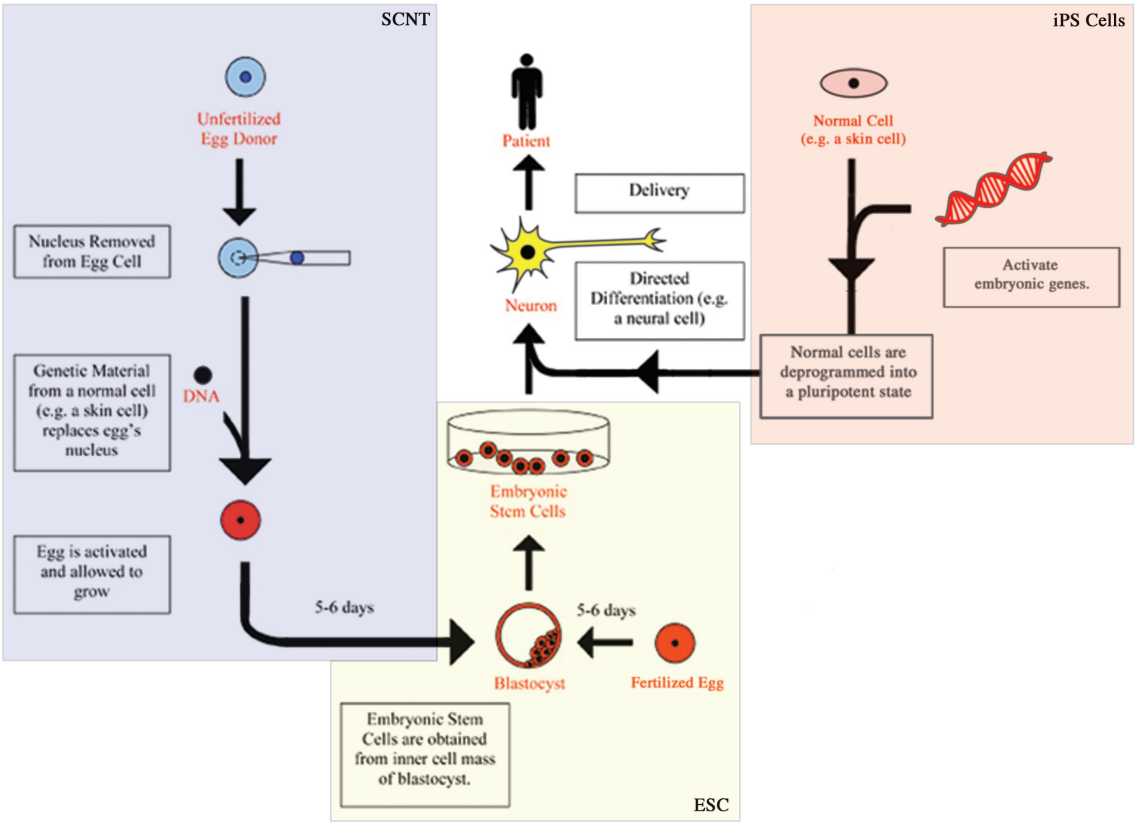
Mason believes that stem cells are a tool for treating and curing diseases instead of just managing them with pharmaceuticals, as we do now. He noted that stem cell therapies already exist. More than 300,000 people have been treated with living cell therapies, and products approved by the U.S. Food and Drug Administration (FDA) are currently on the market. "We're not talking about something particularly new," Mason said, "but we just don't seem to be aware how successful it has been."

In his presentation, Mason described some regenerative medicine therapies that have already attained a degree of success. For instance, leukemia patients can be treated with bone marrow

[3] C. Mason et al., "Regenerative Medicine Glossary," *Regen. Med.* 4, no. 4 (2009): Suppl. no. 1.

[4] K.R. Matthews, "Stem Cell Research: A Science and Policy Overview" (paper published by the James A. Baker III Institute for Public Policy, September 2009), http://www.bakerinstitute.org/publications/stemcell-intro-0208.pdf.

Figure 1: Pathways to Pluripotent Cells: hESCs, SCNT, iPS Cells



K.R. Matthews, "Stem Cell Research: A Science and Policy Overview" (paper published by the James A. Baker III Institute for Public Policy, September 2009), http://www.bakerinstitute.org/publications/stemcell-intro-0208.pdf.

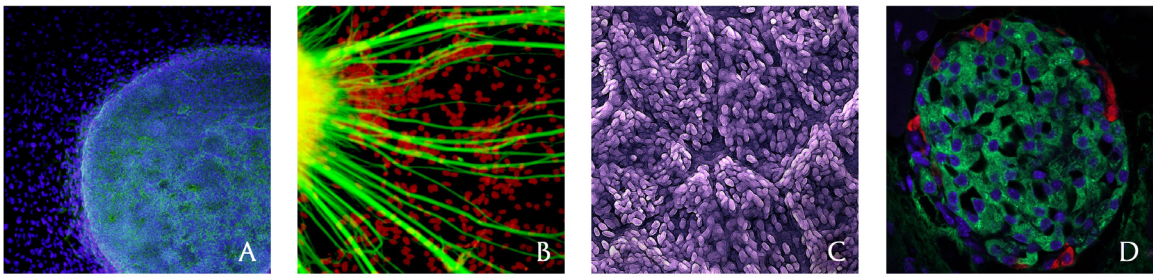
transplants that replace cancerous cells with healthy blood stem cells. There is also a stem cell therapy that helps regenerate damaged cells in the eye to restore sight. In addition, Mason mentioned commercially available tissue-engineered skin and the successful transplant of a tissue-engineered human trachea in 2008. Mason also remarked that a tissue-engineered human bladder is currently in the final stages of clinical trials.

No one stem cell type will be the cure-all, Mason noted. All types (embryonic, adult, cord, iPS, etc.) will be required, but hESCs receive the most media attention. Mason believes this is because they offer the greatest potential to treat debilitating diseases due to their ability to specialize into almost every cell type in the body. However, although there is a great deal of hype surrounding hESCs, scientists have not yet successfully used them to develop a therapy or cure.

A number of applications for hESC in therapies are currently being researched. Mason described research on therapies for spinal cord injuries, heart failure, diabetes, and vision loss due to macular degeneration (see Figure 2: hESCs). Mason feels that regenerative medicine technologies could produce a thriving industry, stating that "stem cells are both health and wealth." Furthermore, he has "no doubt that companies that successfully commercialize this will build a very competitive and sustainable industry in the future."

In 2009, the biotechnology company Geron started the first FDA clinical trial employing hESCs to help patients with spinal cord injuries. Unfortunately, the trial had to be halted after a few months due to complications in the ongoing animal studies. But Geron indicated it will try to start up the trials again in late 2010 after these issues are resolved.[5]

Figure 2: hESCs and Differentiated Cells for Therapies: A) hESCs, B) Neural Cells, C) retinal cells, and D) ß-islet cells



hESC | *hESC derived neural cells* | *hESC derived retinal cells* | *mouse ESC derived ß-islet cells*

Images A-C courtesy of the California Institute for Regenerative Medicine, specifically B) the lab of Fred H. Gage at the Salk Institute for Biological Studies and C) the lab of David Hinton at the University of Southern California. Image D courtesy of authors: Chistin Süß, Jakob Suckale, Michele Solimena.

Mason also described research in which hESCs were differentiated into cardiac muscle cells and implanted after a heart attack to prevent cardiac cell death and heart damage, both of which can lead to heart failure. This research was conducted on animals, but could have great potential if successful in humans.

In addition, Mason pointed out research conducted by several other companies, including Novocell, Advanced Cell Technology (ACT), and Pfizer.[6] Novocell, in collaboration with Pfizer, is using hESCs to develop a treatment or cure for insulin-dependent diabetes. Researchers hope to restore normal pancreatic function in diabetic patients by differentiating hESCs into ß-islet cells, which produce insulin, eliminating the need for frequent insulin injections. Pfizer and ACT are focused on a therapy to restore vision in patients suffering from age-related macular degeneration. Restoring retinal pigment epithelial cells can prevent patients from becoming blind. ACT submitted an application to the FDA in 2009 to conduct clinical trials using hESCs. If approved, it would be the second clinical trial using hESCs.

"No doubt that companies that successfully commercialize this will build a very competitive and sustainable industry in the future."

– Chris Mason

But while there have been some successful applications of regenerative medicine, the full potential for stem cell research has yet to be realized, and there are still many obstacles to overcome in both the science and policy arenas. Mason believes that the biotechnology

5 View the Geron Web site at http://www.geron.com.

6 View the Novocell Web site http://www.novocell.com; ACT at http://www.advancedcell.com/; and Pfizer at http://www.pfizer.com.

industry "need[s] the investment specifically in the translation of basic science into therapies for reaching clinical practice." Mason also remarked that both Texas and the United Kingdom were well-positioned to create and succeed in this type of market.

Mason closed his talk by again emphasizing the potential of regenerative medicine and stem cell therapies to help millions of patients, as well as their families and caregivers. However, Mason expressed the view that patients must be cautious of overhyped and unregulated stem cell therapies offered around the globe. Physicians should communicate to their patients the risks and benefits of a treatment, so they can make an informed decision before traveling to receive these therapies, he said.

TEXAS STEM CELL POLICY

Ellen Arnold, a principal with the public affairs consulting firm Arnold Public Affairs, spoke on the recent activities of the Texas legislature. She is also an adviser to Texans for Advancement of Medical Research (TAMR), an advocacy group that lobbies for all types of stem cell research in Texas. In her presentation, she chronicled proposed state hESC legislation over the past decade and its potential effects on research in Texas.[7]

Arnold found that most of the proposed bills in Texas prior to 2005 were prohibitive in nature. Several would criminalize hESC research or make it illegal to receive therapies derived from hESCs, regardless of where the procedure occurred. The proposed penalties for these actions were $1 million fines and up to 10 years in prison. "Had I taken my niece, who has type I diabetes, to the U.K. for treatment and then come back [to Texas], I would have been subject to criminal charges and possible incarceration—my niece's physician as well," Arnold remarked. She commented that in recent years there have been bills in Texas that would ban both funding for hESC research and appropriations to institutions conducting hESC research. Fortunately, none of these prohibitive bills passed.

Arnold noted that in 2005, Texas legislators began to propose bills that were more permissive to stem cell research. These bills would have allowed hESC research and provided methods to regulate with ethical guidelines. They would have also banned human reproductive cloning (the cloning of a human being), established an oversight committee to monitor research, and funded research using hESCs. However, none of these bills passed.

> *"[Senator Ogden] was not aware that any embryonic stem cell research was being conducted in public institutions in Texas."*
>
> *– Ellen Arnold*

At the same time, legislators filed a number of restrictive bills, Arnold acknowledged. In addition to proposing bills that would prohibit hESC research outright, legislators employed several other strategies, including adding an amendment to an existing bill (i.e., an appropriations bill). One amendment would have prohibited appropriations to universities that conducted hESC research regardless of the funding source. "That was a very serious strategy," Arnold believes.

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7 View the TAMR Web site at http://www.txamr.org.

Arnold also found that university tuition revenue bonds bills provide a way to restrict research. These bonds are very important to universities because they supplement their income. Bills filed would have prohibited the use of any facility for hESC research if that facility was built with bond dollars.

Legislators also attempted to redefine when life begins, and to link hESC research to abortion, Arnold stated. One proposed bill defined life as "a full or complete complement of DNA." Arnold alleged that opponents of hESC research often tried to link hESCs to abortion by claiming that aborted fetuses were a source of stem cells. Opponents also suggested that women were paid to receive abortions to provide an hESC source. Neither of these assertions is true.

All of the attempts to pass prohibitive legislation were ultimately defeated. Arnold believes that this was due to the work of a small, bipartisan group of legislators, staffers, scientists, and citizens. "Had I been asked to predict our success, I would have said, 'not a chance,' but I underestimated their enthusiasm for and commitment to the issue," she remarked.

Arnold remarked that efforts to pass prohibitive legislation have continued. In the 2009 legislative session, State Sen. Steve Ogden, R-Bryan, chairman of the Senate Finance Committee, proposed Texas Senate Bill (SB) 1695, which would prohibit the use of state funds or facilities for research involving the destruction of human embryos, including hESC research. In addition, Ogden attempted to add an amendment to the 2009 General Appropriations Act that would have banned the use of state funds to support any activity that led to the destruction of a human embryo (see box: Ogden Budget Rider). Arnold commented, "I think the thing that startled people was that there was no hearing; there wasn't public input or debate" when the amendment was added to the appropriation bill or afterward.

Ogden Budget Rider — 2009

ARTICLE IX: NO DESTRUCTION OF HUMAN EMBRYOS

Required Action

In Article IX of the General Appropriations Act add the following rider:

*___. **No Destruction of Human Embryos.** No funds appropriated under this Act shall be used in conjunction with or to support any activities whatsoever, including research, which involves the destruction of a human embryo.*

Arnold explained that both the senate and appropriations bills would have prohibited all hESC research, even on hESC lines approved by the Bush administration. In addition, she believes that the legislation would negatively affect the ability of Texas academic and research institutions to recruit and retain premier students and scientists to conduct biomedical research—in all disciplines.

In the end, Ogden did not seek a hearing for Senate Bill 1695 and withdrew his amendment from the General Appropriations Act. Arnold felt that this was because when he wrote them "he was not aware that any embryonic stem cell research was being conducted in public institutions in Texas. He didn't realize what his rider would have done, [that it] would have

had such an impact in Texas." Instead, Ogden proposed a new bill, which called for reports from all publicly funded projects using hESCs. But this bill also did not pass.

However, in 2009 Ogden included an amendment to House Bill 51, which did pass, that authorized a study of how to collect data on research being conducted throughout Texas. This bill required an interim committee to study the feasibility of collecting data and maintaining a searchable database related to technology research performed in public universities. The committee would include representatives from major public universities in Texas, as well as members chosen by the Texas Higher Education Coordinating Board.

Arnold believes that a general lack of understanding in the state house about hESC sources, research, and potential benefits led to multiple attempts to pass restrictive legislation. Arnold also feels that many public research institutions have been reluctant to discuss their research or the economic impacts of criminalizing hESC research, leading legislators to believe that prohibitive bills would not affect Texas. Many legislators were unaware of research being conducted in their districts and Texas as a whole.

U.S. STEM CELL POLICY

Neal Lane, Ph.D., the Baker Institute senior fellow in science and technology policy and the Malcolm Gillis University Professor at Rice University, discussed the U.S. federal policy on stem cell research.[8] Lane acknowledged that U.S. policy "may not appear to be an entirely rational approach to policymaking." But a number of events—largely related to advances in science and our understanding of human cellular biology, medicine, and technology—have brought us to where we are today, he said.

> *"In this country almost 20 years passed between the birth of the first test tube baby and any sort of serious consideration, serious discussion of policy having to do with embryonic research."*
>
> *– Neal Lane*

As with the United Kingdom, U.S. policy on embryonic research began in 1978, when Louise Brown became the first baby born through *in vitro* fertilization (IVF). Lane noted that "in this country almost 20 years passed between the birth of the first test tube baby and any sort of serious consideration, serious discussion of policy having to do with embryonic research." It was only in the past 12 years that the public started discussing policies related to research on or with embryos. But, Lane said, this is not unusual in the U.S. system of government, where power is shared between the president and Congress. Often it takes an extraordinary set of circumstances, a national crisis of some sort, to change the law, he noted.

This is in stark contrast to the U.K. process, which slowly and deliberately developed policies over the past 30 years. Lane stated his belief that "the U.K. has been a leader among nations in demonstrating that there really is a rational approach to policymaking."

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[8] Talk based on K.R. Matthews, "Stem Cell Research: A Science and Policy Overview" (paper published by James A. Baker III Institute for Public Policy, September 2009), http://www.bakerinstitute.org/publications/stemcell-intro-0208.pdf.

At the time of Louise Brown's birth, Title 45, Part 46 of the Code of Federal Regulations titled "Protection of Human Subjects" governed IVF in the United States.[9] In response to the success of IVF, the administration of President Jimmy Carter established the Ethics Advisory Board (EAB) to oversee federal research on human embryos, although private research was unrestricted. Any federally funded research on embryos that was approved by the board could be carried out. But the board only met once and never approved any research projects. It was eventually disbanded in the early 1980s during the Ronald Reagan administration. Since there was no longer a board, no embryo research could be approved. In 1993, the administration of President Bill Clinton rescinded the law creating the EAB, in theory allowing research on embryos to proceed. However, in the end, the federal government funded no such research.

Lane stated his belief that "the absence of a binding law on the books—with appropriate guidelines, oversight, and regulation to guide embryo research—left a void that was addressed a few years later by a Republican Congress using the appropriations process." With the Republican takeover of Congress after the 1994 election, Republican members were anxious to fill the policy gap on embryo research. This was achieved through the Dickey-Wicker Amendment, named for its authors, U.S. Reps. Jay Dickey (R-AK) and Roger Wicker (R-MS), to the Department of Health and Human Services (DHHS) appropriations bill.

More commonly known as the Dickey Amendment, the rider has been attached to the DHHS appropriation bill every year since 1996 (see box: The Dickey Amendment). The National Institutes of Health (NIH), the U.S. biomedical research funding agency, resides inside the DHHS, and therefore the amendment impacted all federally funded biomedical research. The Dickey Amendment bans the use of federal funds for the creation of hESC lines because in this process an embryo is destroyed.

The Dickey Amendment

"Prohibits the use of funds made available in the Act for:
1) the creation of a human embryo for research purposes or
2) research in which a human embryo is destroyed, discarded, or knowingly subjected to risk of injury or death...greater than that allowed for research on fetuses in utero *under 45 CFR 46.208(a)(2) and Section 498(b) of the Public Health Service Act.*

Defines 'human embryo or embryos' to include any organism ... that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells."

– DHHS, FY 2005 Budget

[9] DHHS, Code of Federal Regulations: Title 45 "Public Welfare," Part 46, "Protection of Human Subjects." http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm.

Lane stated that the birth of the cuddly sheep, Dolly, was another key event in the creation of the U.S. stem cell policy (see Figure 3: Dolly).[10] Born on July 5, 1996, Dolly was the world's first cloned mammal, the creation of Ian Wilmut's group at the Roslin Institute in the United Kingdom. Dolly provoked a strong reaction among members of the public as well as policymakers. Many people were afraid the next step would be the cloning of human beings, a very unpopular notion not only among members of the public but among scientists themselves.

Figure 3: Dolly

Following Dolly's birth, Clinton called on his bioethics advisory group, the National Bioethics Advisory Commission (NBAC), to make recommendations on policy options he might consider. There was no federal law, nor is there today, that prevents someone from attempting to clone a human; fortunately, the FDA can monitor cloning research and has promised to regulate any potential cloning. In 1998, the NBAC concluded that reproductive cloning should be prohibited.[11] As a result, Clinton put forward a bill for congressional approval that would ban human reproductive cloning. "Congress, in a moment of wisdom, decided to postpone the passage of the bill so they could determine its impact on valid biomedical research," Lane remarked. In the meantime, science was not waiting for Congress.

In November 1998, James Thomson and his group at the University of Wisconsin–Madison reported that, using nonfederal funds, they had created the first hESC lines from frozen IVF embryos that otherwise would have been discarded.[12] The media coverage that followed gave the general public a better understanding of the new medical treatments possible through hESC research.

"Following the University of Wisconsin breakthrough, Clinton again approached his bioethics commission, which after due deliberation recommended federal funding of hESC research, including the creation of new stem cell lines from IVF embryos, and recommended steps to insure appropriate oversight and regulation," stated Lane. The NBAC did not see an ethical distinction between funding research on hESCs that someone else created and using federal funding to create stem cell lines from discarded embryos. In both cases, an embryo is destroyed.[13]

With Clinton's approval, DHHS began to review the Dickey Amendment to determine if the law would allow the NIH to fund research on existing hESC lines. But Clinton was not willing to go as far as the NBAC recommended and allow the NIH to fund the derivation (creation) of new hESC lines. The NIH lawyers concluded that the Dickey Amendment permitted research on existing lines, but prohibited the use of federal funds to create new hESC lines.

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[10] I. Wilmut et al., "Viable offspring derived from fetal and adult mammalian cells," *Nature* 385 (1997):810–3.

[11] NBAC, "Cloning Human Beings: Report and Recommendations of the National Bioethics Advisory Commission" (1997), http://bioethics.georgetown.edu/nbac/pubs/cloning1/cloning.pdf.

[12] J.A. Thomson et al., "Embryonic Stem Cell Lines Derived from Human Blastocysts," *Science* 282 (1998):1145–7.

[13] NBAC, *Ethical Issues in Human Embryonic Stem Cell Research, Volume I: Report and Recommendations by the National Bioethics Advisory Commission*, 1998, http://bioethics.georgetown.edu/nbac/stemcell.pdf.

After much delay, the Clinton administration was prepared to move forward with hESC research consistent with the law. Guidelines were released and the NIH prepared to review proposals and make grants in the spring of 2001. But before that could happen, George W. Bush assumed the presidency and decided to reassess the policy.

After taking office in 2001, Bush set aside the ruling by the DHHS lawyers and the NIH and halted the funding of hESC research until his administration could determine its policy. On August 9, 2001, Bush announced a new federal policy. Federal funding would be available to support research only on stem cell lines existing before August 9, 2001. No funding would be available to create new lines or carry out research on lines created after that date, regardless of how they were created. The president announced that based on NIH information, there were approximately 60 stem cell lines in existence on August 9, 2001. That was an optimistic estimate. The number of existing lines turned out to be 21.

Lane noted that Bush had tried to be responsive to scientists by allowing some federal funding for hESC research. But the reaction from the research community was mixed; many criticized the new policy as too restrictive. The Bush policy impacted only federal funding; it did not affect privately funded research or state or local government funded hESC research.

Lane stated that, at present, no federal laws restrict hESC research or reproductive cloning; the only limitations are found in executive orders that restrict federal funding. Efforts were made since 1997 to pass laws banning human reproductive cloning; but many conservatives are unwilling to support a bill unless it goes further and also bans other kinds of research involving human embryos. Despite the lack of federal laws relating to stem cell research, any human testing of a new medical treatment or therapy, whether based on stem cells or anything else, is subject to regulation by the FDA and must follow the usual clinical trials procedures.

Each year, from 2001 to 2008, Congress has tried to pass bills that alternated between expanding and prohibiting hESC research. The first bill that came through both houses was the bipartisan Stem Cell Research Enhancement Act of 2005. This bill would allow federal funding of research utilizing hESCs created from donated IVF embryos, specifically those created for reproductive purposes. After years of being pushed aside, the bill was finally passed by the House of Representatives in 2005 and by the Senate a year later.

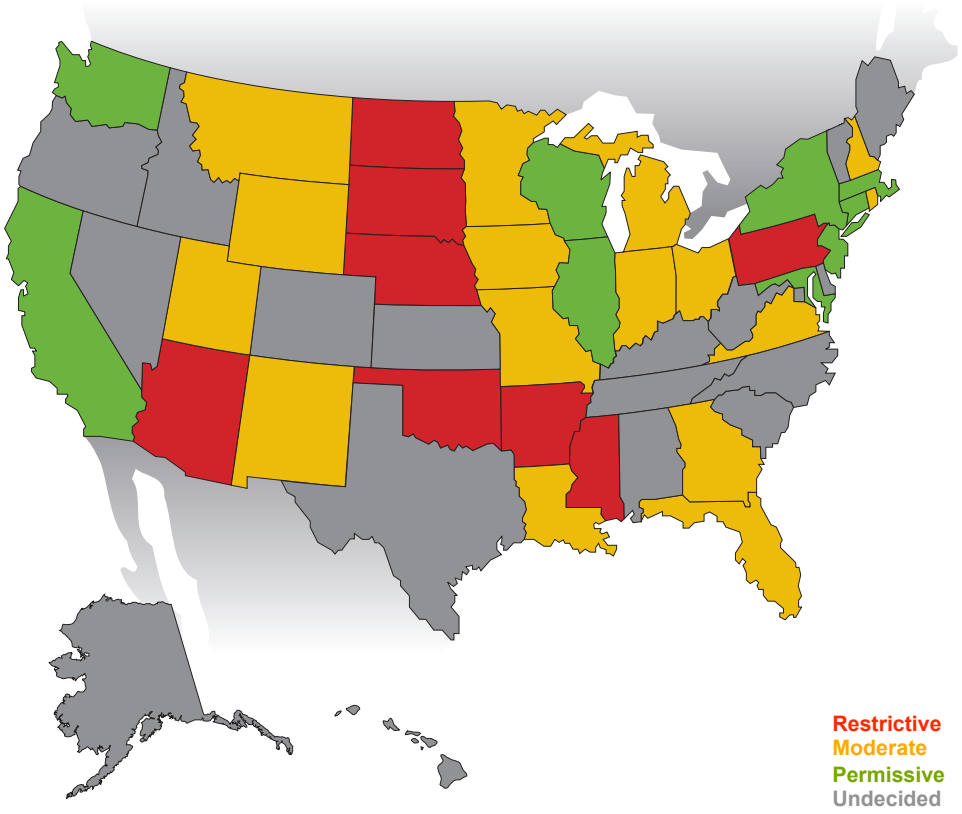
"Obama's policy more closely regulates the informed consent process and, thus, is somewhat more restrictive than that of President Bush."

– Neal Lane

But the bill was ultimately vetoed by Bush, who advocated for embryo adoption programs. Unfortunately, it is estimated that more than 100,000 embryos are currently being stored in IVF clinics all around the country, most of which will be destroyed because they are not needed by their donors. Only a small fraction—less than 1,000—of these embryos have actually been adopted. In 2007, the newly elected Democratic majority in Congress passed the bill, which Bush again vetoed. The president instead issued an executive order in regard to language in the Dickey Amendment to clarify the meaning of "risk of injury or death" so alternative procedures to create hESCs could be federally funded (which could, in theory, risk harm to an embryo).

While the federal government has been unable to establish laws regulating hESC research, states have been more proactive (see Figure 4: State Stem Cell Policies).[14] Some states have passed legislation that restricts or bans hESC research. Other states have adopted restrictions that are short of banning. For example, while Missouri has banned the use of state funds for hESC research, legislators have essentially protected stem cell work by passing a law that allows federally funded hESC research. Several states (including California, Connecticut, and Illinois) have appropriated funds to support in-state hESC research. But the majority of states, including Texas, have no stem cell policy at all.

Figure 4: State Stem Cell Policies



When running for president in 2008, Obama promised to increase federal funding for hESC research. Once in office, he moved quickly to change the policies of his predecessor. On March 9, 2009, Obama signed an executive order titled "Removing Barriers for Responsible Scientific Research Involving Human Stem Cells" (see box: Removing Barriers).[15] The order rescinded all previous executive orders on hESC research and removed the cutoff date for federal funding of hESC research. It also directed the NIH to develop guidelines within 120 days for the regulation of federally funded hESC research.

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[14] K.R. Matthews, "Stem Cell Research: A Science and Policy Overview" (paper published by the James A. Baker III Institute for Public Policy, September 2009), http://www.bakerinstitute.org/publications/stemcell-intro-0208.pdf.

[15] B. Obama, "Removing Barriers for Responsible Scientific Research Involving Human Stem Cells," Executive Order, March 9, 2009. http://www.whitehouse.gov/the_press_office/Removing-Barriers-to-Responsible-Scientific-Research-Involving-Human-Stem-cells/.

Lane suggested that the phrase in the executive order, namely, that hESC research could be funded "to the extent permitted by law," implicitly referred to the Dickey Amendment—which continues to appear on the annual DHHS appropriations bills—and its ban on creating hESC lines using federal funds. "Obama did not intend for his new policy to remove the ban on using federal funds to create these lines, nor did he advocate for its removal," Lane remarked.

As requested by the president, the NIH produced draft guidelines for public comment in April 2009. During the 30-day comment period, more than 49,000 people expressed opinions on various aspects of the guidelines. The NIH then addressed the issues raised by the public and released its final guidelines on July 7, 2009, which are in force today.

The NIH guidelines specifically address hESC research and certain uses of iPS cells. They highlight two basic principles for federally funded hESC research: 1) responsible research on hESC has the potential to improve our understanding of human health, and 2) individuals donating embryos should do so freely.

Removing Barriers for Responsible Scientific Research Involving Human Stem Cells

"For the past 8 years, the authority of the Department of Health and Human Services...to fund and conduct human embryonic stem cell research had been limited by presidential actions. The purpose of this order is to remove these limitations on scientific inquiry, to expand NIH support for the exploration of human stem cell research."

– President Barack Obama, March 9, 2009

For new hESC lines, only lines created from leftover IVF eggs donated with proper consent are eligible for NIH funding. As part of the consent, the NIH requires that no payments or free services for donating are provided and that there is a clear separation between the IVF procedure and the decision to donate. The NIH also stresses that the donor must be fully and completely informed; this includes notification that the embryo will be used to create hESCs; the embryo will be destroyed in the process; the lines will be available for years; and personal information (such as genetic information or disease history) might be provided to the researcher.

For already existing lines, the NIH will review documentation to determine if the investigators followed the spirit and intent of the guidelines. In addition, the investigators must demonstrate that the lines were created from leftover IVF embryos and that donors gave informed consent.

The NIH guidelines also delineated what was not eligible for federal funding. This included hESCs or iPS cells introduced into nonhuman primates (i.e., monkeys); breeding animals where the introduction of hESCs or iPS cells may contribute to the germ line (i.e., in a mouse or hamster where hESC or iPS cell could be passed to progeny); derivation of hESC lines; and hESCs from other sources, such as SCNT, parthenogenesis (the development of an embryo from an unfertilized egg), or any IVF embryos created for research (not reproductive) purposes.

When comparing the policies of the three most recent U.S. administrations (see Table 1: Presidential Stem Cell Policies), Lane noted that the policies of Obama and Bush might appear to be closer than those of Obama and Clinton. Although the Clinton administration never had a chance to fund hESC research, because the clock ran out, the Clinton policy would have allowed the NIH to fund research on hESC created from all sources.

The major difference between the hESC policies of presidents Obama and Bush is the August 9, 2001, cutoff date set by Bush. Obama removed this date. In addition, Lane noted, "Obama's policy more closely regulates the informed consent process and, thus, is somewhat more restrictive than that of President Bush." Over the past eight years, several hESC lines approved by the Bush administration were found to lack proper consent documentation, although federal funding had been permitted. All three presidents have agreed that the NIH should not be permitted to fund the creation of hESC lines.

Table 1: Presidential Stem Cell Policies: Clinton, Bush, and Obama

Federal Funding:	***Clinton***	***Bush***	***Obama***
hESC	Yes†	Yes*	Yes
Create hESC	No	No	No
SCNT	Yes†	No	No
Cloning	No	No	No
Adult SC	Yes	Yes	Yes
Consent	Yes†	Not Enforced	Enforced
IVF only	No	Yes	Yes
Guidelines	NBAC, DHHS	PCB	NIH 2009

† – Did not fund any grants ** – Created before August 9, 2001*

Looking towards the future of U.S. policy, Lane said, "Alternatives to hESCs are still being researched and could limit the need to create new lines of hESCs, having an impact on the current policy." Furthermore, Lane acknowledged that politics is never over—in Washington or at the state level. After Obama's executive order expanded federal funding, many anti-stem cell groups moved their campaigns to the states (including Texas) to promote legislation that banned all hESC research or a portion of such research (e.g., state funding of hESC research).

Lane also said that more policy developments could occur in Washington. Congress still has not successfully passed a law that regulates embryonic research. Legislators might propose their own set of policies and regulations governing federal funding for hESC research. Or Congress might decide to restrict research being pursued by researchers using private or state funding. Furthermore, Lane stated his belief that the lack of a federal law dealing with reproductive cloning techniques "is a very serious flaw in our policy." In addition, Lane remarked that with the economic and international challenges facing the country, "Congress won't spend much time on embryo research policy unless something major happens that gets the public's attention."

U.K. STEM CELL POLICY

Three U.K. speakers—Lord Naren Patel, M.D., D.Sc., chairman of the UK National Stem Cell Network Steering Committee; James Lawford Davies, partner at Lawford Davies Denoon and lecturer in law and medicine at the University of Newcastle; and Robin Buckle, Ph.D., head of the Regenerative Medicine and the Neurosciences and Mental Health Board for the Medical Research Council (MRC)—offered insight into embryo legislation in the United Kingdom. Patel stated that, as in the United States, embryo policy in the United Kingdom began with Louise Brown, the first child born as a result of IVF. Patel felt that anxieties over "test tube babies" led to a voluntary licensing authority in the United Kingdom.

As a result of the Brown controversy, a committee of inquiry was formed and chaired by Baroness Mary Warnock, a philosopher. In 1984, the committee released what became known as the Warnock Report, which made recommendations for embryo research legislation and regulation. The report concluded that embryo research and IVF should be allowed, with appropriate safeguards. The committee was also the first group to recommend limiting the development of an embryo to 14 days, when the primitive streak appears, marking the start of neural development. In addition, the committee recommended the establishment of a regulatory authority to oversee and grant licenses for research and IVF treatments.

Lawford Davies acknowledged that the public was not entirely in favor of these recommendations. In 1985, the Unborn Children (Protection) Bill, introduced by Member of Parliament John Enoch Powell, was put forward to outlaw any research involving embryos. The bill would have also put significant restrictions on the use of IVF. Fortunately for scientists, the bill was defeated, although only narrowly and essentially on a technicality. Lawford Davies emphasized that the United Kingdom very nearly banned embryonic research, which was a wake-up call to the research community.

> *"At the end of the day, if the research does not require [the use of] embryos, human embryos, then the regulatory authority will not allow that research."*
>
> *– Lord Naren Patel*

After several years of voluntary guidelines, the legislation that finally regulated embryo research in the United Kingdom was the Human Fertilisation and Embryology Act of 1990 (HFE Act).[16] This act permitted embryo research and the creation of embryos for research purposes; it also established a regulatory agency, the Human Fertilisation and Embryology Authority (HFEA), to monitor embryonic research and use, as recommended by the Warnock Report. Patel remarked that the legislation at this time focused on IVF and the regulation of embryo research for fertilization purposes. The act also required the monitoring of use and storage of embryos.

HFEA's main duty is to grant licenses that permit embryo creation, both for IVF and research purposes. It is a criminal offense to create embryos without such a license. Patel stated that licenses are given only for research that is "necessary and desirable." This includes research involving infertility treatments, congenital diseases, miscarriages, contraception, or detection of gene chromosome abnormalities (see box: Research Purposes).

[16] See The Human Fertilisation and Embryology Act of 1990 at http://www.hfea.gov.uk/134.html.

Based on recommendations from the Warnock Report, the HFEA also requires that no embryos be created and maintained past 14 days of development. The authors of the Warnock Report believed it would be inappropriate to do research after that point because it marks the start of neural development.

Extensive discussions on the status of the human embryo by a House of Lords committee, which included Patel, eventually led to the decision to permit embryo creation. The committee determined that the human embryo has a special status, but one that is different from a living child or adult. Human embryos are entitled to a measure of respect, but such respect is not absolute and must be weighed against the benefits arising from the proposed research. Patel emphasized, "At the end of the day, if the research does not require [the use of] embryos, human embryos, then the regulatory authority will not allow that research. There will be no license granted if that research can be done any other way."

Research Purposes Permitted Under the Human Fertilisation and Embryology Act of 1990

A licence under this paragraph cannot authorize any activity unless it appears to the Authority to be necessary or desirable for the purpose of —

a) promoting advances in the treatment of infertility,
b) increasing knowledge about the causes of congenital disease,
c) increasing knowledge about causes of miscarriage,
d) developing more effective techniques of conception, or
e) developing methods for detecting the presence of gene or chromosome abnormalities in embryo before implantation,

or for such other purposes as may be specified in regulations.

– HFE Act of 1990, schedule 2, paragraph 3(2)

Patel noted that it is not easy to obtain a license. At the time of his presentation, the HFEA had granted just 124 licenses since its inception in 1991. In 2008 and 2009, only 34 licenses were granted. Approximately half of the licenses went to researchers creating new hESC lines; the rest were granted for the study of embryo development or specific diseases, Patel said.

In 2001, the HFE Act was amended to account for scientific developments that included the creation of the first hESC line, according to Buckle. The amendment prohibited human reproductive cloning, but allowed SCNT in certain cases, provided that the HFEA issued a license. Patel noted that SCNT was permitted because of its potential to create specialized or individualized hESC treatments.

Buckle stated that the 2001 amendment acknowledged that hESC lines derived from an embryo were not within HFEA's regulatory domain and that there was a need to oversee hESC research. Consequently, the United Kingdom established The Steering Committee for the UK Stem Cell Bank and the Use of Stem Cell Lines, chaired by Patel and composed of scientists, ethicists, and

laypersons. The committee was charged with drawing up a Code of Practice to provide guidelines for those working with hESC lines in the United Kingdom. The amendment also established the UK Stem Cell Bank and required that all hESC lines derived in the United Kingdom be put in the bank. The latter requirement was a condition for receiving an HFEA license.

One of the main functions of the UK Stem Cell Bank is to maintain and store ethically sourced hESC lines under high levels of quality control, according to Buckle. In 2009, 70 hESC lines were being stored in the bank, 28 of which were from overseas. The bank also makes these lines accessible to the research community. At the time of the talk, 16 quality-controlled lines were being distributed to researchers across the globe. Buckle stated, "I think it's important, obviously, that the number of cell lines out there doesn't proliferate out of control with no purpose, because the reality is that actually probably only 20 or 30 lines are typically used by 90 percent of the researchers in the world at the moment."

2001 HFE Act Amendment

(1) The Authority may issue a licence for research under paragraph 3 of Schedule 2 of the Act for any of the purposes specified in the following paragraph:

(2) A licence may be issued for the purposes of —

a) increasing knowledge about the development of embryos;
b) increasing knowledge about serious disease; or
c) enabling any such knowledge to be applied in developing treatments for serious disease.

– HFE Act Amendment, 2001

Buckle commented that researchers inside and outside of the United Kingdom are permitted to obtain hESC lines from the bank at no cost. An HFEA license is not required. However, he emphasized, there is a robust review process both to access the lines from the bank and to use hESC lines from other sources for research within the United Kingdom. Applications for in-country use of hESC lines, importing and exporting hESC lines, and depositing and accessing stem cell lines in the bank are reviewed by the committee four times a year. Researchers must write a proposal that includes where the research will be done, which cell line(s) will be used, and the aims of the research. The steering committee does not review the research proposal itself, but ascertains whether the research plans and environment are in accordance with the HFE Act. If the proposed hESC lines are to be imported, the committee must ensure the lines were derived with appropriate informed consent and meets other conditions set by the United Kingdom. The committee does not review the ethics of the research, but requires that all ethical approvals, including relevant licenses for animal use, are submitted with the application.

Essential licenses, consents, and approvals are also needed to deposit hESC lines into the bank, noted Buckle. To make a deposit, the derivation of the stem cell line must be done in accordance with the UK Code of Practice; if the cell lines are from overseas, they must have been derived with equivalent standards. Information related to donor consent must be included with the cell line, and a description of any restrictions on future use of the lines is

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>
> *– Robin Buckle*

required. Buckle added that the steering committee must also determine if the cells are bona fide cells for research use. Buckle noted that any intellectual property arrangements must also be worked out prior to depositing the cells to avoid conflicts in distributing the cell lines.

Buckle remarked that at the time of the presentation that the UK Code of Practice for the Use of Human Stem Cell Lines was under revision. A number of factors contributed to the need for an update. One was that researchers perceive the committee's review procedures to be overly bureaucratic. Another consideration was that changes in the research landscape—for example, the discovery of induced pluripotent stem cells—must be accounted for. Finally, there was a need to accommodate the increasing push both to commercialize hESC lines and to use their derivatives in clinical settings.

Buckle noted that the United Kingdom is working on creating six good manufacturing practices (GMP) grade facilities for the production of clinical-grade hESC lines. This would provide quality assurance for eventual transplantation in humans. Buckle acknowledged that there are currently no existing clinical-grade lines that have been derived free of animal products (such as serum, cells, or proteins), but the hope is to have clinical trials with such lines within the next five years.

Embryonic research was again addressed during the scheduled 2008 review of the HFE Act. Patel explained that under the revised act, the United Kingdom permits the generation of hybrid embryos in exceptional circumstances and under strict regulations. Hybrid embryos could be created through SCNT using animal eggs and human DNA (see Figure 1: Pathways to Pluripotent Cells, SCNT Pathway). Hybrid embryos offer the potential to study disease mechanisms where no other opportunities to do so currently exist, as is the case for mitochondrial diseases. Patel added that the use of animal eggs would be useful because of the shortage of available human eggs.

The HFE Act of 2008 expanded the definitions of embryo, gamete, and hybrid embryos. But Patel also noted that it still remained illegal to place embryos in a woman for any reason other than those permitted under the HFE Act, namely IVF to treat infertility. Embryos could only be generated and used for research that would increase knowledge or help develop treatments relating to infertility, serious disease, or serious medical conditions. No such embryos could be kept for more than 14 days, and all research would require an HFEA license.

Patel and Buckle also briefly discussed regulations of iPS cells and adult stem cells. iPS cells do not fall under the purview of HFEA or the steering committee. Buckle acknowledged that even though the process of deriving iPS cells did not involve the use of human embryos, there

remained a number of ethical issues associated with these cells, such as the informed consent process related to the source of the donor tissue and cells derived from it. Some guidance will be published as part of the revision of the UK Code of Practice.

Buckle remarked that ethics and standards governing the use of adult stem cells have been in place for a long time. He cited the example of bone marrow transplants, and emphasized that adult stem cells do not carry the same ethical weight as hESCs. Buckle also noted that the Medical Research Council (MRC), the U.K. funding agency for biomedical research, funds more adult stem cell research than hESC research. He added that the MRC is currently funding a number of clinical trials with adult stem cells, but none as yet with hESCs. Patel also acknowledged the need to promote all types of stem cell research, stating, "[The U.K.] promote[s] active research in all types of stem cells ... because at this stage we cannot be sure which of the ones will deliver the treatments, and it is likely that all of them will deliver treatments but of a different nature and of different diseases."

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– Lord Naren Patel

Patel concluded his talk by emphasizing that the most important part of the regulatory system is the constant dialogue with the public, including both laypersons and scientists. The United Kingdom has educated the public about the developments, challenges, and uncertainties in stem cell research. According to Patel, this has led to strong support for the legislation. In 2008, a public opinion survey—conducted over 18 months—found 70 percent of the population to be fairly comfortable with the legislation. Patel attributed this to the fact that the public understands what researchers are doing, the United Kingdom has the regulatory authority to curb abuse, and scientists know that there are severe penalties for breaking the rules. In addition, as we saw in 2008, the United Kingdom's policies are reviewed on a regular basis with input from researchers and the general public.

Patel stated,

> "Our legislation is sometimes said [to be] liberal, but it isn't. It is highly regulated. Not only is the research regulated on human embryos, the whole area of *in vitro* fertilization is regulated. And research can only be carried out if the Authority gives a license, and it has to be satisfied that the research cannot be carried out by any other means and the research can't be carried out without using human embryos ... [or] embryos not required for infertility treatment. If all of this cannot be done, only then it might grant a license to do research on human embryos or create embryos for research."

EUROPEAN UNION STEM CELL POLICY

During his presentation, Lawford Davies also reviewed hESC policies in several European countries, as well as policies related to the European Union (EU) and a few key places around the world. From these regulations, Lawford Davies perceived four categories of hESC policy: restrictive regulation, permissive regulation, self-regulation, and no regulation.

Several countries, including Germany and Italy, have what Lawford Davies classifies as restrictive or prohibitive regulations, but still allow hESC research. Germany's 1990 Embryo Protection Act outlawed embryo destruction, making it a criminal offense. Thus, hESCs cannot be created in Germany because the process destroys the embryo. However, the country's Stem Cell Act of 2002 allowed researchers in Germany to import and utilize hESC lines created in other countries before 2002. This law was amended in 2008 to set a new cutoff date of May 2007.[17]

> *"If you are going to regulate in this area, then you need to do it in a way that allows progress to happen and allows change to be taken into account."*
>
> *– James Lawford Davies*

Another country Lawford Davies classifies as restrictive is Italy. Italian law regulates assisted reproduction technologies by, for instance, limiting the number of IVF embryos that may be created at any one time (only three). The law also prohibits storing embryos, requiring all embryos to be implanted into a woman.[18] Similar to Germany, no hESCs can be created in Italy, but the law does not prevent researchers from studying them.

Countries Lawford Davies described as permissive usually regulate research through licenses. He believed that the United Kingdom formed this model with the establishment of HFEA and regulations on embryonic research. Both Australia and Canada followed the United Kingdom's model when developing their own licensing systems.

Some countries with permissive policies, such as China, do not regulate, but utilize a system of guidance or self-regulation with regard to hESC policy. Lawford Davies noted that China does a great deal of hESC research, both good and bad. During a recent trip to China, he observed that several Chinese researchers were advocating for a regulatory system to improve the overall quality and reputation of the country's hESC research.

Lawford Davies considers U.S. policy to be self-regulating, since no regulations cover the creation or use of hESCs, and no research is actually banned; there are only limits on federal funding. He acknowledged that limiting funding is a form of restriction, but he believes the United States has continuously remained out of the hESC debate on the world stage. According to the President's Council on Bioethics 2004 report on the subject, "the federal government

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[17] H. Gottweis, B. Salter and C. Waldby, *The Global Politics of Human Embryonic Stem Cell Science: Regenerative Medicine in Transition* (Palgrave Macmillan, 2009).

[18] B. Fineschi, M. Neri and E. Turillazzi, "The new Italian law on assisted reproduction technology (Law 40/2004)," *J Med Ethics* 31 (2005): 536–539, http://jme.bmj.com/content/31/9/536.abstract.

has pursued a policy whereby it does not explicitly prohibit embryo research but also does not officially condone it, encourage it, or support it with public funds."[19] However, policies at the state level are both restrictive and permissive, with states like California supporting and funding research while states like South Dakota prohibit any research on embryos or with hESCs.

Lawford Davies commented that the four categories span the extremes of regulation: on one end, all research is prohibited while at the other end, research is completely unregulated. Yet similar factors are considered when regulations are devised: the welfare of the child born through assisted conception, safety of assisted conception or hESC clinical use, and the status of the human embryo, the latter being the most controversial and debated. Countries that regulate or legislate embryonic research accept that there is a special status attached to the embryo, Lawford Davies believes. "There is a consensus that there is a special status. But there is no consensus, nor will there ever be, as to how that status should be protected or what the status should be, and that is where the real problem arises," he stated.

Lawford Davies also acknowledged that legislation has always seemed to involve a compromise. Even in the United Kingdom, which has a well established policy, there are groups that still oppose embryonic research. Beginning in 2003, Josephine Quintavalle, on behalf of the ProLife Alliance, brought a series of lawsuits against the U.K. government regarding its right to govern embryonic research. The court ultimately decided that HFEA did have the authority to grant licenses. HFEA has been subject to other ethical and legal scrutiny since its creation, but still remains intact.

The EU also has regulations on cells, tissues, and advanced therapies that impact hESC research in member states. Lawford Davies remarked that the EU only takes action where it has legal authority to do so and usually only in relation to matters of pan-European significance. Examples include public health issues, cross-border health threats, and medical tourism (when patients cross borders to obtain health care). He stated that the direct effect of this was that certain EU laws are binding regardless of whether or not a member state implements them properly.

Lawford Davies expressed the view that the EU regulates tissues and cells in a limited but important manner. In 2004, the EU implemented Directive 2004/23/EC to set standards of quality and safety for the donation, procurement, testing, processing, preservation, storage, and distribution of human tissues and cells. The regulation specifically applied to cells for use in humans, but not for *in vitro* research. Lawford Davies stated that while hESCs fall under this regulation, autologous treatments (tissues used in the same patient who donated them) do not. But the EU directive includes other regulations—including patient consent, package labeling, and several other technical directives—to maintain basic quality and safety. He noted that the EU regulations ensure that anywhere in the EU there is a minimum standard in place. He also stressed that the EU does not require member states to permit a specific type of research or therapy, such as hESC research; however, if states want to do this type of research, the regulations mandate that the states fulfill the minimum safety requirements.

Lawford Davies also discussed the European Commission's (EC) regulation of advanced therapies and medicinal products (ATMP).[20] He stated that this includes therapies with cells

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[19] See PCB, "Monitoring Stem Cell Research," Washington, D.C. (2004), http://www.bioethics.gov.

[20] See the preamble to EU Directive 2001/83/EC; http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2007_1394/reg_2007_1394_en.pdf.

and tissues. While well-established regulations of medical devices and drugs existed prior to ATMP, there were gray areas that included cell and tissue engineering and gene therapies that were not regulated previously. Lawford Davies remarked that the EC wanted to facilitate the introduction of these types of therapies with standards that were relevant. He again emphasized the point that the EU cannot force member states to develop these types of therapies.

Lawford Davies explained that the ATMP regulation established a single authorization for ATMPs in the EU. It also created technical requirements for ATMPs as well as a committee to provide scientific advice. Lawford Davies described the regulation as a way to foster competitiveness and facilitate access while maintaining a high level of health protection. He cautioned that a consequence of the regulation was that some responsibilities were passed on to other regulators, putting them outside of the EC's direct control.

Advanced Therapies and Medicinal Products

The regulation of advanced therapy medicinal products at Community level should not interfere with decisions made by Member States on whether to allow the use of any specific type of human cells, such as embryonic stem cells, or animal cells. It should also not affect the application of national legislation prohibiting or restricting the sale, supply or use of medicinal products containing, consisting of or derived from these cells.

– Regulation (EC) No. 1394/2007, Preamble Section 7

Lawford Davies closed by offering his insight into how best to regulate hESCs and other therapies. He believes that "If you are going to regulate in this area, then you need to do it in a way that allows progress to happen and allows change to be taken into account." He also felt that the regulation has to be proportionate to the sensitivity of the project or research could be unnecessarily crippled by delays. Lawford Davies also noted that the regulator must be impartial and objective and cannot be subject to bias or intimidation. He recommended that the regulators have expertise and efficiency in order to make educated legislative decisions.

CONCLUSIONS

From the policy presentations and discussions at the Texas-UK Collaboration workshop, attendees were able to learn more about hESC research and policies in Texas, the United States, and the United Kingdom. Though the policies vary throughout these regions, some common themes became apparent over the course of the program. While the United Kingdom did most of the work to create a policy in the early 1990s, the U.S. government did not stop debating the subject until 2009, and the state of Texas has yet to implement stem cell legislation. Yet all three governments have been challenged to put policies into place that respect the feelings and beliefs of the public, scientists, and laypersons alike—and that find the most appropriate compromise to satisfy their constituencies. Governments have also opened a dialogue with the public, and scientists are often called upon to directly explain how their research could lead to new therapies for debilitating diseases.

William Brinkley, Distinguished Service Professor in the Department of Molecular and Cellular Biology and dean of the Graduate School of Biological Sciences at Baylor College of Medicine, noted in his opening remarks before the panel discussion that the complex regulatory schemes and laws in the United States are "a maze of conflicting, controversial, and confusing policies that continue to evolve within the federal government and also at the state government levels." Lane agreed with this sentiment in his talk, stating, "It is usually better to have a thoughtful policy on the books—a real federal law—than to take chances, as political winds can change very rapidly here in the U.S." One of the major issues facing the United States in the past decade was deciding exactly which policy to put into place.

Patel attributed the success of U.K. policies to a constant dialogue with the public before and after the policies were put in place. These discussions helped all parties remember why there was a need for research and why it was essential to regulate it. It also allowed for swift changes to policies in response to scientific advancements.

Many of the speakers also noted that a permissive hESC policy requires the participation of scientists in the policymaking process. In the United States, Lane believes that scientists are needed to effectively communicate the state of hESC and embryonic research, but stresses the need to respect individual beliefs and views to allow for progress on the policy front. In Texas, Arnold and the other members of TAMR have been able to reach out to policymakers and the public to prevent the passage of prohibitive legislation. But in order to get permissive legislation, she needs more scientists to speak about their research and the positive impact it has had on the state. Brinkley remarked that one of the best ways to promote hESC research would be to show research successes to the public. "Communication of accurate information in a dispassionate way with the general public is always a good idea," noted Lane, as well. However, Lane cautioned that there would also be failures in clinical trials involving hESCs, and policymakers must be prepared to respond to any public outcry.

It is important to keep in mind that not everyone is going to agree on the best way to regulate ESC research. Lawford Davies stated that there must be a compromise between differing viewpoints on the issue. He stated that this compromise was reached in the United Kingdom by allowing hESC research to go forward, but making it highly regulated. The United States has attempted to compromise by remaining neutral on the legality of hESC research and allowing states to make their own regulations. In Texas, Arnold noted, none of the proposed bills have been compromises; they have come from proponents on each side of the issue. By talking with and educating the public about the need for research and regulation, a compromise that satisfies all parties could be reached, especially here in Texas.

With this in mind, the Baker Institute, in collaboration with the British Consulate-Houston and the Texas-UK Collaborative at Rice University, hosted this policy discussion at the Texas-UK Collaboration workshop to allow for an open discussion about hESC research and policy. The event included state policymakers and staff to give them an opportunity to learn more about current research and potential therapies and to interact with scientists and policy scholars. It also offered the general public a forum to ask questions and express their concerns. These discussions with scientists, policymakers, ethicists, and policy scholars, as well as with community and business leaders, help improve the overall dialogue. The Baker Institute and its partners are committed to helping facilitate these conversations to better develop and guide policies on stem cell science and societal applications now and in the future.

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The workshop was part of the Baker Institute International Stem Cell Policy Program, which seeks to bring together scientists, ethicists, policymakers, media experts, and community and business leaders to engage the public on issues related to stem cell research. The program is part of the Science and Technology Policy Program, led by senior fellow Neal Lane, Ph.D., and fellow Kirstin Matthews, Ph.D., and is supported by the State of Qatar Endowment for International Stem Cell Policy.

Appendix A — Workshop Agenda

Monday, September 14, 2009

2:00 pm — Welcoming Remarks
May Akrawi, Ph.D.
Consul, Science and Innovation, British Consulate-General, Houston

Panel: Policy, Regulation, Ethical, and Collaborative Issues

Moderator: **William Brinkley, Ph.D.**
Distinguished Service Professor, Department of Molecular and Cellular Biology; and
Dean, Graduate School of Biomedical Sciences, Baylor College of Medicine

2:15 pm — Texas Politics and Policy
Ellen Arnold
Principal, Arnold Public Affairs

Governance of Stem Cell Regulation in the U.K.
Rob Buckle, Ph.D.
Head, Neurosciences and Mental Health Board, Medical Research Council

Question & Answer Session

3:30 pm — Break

3:45 pm — International Stem Cell Policies
James Lawford Davies, L.L.M.
Partner at Lawford Davies Denoon and Lecturer in Law and Medicine, University of Newcastle

Medical Tourism and Stem Cell Research
Chris Mason, M.D., Ph.D.
Professor of Regenerative Medicine Bioprocessing, University College London

Question & Answer Session

5:00 pm — Reception

6:00 pm — Dinner

7:00 pm — Introduction and Welcoming Remarks
May Akrawi, Ph.D.
Consul, Science and Innovation, British Consulate-General, Houston

Malcolm Gillis, Ph.D.
Ervin K. Zingler Professor of Economics; Executive Director, TX-UK Collaborative; and
Former President, Rice University

Paul Lynch
H.M. Consul-General, British Consulate-General, Houston

Keynote Presentations

Stem Cell Policy in the Obama Age
Neal F. Lane, Ph.D.
Senior Fellow, James A. Baker III Institute for Public Policy; and
Malcolm Gillis University Professor, Rice University

Human Reproduction and Embryonic Research: A U.K. Perspective on Legislation and Regulation
Lord Naren Patel, M.D., D.Sc.
Chairman of the UK National Stem Cell Network Steering Committee

Appendix B — Participant Biographies

May Akrawi, Ph.D., is the British consul for science and innovation of the British Consulate-General, Houston. Akrawi has a keen interest in technology transfer and development, and before her appointment to the British Consulate she worked with In Vitro Technologies to head up their first European office in London. In that position, she worked in a scientific and business development and marketing role to establish a network of pharmaceutical and biotechnology clients for the company, as well as initiate collaborations on new R&D projects. Akrawi also worked with the Wellcome Trust promoting "The Public Understanding of Science" and conducting genomics workshops for visitors and students. Additionally, she was a scientific research analyst at a U.S. law firm, specializing in scientific issues relating to product liability litigation for blue-chip clients and establishing networks of scientific and medical consultants worldwide. Akrawi has also held the position of program manager for pharmaceutical discovery at a business information company. She received her B.Sc. in biochemistry and Ph.D. in molecular biology, both from University College London, followed by a postdoctoral fellowship at the Institute for Molecular Biology in Barcelona investigating genomic microsatellite sequences.

Ellen Arnold is a principal with Arnold Public Affairs, a public affairs consulting firm specializing in advocacy in Texas, the southeast United States, and Washington, D.C. Arnold represents nonprofit entities before the Texas Legislature, assisting clients with their goals to pass legislation, obtain state appropriations, and influence or impact potential legislation affecting their organizations. She works to improve circumstances for children, for elderly Texans, and for persons with disabilities, chronic illnesses, and diseases.

In addition to nonprofits such as National Multiple Sclerosis Society, Boys and Girls Clubs, Goodwill Industries, and Texas PTA, Arnold has represented Texans for Advancement of Medical Research (TAMR) since its inception. TAMR has led efforts since 2003 to educate policymakers and citizens about all forms of regenerative medical research in Texas, and has successfully prevented bans to human embryonic stem cell research and bans to funding for such research.

In addition to representing single entities, Arnold has managed several projects on behalf of coalitions formed to achieve a common goal. In that role, she has helped develop and implement strategies that included grassroots organization, grasstrops identification and use, radio and print media—both earned and paid utilization, and legislative advocacy.

William R. Brinkley, Ph.D., is senior vice president for graduate sciences and dean of the Graduate School of Biomedical Sciences at Baylor College of Medicine (BCM). He is also the Distinguished Service Professor in the Department of Molecular and Cellular Biology and serves as co-director of the W.M. Keck Center for Computational and Structural Biology. Brinkley began his career at BCM in 1976 as the director of the Division of Cell Structure and Function in the Department of Cell Biology. In 1985, he became chair of the Department of Cell Biology and director of the Gregory Fleming James Cystic Fibrosis Center at the University of Alabama at Birmingham. He returned to BCM in his present position in 1991. As dean, Brinkley is interested in the training of future scientists, and he is active in the curriculum development and analysis of career opportunities. Brinkley received his Ph.D. from Iowa State University, and completed his post-doctoral fellowship at the University of Texas M. D. Anderson Cancer Center.

Rob Buckle, Ph.D., is the head of the Neurosciences and Mental Health Board of the Medical Research Council (MRC) Head Office in London. He is also the lead on Stem Cells and Regenerative Medicine. Buckle's responsibilities span research strategy and funding, as well as policy and public communications. In addition to the MRC's role in supporting stem cell research, it also provides the secretariat to the independent steering committee for the UK Stem Cell Bank and the Use of Stem Cell Lines, which has an important role in the oversight of ethical embryonic stem cell research in the United Kingdom. In addition, the MRC chairs two

strategic coordination committees—the UK Stem Cell Funders Forum, which encompasses all major funders of stem cell research in the United Kingdom, and the International Stem Cell Forum, which currently has 22 member organizations from 20 different countries.

Malcolm Gillis, Ph.D., is the Ervin K. Zingler Professor of Economics at Rice University and the executive director of the TX-UK Collaborative. After distinguished careers at Harvard and Duke Universities, Gillis served as president of Rice for more than a decade. He has dedicated more than 25 years of his professional career to teaching and applying economic analysis to important issues of public policy spanning nearly 20 countries. He has published more than 70 journal articles and authored several leading economic textbooks. He was co-founder and chair of the board of trustees of the Center for World Environment and Sustainable Development and the Duke Center for Tropical Conservation. From 2005 to 2008, Gillis was chair of BIOHOUSTON, an organization promoting Houston as a major center for the biotechnology industry. In 2008, Texas was ranked in the top five locations in the world for the development of the biotech industry. In March 2008, he was appointed by the governor of Texas to serve as vice chairman on the Cancer Prevention and Research Institute of Texas Oversight Committee, a $3 billion effort over the next decade. Gillis holds several degrees, including a B.A. and an M.A. from the University of Florida and a Ph.D. from the University of Illinois.

Neal F. Lane, Ph.D., is the senior fellow in science and technology policy at the Baker Institute. He is also the Malcolm Gillis University Professor at Rice University and professor in the Department of Physics and Astronomy. Previously, Lane served in the federal government as assistant to the president for science and technology and director of the White House Office of Science and Technology Policy (OSTP) from August 1998 to January 2001, and he served as director of the National Science Foundation (NSF) and member (ex officio) of the National Science Board from October 1993 to August 1998. Before his post with NSF, Lane was provost and professor of physics at Rice, a position he had held since 1986. He first came to the university in 1966, when he joined the Department of Physics as an assistant professor. In 1972, he became professor of physics and space physics and astronomy. He left Rice from mid-1984 to 1986 to serve as chancellor of the University of Colorado at Colorado Springs. Additionally, from 1979 to 1980, while on leave from Rice, he worked at the NSF as director of the Division of Physics. He is a fellow of the American Academy of Arts and Sciences and other honorary and professional associations. In 2009, he was awarded the National Academy of Sciences Pubic Welfare Medal, the American Institute of Physics K.T. Compton Medal, and the Association of Rice Alumni Gold Medal. Lane received his Ph.D., M.S., and B.S. in physics from the University of Oklahoma.

James Lawford Davies, L.L.M., is a partner at Lawford Davies Denoon and a lecturer in law and medicine at the University of Newcastle. He specializes in the law relating to reproductive and genetic technologies, human tissue and cells, and related research. Lawford Davies advises a large number of clinics and research centers licensed by the Human Fertilisation and Embryology Authority (HFEA) and has been involved in most of the leading cases relating to assisted reproduction and related research. He has advised widely on the regulatory and commercial issues relating to embryo and embryonic stem cell research, including cell nuclear replacement, human-animal hybrids research, import and export, and the implications of European Union law.

Paul Lynch serves as the British Consul-General in Houston, Texas. He joined the Diplomatic Service in 1999 after several years of policy jobs in the Home Office and Cabinet Office in London. Lynch served in Tokyo from 1996 to 2000 as first secretary for science and technology and was on full-time language training at the British Embassy Japanese Language School from 2000 to 2001. In late 2001 he worked in the Commercial Section of the British Embassy in Tokyo, before taking up the position of commercial consul in Osaka from 2002 to 2005. Lynch took over as Consul-General Osaka in 2005 until his departure in April 2007. Before joining the Diplomatic Service, Lynch worked in the Home Office on prisoners' rights,

the police and race relations, the government response to the Royal Commission on Criminal Justice, and the Criminal Justice Act 2004, with a particular focus on the provisions relating to the accused's right to silence. From 1994 to 1996, Lynch was private secretary to the parliamentary secretary in the Cabinet Office, with a portfolio including public services and science policy. Lynch was educated at The Hatfield Polytechnic and the London School of Economics.

Chris Mason, M.B.B.S., Ph.D., is a professor of regenerative medicine bioprocessing at University College London (UCL). He is internationally recognized as a leader in stem cell and regenerative medicine translation and commercialization. His background in basic science, clinical medicine, bioprocessing, and business provides unique insight and understanding of the challenges facing the regen sector as it grows into a competitive and sustainable global health care industry. Mason was a fellow of the Royal College of Surgeons, both of England and in Ireland. He currently holds a personal chair in Regenerative Medicine Bioprocessing, leads the Regenerative Medicine Bioprocess Group in the Advanced Centre for Biochemical Engineering at UCL, and is on the steering committee for the UCL Centre for Stem Cells and Regenerative Medicine. Other accomplishments include being senior editor of the journal Regenerative Medicine, co-founder and director of the London Regenerative Medicine Network, and founding steering committee member of the UK National Stem Cell Network. Mason is also on a number of national and international committees, working groups and initiatives related to the academic, clinical, and commercial advancement of cell therapies and tissue engineering. He has a broad range of expertise in commercial consultancy and is presently on scientific advisory boards of a number of regen companies based in North America. Mason also led the U.K. government-sponsored "Advanced Cells and Tissue Therapy Global Watch Mission" to the United States in 2006. Mason holds a clinical sciences degree from Imperial College London, a medical degree from the United Medical and Dental Schools of Guy's and St. Thomas' Hospitals (now King's College London) and a Ph.D. from UCL.

Lord Naren Patel of Dunkeld, M.D., D.Sc., is chairman of the UK National Stem Cell Network Steering Committee of the Stem Cell Bank and the Use of Stem Cell Lines. He is also chairman of the National Patient Safety Agency of England and Wales and chancellor of the University of Dundee. His academic and clinical interests were in the field of high-risk obstetrics. He has published on preterm labor, fetal growth retardation, and obstetric epidemiology. He is a fellow of the Academy of Medical Sciences and the Royal Society of Edinburgh, honorary fellow of several Royal Colleges in the United Kingdom, Ireland and overseas, and has received honorary doctorates in the United Kingdom and overseas. Previously, Lord Patel was also a member of the board of the Armed Forces Pay Review. He currently sits in the House of Lords having received a knighthood in 1997 and elevation to the peerage in 1999. There, he is a member of the Science and Technology Committee. He is currently chairman of the UK Stem Cell Oversight Committee and the UK Stem Cell Network. Lord Patel studied medicine at Queen's College, University of St. Andrews and has worked in the medical field for more than 30 years.

Appendix C — Organizing Partners

International Stem Cell Policy Program

Human stem cell research—encompassing embryonic, adult, and induced pluripotent stem cell research—is viewed as a critical area of study by much of the science and medical community. While a significant amount of research is needed before embryonic or induced pluripotent stem cells can be used in therapy, these cells have the potential to cure or treat debilitating injuries and diseases such as spinal cord injury, Parkinson's disease, and diabetes. Understanding stem cells can impact developmental biology, cancer biology, regenerative medicine, and other fields of biomedical research.

The mission of the Baker Institute International Stem Cell Policy Program is to bring together scientists, ethicists, policymakers, media experts, and community and business leaders to find new ways to engage the general public in a dialogue on international stem cell policies and the ethical use of stem cells for research. The program includes an international conference series titled "Stem Cells: Saving Lives or Crossing Lines." The program also sponsors local events; workshops that bring together scholars and scientists from the international community, and conference reports on the workshops; and major public policy research. The program is part of the Baker Institute Science and Technology Policy Program, led by senior fellow Neal Lane and fellow Kirstin Matthews.

Support for this program has been generously provided 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.

Science and Technology Policy Program

The mission of the Science and Technology Policy Program is to provide a space for policymakers and scientists to engage in substantive dialogue on pressing scientific issues facing the nation and the world. Through this program, the Baker Institute sponsors a series of workshops, lectures, research projects, and conferences designed to address a broad range of policy issues that affect scientists and their research, as well as the application of science for the public good. These issues include space, health and medicine, energy and the environment, national and domestic security, science education, and the federal government's support of science and technology. The program is run by Neal Lane, senior fellow in science and technology policy, and Kirstin Matthews, fellow in science and technology policy and program manager. Details and descriptions of the Science and Technology Policy Program's projects can be found at http://science.bakerinstitute.org.

Science & Innovation Team, British Consulate-General Houston

The Science & Innovation Team in Houston is part of the British Foreign and Commonwealth Office's network of global science attachés. They work to facilitate collaborations between science and innovation providers and users in the United Kingdom and the United States in industry, academia, and research institutions. In addition, they keep U.K. policymakers fully informed about research and policy developments in the United States, as well as promote the United Kingdom as a world-class leader in science and innovation. The S&I Network also reports on policy developments, strategy and emerging priorities, and facilitates international negotiations and collaborations in areas such as climate change, stem cell research, nanotechnology, and low-carbon technologies. For more information, please contact S&I Consul May Akrawi at may.akrawi@fco.gov.uk or 713.659.6270 (x2134).

TX–UK Collaborative

The TX–UK Collaborative fosters cross–disciplinary collaborations among researchers in world–class institutions in Texas and the United Kingdom, building new areas of research and building capacity. The cross–disciplinary research at the interface of the nano, bio, and info sciences creates new ideas, techniques, products, and opportunities. The collaborative supports thematic workshops and research planning meetings bringing researchers from diverse backgrounds together focusing on specific problems, as well as exchange visits to facilitate research programs. It has contributed significantly to the establishment of research alliances and centers and to the development of technologies. For additional information regarding the collaborative, contact Denis Headon, director, at headon@rice.edu, 713.348.4118, or visit our Web site at www.texasukcollaborative.com.