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FEDERALISM BY NECESSITY: STATE AND PRIVATE SUPPORT FOR HUMAN EMBRYONIC STEM CELL RESEARCH

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Introduction

Supporting basic biomedical research has traditionally been a primary function of the federal government. The federal National Institutes of Health have long been the major funder of biomedical research, spending over $25 billion annually to support researchers in a wide variety of fields. State governments, by contrast, have historically spent little or no money on basic research and have little experience in managing cutting edge scientific research programs.

This traditional division of labor has been inverted in the case of human embryonic stem cell research (hESC). hESC has come to be among the most controversial of scientific research topics, producing widespread, visible, and often rancorous debate in Congress, state legislatures, the mainstream and alternative media, political campaigns, and a variety of other forums. Because of national conflicts over the virtues of this research, the federal government's role in financing hESC research has been limited both in scope and scale. Only certain embryonic stem cell "lines" are currently eligible for federal research support. Federal regulations also prohibit the direct or indirect use of federal funds to finance research using other stem cell lines, so that laboratory space or equipment initially purchased with federal funds cannot be used to support research on ineligible stem cell lines. Congressional attempts to either restrict this research further or to significantly expand the scope and scale of federal support have both been unsuccessful.

In response to this deadlock in Washington, stem cell advocates of different persuasions have turned to state political systems — governors, legislatures, and bureaucracies — to continue to pursue their agendas, with varying degrees of success. This pattern of "federalism by necessity" — seeking support at one level of government when desired policies have been blocked at another — is a long-standing feature of American domestic policy making frequently exploited by liberals and

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conservatives alike.[1] In some states, hESC has been prohibited or severely restricted; in others, however, state governments and private philanthropists have established a variety of funding mechanisms to support stem cell research in general and hESC in particular. These efforts have both increased the amount of money devoted to hESC research and established infrastructure — laboratory space, training programs, and the like — that is not subject to federal spending restrictions. States and private donors now spend significantly more money than the federal government to support hESC research, a situation that seems likely to persist even past the next presidential election in 2008.

This paper examines the current and likely future funding picture for hESC research. It outlines the current federal regulatory and funding situation, inventories state and private funding for stem cell research, and evaluates the factors likely to shape future stem cell funding.

Stem Cells — Embryonic and Others[2]

Stem cell research is a complex scientific and political undertaking in which some aspects are extremely controversial and others are not. In the most general sense, stem cells are undifferentiated "blank" cells that do not have a specific biological function, but which can, at least in theory, be turned into more specialized cells that perform desired functions. Developing therapies from these cells involves turning them into specialized types of cells that can replace those damaged or destroyed by disease that cannot be replaced by natural processes. If stem cells can be turned into the specialized cells that produce insulin, for example, they can be used to replace cells that have been damaged by diabetes.

Stem cell research uses a wide range of these types of cells and only some of them are controversial. Scientists use a wide variety of animal stem cells, both embryonic and others, to study disease processes and experiment with various techniques that may eventually have applications in the treatment of human disease — the techniques that were used to isolate human embryonic stem cells, for example, were first developed in animal models. Research using animal stem cells of different types is not controversial and has been routinely supported by the National Institutes of Health.

Research using human stem cells is more politically complex. So-called "adult" stem cells,[3] which are typically more specialized in that they can generally only be turned into a limited range of more specialized cells, were initially isolated in the 1950s and have come to be used as part of treatment regimes for some diseases, particularly those that require the replacement of the immune system. Hematopoietic stem cells, for example, which can be isolated from bone marrow, are regularly used to replenish the blood cells that are destroyed by treatments for leukemia and other forms of cancer. Research using these types of stem cells, which naturally occur in the body and can be

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1 James W. Fossett, "Managing Reproductive Pluralism: The Case for Decentralized Governance," *Hastings Center Report* (July/August 2007): 20-22.

2 This section is drawn largely from two publications of the International Society for Stem Cell Research, "Frequently Asked Questions" and "Stem Cell Primer," both online at http://www.isscr.org/public/.

3 The term "adult" is confusing, since these cells do not necessarily come from chronological adults. Some varieties of "adult" stem cells, in fact, can be isolated from the blood in the umbilical cords of newborn infants or the pulp under baby teeth. The use of the term "adult" comes from the fact that these stem cells are found in tissue that has already developed.

isolated without any adverse effects, is not particularly controversial and is regularly funded by NIH and other organizations that support biomedical research.

By contrast, research using human embryonic stem cells has become extremely controversial. These cells, which were isolated in the late 1990s, form in the development of a fertilized human embryo and are extracted in the first few days of the embryo's growth. These cells are, at least in theory, capable of being turned into all of the body's specialized cell types and thus are potentially usable to treat a broader range of diseases than more specialized or less flexible adult stem cells. The controversy surrounding research using these cells arises from the fact that the extraction of the stem cells destroys the embryo, which many advocates find unacceptable.

Federal Regulation and Funding

The funding pattern of "federalism by necessity" has emerged from the political gridlock around national human embryonic stem cell research policy. In spite of considerable attention to these issues over the course of the last fifteen years by two separate presidential commissions and several scientific advisory panels, as well as considerable Congressional discussion, there is little consensus about the appropriate scope and financing for this research.[4] Debate in Washington has generally not addressed the permissibility or legality of embryonic stem cell research, but has rather focused on the narrower question of what stem cell "lines" should be eligible to receive federal financial support through the National Institutes of Health and other federal agencies.[5] The Bush administration, together with some (though not all) religious and prolife groups, have argued consistently that human embryos have the same moral status as human life and research that destroys embryos should be restricted, if not entirely prohibited. Many (though not all) Democrats, together with disease advocacy groups and some prolife Republicans, have disputed this characterization of the moral status of the embryo and argued that hESC presents considerable potential in the treatment of a wide range of diseases. The use of federal funds to create embryos for research purposes or to destroy or harm embryos has been routinely prohibited in appropriations bills since the mid-1990s through the so-called Dickey amendment.[6] Subsequent debate, however, has relied on arguments that this prohibition does not extend to research using stem cell lines created using other funding sources.[7] The Clinton administration advocated an expansive view of this argument, which would have encouraged researchers to fund the creation of stem cell lines from

4 For a history of federal policy in this area, see The President's Council on Bioethics, *Monitoring Stem Cell Research*, Chapter 2, "Current Federal Law and Policy," http://www.bioethics.gov/reports/stemcell/chapter2.html.

5 See, e.g., Rich Weiss, "Bill Renews Fight on Stem Cells," *The Washington Post*, February 17, 2005, A6; Rick Weiss, "Approved Stem Cells'Potential Questioned," *The Washington Post*, October 29, 2004, A3; Ceci Connolly, "2 GOP Senators Defend Bush on Stem Cell Research," *The Washington Post*, August 13, 2004, A2; *The Stem Cell Debate*, CNN.com in Depth Special, http://www.cnn.com/SPECIALS/2001/stemcell/.

6 The original amendment can be found in Section 128 of P.L. 104-99; it affected NIH funding for FY1996 contained in P.L. 104-91. For subsequent fiscal years, the rider is found in Title V, General Provisions, of the Labor, HHS, and Education appropriations acts. See CRS Report for Congress, *Stem Cell Research,* n. 19, http://fpc.state.gov/documents/organization/51131.pdf.

7 See Judith A Johnson and Erin D. Williams, "CRS Report for Congress: Stem Cell Research," Updated August 10, 2005, http://fpc.state.gov/documents/organization/51131.pdf; George Q. Daley, "Missed Opportunities in Embryonic Stem-Cell Research," *The New England Journal of Medicine* 351 (August 12, 2004), 627-628, http://content.nejm.org/cgi/reprint/351/7/627.pdf.

other sources and then apply for federal funds to continue research on these "pre-existing" lines.[8] The Bush administration, by contrast, has limited federal funding support to the small number of lines existing before 2001. The Bush administration has given rhetorical support to procedures which attempt to create stem cell lines without destroying embryos, but NIH has to date been unwilling to fund research into the development of such techniques.[9]

The Bush administration has also adopted an unusually restrictive policy that prohibits the "direct or indirect" use of federal funds to support research on ineligible stem cell lines.[10] In order to avoid jeopardizing their other federal funds, many universities and other research institutes have found it prudent to build separate new labs and purchase completely new equipment to be used in hESC research from nonfederal sources in order to avoid charges that they are using, for example, lab equipment originally purchased with federal funds to indirectly support research on ineligible stem cell lines.[11]

Despite considerable effort, the federal policy-making process has not been successful in moving hESC policy in any particular substantive direction. By one count, more than 40 separate pieces of legislation have been introduced since 2001 in this general area, ranging from attempts to prohibit or even criminalize any kind of cloning research to efforts to expand the scope and scale of federal support for hESC research.[12] None of these initiatives have become law. Congress has twice passed, and President Bush has twice vetoed, legislation which would expand federal support to cell lines derived from embryos created, but not used, for *in vitro* fertilization. Current federal law continues to impose no restrictions on research funded by private or other nonfederal funds, but limits federal support to a small number of pre-existing lines.

As a result of these limits, federal support for hESC has been historically small. Table 1 displays past and estimated funding levels by the National Institutes of Health for hESC and other kinds of stem cell research for the last four fiscal years. Total NIH funding for all kinds of stem cell research has remained relatively flat over most of this period, at approximately $640 million annually. This amount is relatively small compared to NIH support in such areas as cancer, genetics, biotechnology, and cardiovascular research, and is roughly comparable to NIH spending on Alzheimer's disease, diagnostic radiology, and eye diseases.

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8 See the Clinton administration "National Institutes of Health Guidelines for Using Human Pluriptent Stem Cells," 65 Fed. Reg. 51,975 (August 25, 2000), reprinted in The President's Council on Bioethics, *Monitoring Stem Cell Research*, Appendix D, available at http://www.bioethics.gov/reports/stemcell/appendix_d.html.

9 Rick Weiss, "Future of Stem Cell Tests May Hang on Defining Embryo Harm" *The Washington Post*, July 29, 2007, A8.

10 Roger Noll, "The Politics and Economics of Implementing State-Sponsored Embryonic Stem-Cell Research" (Stanford Institute for Economic Policy Research Discussion Paper 04-28), June 2005, 20-21.

11 See, for example, Claudia Dreifus, "At Harvard's Stem Cell Center, the Barriers Run Deep and Wide," *The New York Times*, January 24, 2006.

12 Francis Fukuyama and Franco Furger, "Beyond Bioethics. A Proposal for Modernizing the Regulation of Human Biotechnologies." The Paul H. Nitze School of Advanced International Studies, Washington D.C., Chapter 5.

Table 1
Stem Cell Spending—National Institutes of Health

	Allocations, $ millions			
	FY2005	*FY2006*	*FY2007 (Est)*	*FY2008 (Est)*
Human Embryonic	$40	$38	$37	$37
Human Nonembryonic	$199	$206	$206	$205
Nonhuman Embryonic	$97	$110	$110	$109
Nonhuman Nonembryonic	$273	$289	$288	$287
Total, NIH Stem Cells	$609	$643	$641	$639

Source: National Institutes of Health, "Estimates of Funding for Various Diseases, Conditions, Research Areas" (Updated 2/5/07)

As might be expected, NIH support over this period for hESC research has remained small, amounting to something less than $40 million annually, or only about six percent of all stem cell research funding. Other forms of stem cell research are not particularly controversial and there are no limits on research activities of the sort that have been attached to hESC. Treatments have been developed using other types of human stem cells, and many of the techniques used to isolate or manipulate embryonic stem cells have been developed using animal cells, but direct federal support to date for hESC research has been limited.

State Actions and Funding

While decisive federal action around hESC has proven impossible to date, more than a few states have been able to establish coherent state research policies. As in numerous other areas, advocates who have been frustrated by the current deadlock in Washington have been able to move their agendas forward at the state level. While policymakers in many states have avoided becoming involved in the complex and controversial issues surrounding hESC, others have been able to construct majorities around particular approaches to this research. The resulting legislation has been extremely diverse in scope and intent, ranging from legislation to prohibit and even criminalize hESC research to active encouragement of hESC research inside their state borders and authorization of considerable amounts of state funds to support such research.[13] Six states currently ban hESC research, while as many as ten have supported stem cell research in some form.

State financial support for stem cell research is particularly significant since few states have any experience with supporting biomedical research on a large scale. While some states have supported various kinds of targeted research initiatives at state universities to encourage other types of technology, almost no states have experience with operating competitive, peer-reviewed research programs in medicine or genetic research. Funding from the National Institutes of Health and other federal agencies has been ubiquitous in biomedical research, so states have not previously felt compelled to support research in these areas.

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13 For an excellent recent review of state activities, see Christine Vestal, "Embryonic Stem Cell Research Divides States," *Stateline.org*, June 21, 2007, http://www.stateline.org/live/details/story?contentId=218416.

Table 2
State Government Support for Stem Cell Research ($ million)

States	*Allocated to date*				
($ million)	*Human Embryonic Stem Cells*	*Other Stem Cell/Unallocable*	*Appropriated/Authorized But Not Allocated*	*Proposed, But Not Appropriated*	*Projected Annualized*
California[a]	$208		$3,000		300
New Jersey[b]	$4.30	$0.70	$210	$450	45
Connecticut[c]	$20		$100		10
Illinois[d]		$15			
Maryland[e]		$15	$23		23
Wisconsin[f]					
New York			$100	$500	50
Ohio[g]		$27			
Massachusetts				$1,000	100
Minnesota[h]		$15			
Total	$232	$73	$3,333		528

Notes/Sources

a California allocations financed by loans from general fund and private parties; part of $3 billion in bond proceeds that have been authorized by voters but not issued to be used to pay back loans. Source: California Institute of Regenerative Medicine press release, June 5, 2007; http://www.cirm.ca.gov/press/pdf/2007/06-05-07.pdf

b One round research grants in 2005; appropriated/authorized amount includes $10 million for research grants and $200 million for stem cell lab construction. Source: New Jersey Commission for Science/Technology; http://www.state.nj.us/scitech/stemcell/. There is a bill authorizing vote on $450 million bond issue over 10 years moving through the state legislature; see http://www.politicsnj.com/cohen-new-jersey-stem-cell-research-bond-act-released-assembly-budget-committee-9606.

c $19.78 million awarded 11/06; $100 million authorized by Public Act 05-149. Source: http://www.dph.state.ct.us/StemCell/About.htm.

d Two rounds of awards in 2006; unable to allocate between hESC and other stem cell types. Source: Illinois Regenerative Medicine Institute press releases, http://www.idph.state.il.us/irmi/news_081706.html and http://www.idph.state.il.us/irmi/news_042406.html.

e No details beyond titles available. Source: Christine Vestal and Maryland Stem Cell Commission press release, http://www.marylandtedco.org/_media/pdf/StemCellsMDComissionFundingDecisionspressrelease5-17-07FINAL.pdf.

f The University of Wisconsin is a major center for hESC research. However, defining the value of the state's contributions is impossible from publicly available data

g Separate allocations for nonembryonic stem cell research in 2003 and 2006 to Center for Stem Cell & Regenerative Medicine at Case Western Reserve University. Source: http://ora.ra.cwru.edu/stemcellcenter/.

h Capital grant by University of Minnesota to Minnesota Stem Cell Institute. Source: Stem Cell Institute press release, http://www.stemcell.umn.edu/stemcell/about/home.html.

In spite of this limited experience, several states have approved, and more have proposed, substantial spending from state sources to support stem cell research. A summary of state activity to date is presented in Table 2. There is no authoritative source of comparable data on state spending on stem cell research, and it is frequently difficult from publicly available information to apportion various forms of state spending between hESC and other forms of stem cell research.

By far the largest state initiative to date has been in California. In 2004, California voters approved an initiative to spend $3 billion, financed by state general obligation bonds, over a period of ten years to support stem cell research. Issuance of the bonds has been prevented by legal challenges until relatively recently, but the California Institute for Regenerative Medicine (CIRM), the agency that manages the state's stem cell program, has been able to secure funds via a loan from the

state's general fund and the sale of bond anticipation notes to private investors. Using these funds, which will have to be repaid from the proceeds of the bond issue, CIRM has already allocated over $200 million in hESC research support, or more than five times what NIH is allocating annually to support this research.

Other state allocations to date have been smaller. Ohio and Minnesota have made "one time" appropriations for adult stem cell research and capital construction, respectively. New Jersey, Illinois, and Connecticut have allocated research grants of varying sizes and New Jersey has also approved funds for the construction of a stem cell laboratory. Connecticut has already approved and New Jersey is considering ongoing support for stem cell research programs, while Illinois has only been able to make two separate rounds of research awards to date. Maryland has made one round of research awards, and the governor has recently signed a FY2008 budget that authorizes over $20 million in research grants. Wisconsin has not made separate appropriations of state funds to support hESC research, but Governor James Doyle has been aggressively promoting stem cells as an economic development strategy. The University of Wisconsin is a major center for hESC research — the university is one of the places where hESCs were first isolated in the late 1990s — and the state holds important patents in hESC technology. The university also houses the National Stem Cell Bank, established by NIH to maintain and distribute many of the stem cell lines that can be supported by federal funds. The state is aggressively attempting to capitalize on these assets and develop networks of companies pursuing stem cell therapies, but defining the value of the state's contributions is impossible from publicly available data.

Larger state stem cell programs are in the works. The FY2008 New York State budget includes $100 million in state funding to establish a stem cell research program, and there appears to be considerable political support for an additional $500 million in state support, although the source of further funding remains unclear. Governor Deval Patrick has recently proposed $1 billion in state support to support stem cell research in Massachusetts. Both states are major centers for hESC research, and there appears to be bipartisan political support for large, ongoing state funding.

At least some of these state initiatives appear to be sustainable past the 2008 presidential election, which some observers have argued will dramatically improve the federal funding picture. California's Proposition 71 authorizes the disbursement of $3 billion in research funds over ten years, and CIRM management has begun to lobby for additional funding sources past this time horizon. Connecticut has earmarked $100 million in state funds over a decade. Proposals in New York, New Jersey, and Massachusetts would also establish stable funding for stem cell research over a ten-year time horizon, with Massachusetts and New Jersey contemplating issuing state bonds to support this research. Maryland, by contrast, appears to be relying on annual state appropriations to support stem cell research. While this funding source is less reliable than earmarked bond proceeds, strong political support may produce stable funding. Aggressive efforts by governors in Illinois and Wisconsin to secure a stable state source of hESC funding have to date been unsuccessful, but might be expected to persist and may be at least partially successful in the future. This research remains politically controversial in many states, however, and changes in political or budgetary circumstances may jeopardize continued funding in states that fund stem cell research through annual appropriations.[14]

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14 Stephanie Simon, "Stem Cell Dissent Roils States" *Los Angeles Times,* August 1, 2007.

The existence of committed state funds over extended periods of time may well turn state governments into a significantly larger source of funding for hESC research than NIH on an ongoing basis. The last column of Table 2, labeled "Projected Annualized," displays potential annual flows of funds from state programs that have already been approved or appear to have strong political support. Under these assumptions, state support for stem cell research could amount to over $500 million annually over the next decade. While not all of these funds will be used to support hESC as opposed to other forms of stem cell research, it does seem likely that most states will follow California's lead and tilt their funding support disproportionately toward hESC. The Massachusetts initiative, for example, lists "overcoming federal prohibitions" as a major funding goal. Even if as little as half of potential state funding is devoted to hESC research, states would be outspending NIH by a factor of six in this area. California is already the single largest supporter of hESC research in the world, and sustained support from other states may come to mean a diminished role for the federal government in setting stem cell research policy.

Private Philanthropy and Stem Cell Research

A second major source of funding for hESC and other forms of stem cell research has been private philanthropy. While private support, even on a large scale, to support biomedical research is nothing new, private support for stem cell research in general, and hESC in particular, has been both unusually large relative to the scale of the research enterprise and the level of federal support, and has been used for a broader array of activities than has been typical.

While a comprehensive accounting of private contributions to stem cell research is impossible, a listing of some recent large, visible gifts is provided in Table 3. This list is incomplete. Many national foundations that finance research into particular diseases, such as the Juvenile Diabetes Research Foundation, the Michael J. Fox Foundation for Parkinson's Research, and the Leukemia and Lymphoma Society fund stem cell research projects, and other foundations and donors may also fund stem cell projects at individual institutions. The overall size of these donations is difficult to identify, although a recent *Wall Street Journal* article claims that private funding currently constitutes the primary source of support for hESC research.[15] Nonetheless, the gifts on this list amount to some $1.7 billion, a very large amount given the current scale of federal funding and the overall size of the stem cell research enterprise. Itemizing the activities these funds are intended to support, separating support for hESC research from other stem cell research, or identifying the time period over which these funds are to be spent is impossible with any degree of precision. It seems reasonable, however, to infer that much of this funding, particularly to institutions in California, Massachusetts, New York, and Maryland that are already major centers of hESC research goes to support hESC research in various ways. Contributions to establish stem cell research centers at particular universities are common, which may mean that these funds support the acquisition of lab space and equipment, salaries for key center personnel, and other "overhead" or "start-up" functions, as well as activities more directly related to biomedical research. Rather than support the construction of new lab space at a particular university, the New York Stem Cell Foundation has established a free-standing "safe haven" lab with no federal support that is being used by researchers from several in-

15 Robert J. Hughes, "Stem Cell Funding's Private Side," *The Wall Street Journal*, July 28, 2006.

Table 3
Private Donor Support for Stem Cell Research

State	*Institution*	*Donors*	*Amount Donated ($ million)*	*Comments*
Massachusetts[a]	Harvard Stem Cell Institute	Howard Hughes Medical Institute; Juvenile Diabetes Research Foundation; Harvard; other philanthropists	$40	$100 million target
	In conjunction with state life sciences initiative[b]	unspecified	$250	Unclear if donations already made or contingent on state support
	Two Harvard professors — Eggan and Cowen[c]	Stowers Medical Institute	$10	
New York	Rockefeller University; Cornell Medical School; Memorial Sloan-Kettering Cancer Center[d]	Starr Foundation	$50	
	Mount Sinai School of Medicine — Black Family Stem Cell Institute[e]	Leon Black	$10	
	Columbia Stem Cell Center[f]	Various private philanthropists	$25	Total $50 million campaign
	Cornell Medical School Center for Stem Cell Therapeutics[g]	Shahla and Sushang Ansary	$15	
	Post doctoral research fellows[h]	New York Stem Cell Foundation	$5	Foundation also established "safe haven" lab
Maryland[i]	Johns Hopkins University	Michael Bloomberg	$100	Amount for hESC unclear
	Johns Hopkings University Institute for Cell Engineering	Anonymous donor	$58.5	
California[j]	California Institute for Regenerative Medicine (CIRM); various universities	Variety of foundations; individual donors	$100	
	CIRM[k]	Private placement of bond anticipation notes	$45	Proceeds used for research grants; to be repaid from bond proceeds
Missouri[l]	Stowers Medical Institute	James and Virginia Stowers	$985	Unrestricted donation of stock
Texas[m]	University of Texas Health Sciences Center -Houston	anonymous patient	$25	
Washington[n]	University of Washington stem cell institute	multiple donors	$17	$100 million campaign
			$1,735	

Sources:

a Robert J. Hughes, "Stem Cell Funding's Private Side," *The Wall Street Journal*, July 28, 2006.
b Governor Deval Patrick press release, http://www.mass.gov/Agov3/docs/mass_life_sciences_strategy.rtf.
c *Science* magazine, April 28, 2006.
d Press release, "Stem Cell Research in New York City Receives Pivotal Boost from Starr Foundation," Memorial Sloan-Kettering Cancer Center, May 23, 2005.
e "Mount Sinai School of Medicine Estables Stem Cell Institute," *Medical News Today,* May 6, 2005.
f Press release, "Columbia University Medical Center Launches Multi-Year campaign To Support Stem Cell Research," June 15, 2005.
g Robert Kolker, "The California Stem-Cell Gold Rush," *Wired New York Forum*, 2004, http://wirednewyork.com/forum/showthread.php?t=5550.
h New York Stem Cell Foundation, "NYSCF Laboratories: Creating Tools for Accelerating Stem Cell Research Through Scientific Collaboration," http://www.nyscf.org/Laboratory.php
i Sonya Geis, "Rich Donors Help Calif Fund Stem Cell Research," *The Washington Post,* December 19, 2006.
j Geis, 2006; David Hamilton, "Donors Sustain Stem-Cell Effort in California Amid Funding Battle," *The Wall Street Journal*, August 16, 2006).
k CIRM Annual Report, p. 24, http://www.cirm.ca.gov/press/pdf/annual_rpt.pdf.
l Stowers Institute for Medical Research Financial Statements, 2001-2005.
m UT Houston press release, http://publicaffairs.uth.tmc.edu/Media/newsreleases/nr2004/25million_stemcell.html.
n Eric Engelman "$5 million given to stem cell center," *Puget Sound Business Journal*, June 29, 2007, http://masshightech.bizjournals.com/masshightech/othercities/seattle/stories/2007/07/02/story5.html?b=1183348800%5E1484234.

stitutions.[16] The Harvard Stem Cell Institute, for example, has developed several hESC "lines" that are not eligible for federal support, but are available to other researchers, in addition to supporting its own research program. The largest gifts in this table, however, are donations of stock to the Stowers Research Institute in Missouri that can't be allocated easily to any particular activity.[17]

Two novel trends have emerged in the pattern of private support for stem cell research. One, at least in California, is the use of private money to directly support the activities of government agencies. CIRM management actively solicited donations amounting to some $16 million from private parties to pay the organization's initial operating expenses, and the agency occupies office space in downtown San Francisco rent- and utility-free for a decade as a result of private contributions.[18] Private donors have also supported CIRM's research program through the purchase of $45 million in low-interest Bond Anticipation Notes (BANs), which will be repaid once the bond issue authorized by Proposition 71 is actually sold. The Massachusetts proposal for state support of hESC research also includes $250 million in private matching funds to be used in conjunction with state funding.[19]

A second noteworthy trend is the large role of private parties in financing advertising and other activities in support of campaign efforts to legalize or finance stem cell research. While disease advocacy groups and similar organizations have long supported political efforts to secure support for their particular cause, recent spending for stem cell campaigns has been significantly larger than previous efforts. Total private contributions to the campaign to pass Proposition 71 in California, for example, have been estimated at $25 million. More dramatically, the successful campaign in 2006 to pass an amendment to the Missouri constitution that unambiguously legalized stem cell research spent over $28 million, more than had previously been spent by all candidates combined in any statewide race. Almost all this spending was supported by one couple — James and Virginia Stowers, who made the enormous donations to the Stowers Research Institute.

The sustainability of private donations at this level to support stem cell research in general and hESC in particular is unclear. Many disease foundations support stem cell research, including hESC, as part of their on-going research funding activities, and total hESC funding from this source may well exceed that of the federal government. While disease foundations typically do not report funding amounts for stem cell or any other particular line of research in their annual reports or

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16 New York Stem Cell Foundation, "NYSCF Laboratories: Creating Tools for Accelerating Stem Cell Research Through Scientific Collaboration," http://www.nyscf.org/Laboratory.php

17 The Stowers Research Institute situation is complicated. As described in Institute publications, "far more" of the Institute's research program to date has involved adult and germ-line stem cells than embryonic stem cells. Institute management has attempted to expand its embryonic stem cell research program, but persistent attempts by the Missouri legislature to restrict or criminalize this research has made it difficult to attract researchers to the Institute's Kansas City campus. In response to the ongoing political debate in Missouri, the Institute has funded embryonic stem cell research underway at Harvard, which is listed in Table 2; moved significant endowment assets from Missouri to a Delaware-based nonprofit; and has recently announced it is putting further expansion plans in Missouri on hold until the political environment stabilizes. For details, see William Neaves, "Why the Stowers Institute Supports Stem Cell Research" *The Stowers Report*, Fall 2006; "Stowers Puts Expansion Plans on Hold," *St. Louis Business Journal*, June 29, 2007; and Simon, "Stem Cell Dissent Roils States."

18 David Hamilton, "Donors Sustain Stem Cell Effort in California Amid Funding Battle," *The Wall Street Journal,* August 16, 2006.

19 Office of Governor Deval Patrick, "The Massachusetts Life Sciences Initiative, http://www.mass.gov/Agov3/docs/mass_life_sciences_strategy.rtf.

financial statements, the Juvenile Diabetes Research Foundation, one of the larger disease foundations, by itself spends approximately $11 million annually on hESC research,[20] or more than 25 percent of NIH spending. Even if support from other individual disease foundations is smaller, it would not be difficult for total foundation support to exceed federal funding. As noted in Table 3, several universities have also established large fund-raising campaigns to support hESC and other stem cell research, which may be successful to a greater or lesser degree in establishing a stable flow of funds at individual campuses. While there may be fewer large grants to establish new research programs or build labs independent of the current NIH funding restrictions, there may well be enough ongoing support for foundations and other private donors to continue to outspend NIH on hESC research.

While a conclusive accounting appears impossible, the available circumstantial evidence suggests strongly that both state governments and private foundations are significantly outspending the federal government in the support of hESC research. Some observers have suggested that this picture may change after the election of 2008, when the current administration may be replaced by one less hostile to hESC. We now turn to an examination of the likely future of hESC policy and funding.

The Outlook for Stem Cell Funding

Some observers have argued that this picture will change after the election of 2008. The Bush administration will be replaced by one that will likely be less hostile to hESC funding. Almost all of the current Democratic candidates, and more than a few of the Republican ones, are likely to sign the bill expanding the number of stem cell lines eligible for federal funding that President Bush has vetoed twice. There have also been claims that a new election will result in increases in federal funding for hESC research, obviating the need for continued state activity.

These claims may well be overly optimistic. While most potential presidential candidates may well sign the bill Bush has vetoed and may likely eliminate the onerous prohibitions on direct or indirect federal support for research on ineligible lines, it is far from clear that the election of 2008, regardless of who wins, will result in a major increase in federal support for hESC research. Whoever gets elected president in 2008 will have to deal with a ongoing war in Iraq, a $400 billion on-budget deficit, large expiring tax cuts, and a serious health care coverage problem. The Bush administration has recently promised to veto a bipartisan expansion of the popular State Children's Health Insurance Program (SCHIP) currently being considered by Congress, which may mean that further expansions of this program may be put off until after the election as well.

Under these conditions, the odds of a major expansion of the federal role in stem cell research are pretty slim. A Democratic president, and at least a couple of the potential Republican ones, will very likely sign a version of the bill Bush has vetoed, and may well eliminate the regulations on avoiding federal support of ineligible stem cell lines. These are not small things, but they're a long way from putting the feds back in the driver's seat on stem cell policy. Restrictions on the stem cell lines that federal funds can be used to support would still remain, and these actions would not increase the amount of federal support for hESC research.

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20 Hughes, July 28, 2006.

The odds of a major bump in stem cell funding — and it would take a major one to establish the feds as the dominant actors in stem cell policy — have to be rated as slim. The overall budget picture is very tight, and there are a lot of popular programs in the funding queue. Every one of the major Democratic contenders already has a proposal to significantly expand health care coverage, which should provide a pretty good clue about what their primary domestic priority is likely to be. Any proposal to expand health care is likely to be expensive, which means that much less for other purposes. In a further development unlikely to have been noticed by anyone besides budget geeks, both Houses of Congress have adapted "pay-as-you-go" budget rules under which tax cuts or changes in popular entitlement programs have to be offset by spending cuts or tax increases somewhere else. These rules mean, for example, that expanding SCHIP coverage will have to be paid for by cutting something else or raising taxes in some form.[21] This requirement lessens the amount of money available in the rest of the budget. Finding the resources to finance an expansion of hESC research under these conditions is likely to be difficult.

Proposals to dump a lot of additional money into hESC are likely to be controversial, even if both Congress and the administration are favorably disposed. Opposition will come from the same groups that have opposed this research all along, and will likely even come from elsewhere in the scientific community. After doubling between 1999 and 2003, NIH's overall budget has remained flat and even declined in real terms in recent years. As a result of these financial pressures, overall grant success rates have fallen from 30 percent to less than 20 percent, and as low as ten percent in some fields.[22] Scientists who are having trouble supporting their own research are likely to protest vehemently if their stem cell colleagues, who are already getting money from states and private foundations, now get additional support from NIH as well. Funding for stem cell research in general or hESC in particular, does not have a separate budgetary identity inside NIH, but is scattered across the separate budgets of the NIH's component institutes that fund research on a wide range of different diseases. NIH officials in some of these institutes may find it more sensible to steer any new funding away from stem cell research and to other research areas that do not have substantial state or private foundation support. Stranger things have happened, but the odds of a lot of additional federal money being devoted to stem cell research seem slim. Even if NIH is able to expand support for stem cell research, it will only be one payer among many, and not even the largest one.

Even if stem cell supporters are successful in expanding federal hESC funding, it seems unlikely that states will diminish their efforts. As noted above, many states have legally obligated funds with an extended time horizon, over which it may be difficult to divert funds from their intended uses. If the NIH funding picture remains tight, scientists and universities in some states may push to institutionalize or expand state stem cell programs as an alternative source of research funding. A second factor that is likely to encourage states to persist is competition both between states, and between states and several foreign countries that have begun stem cell initiatives of their own. States see themselves, at least rhetorically, as competing with each other for jobs, tax revenue,

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21 The SCHIP expansions currently being considered by Congress, for example, are financed by major increases in the federal cigarette tax and reductions in payments to certain types of Medicare HMOs.

22 For reviews of NIH's recent funding problems, see David Korn et al, "The NIH Budget in the 'Postdoubling' Era," Science, 296 (May 24, 2002); David G. Nathan and Alan Schechter, "NIH Support for Basic and Clinical Research: Biomedical Researcher Angst in 2006," *Journal of the American Medical Association* 295 (2006): 2656-2658; and Joseph Loscalzo, "The NIH Budget and the Future of Biomedical Research," *New England Journal of Medicine* 354 (April 20, 2006): 1665-1667.

economic development, and, in the case of hESC research, research talent and prestige. Particularly after the passage of Proposition 71 in California, much of the public rhetoric in support of state funding for hESC research has focused on the need for states to remain "competitive" with California and other states to attract or retain scientific talent and prestige. CIRM's latest annual report lists some 25 stem cell scientists who have relocated to California from elsewhere, and there is some systematic evidence that stem cell researchers have recently received more job offers than other types of scientists.[23] The Republic of Singapore, among other countries, has also mounted a highly publicized stem cell program of its own that has recruited American and other scientists with subsidized lab space, ready access to stem cell lines, and other inducements.[24] While it is easy to overstate the effectiveness of such efforts, it seems clear that many state politicians have found concerns over "brain drains" to California or other more congenial locations to be effective arguments in pressing for state support for hESC and other forms of stem cell research.

What seems most likely, in short, is that the immediate future will be like the recent past, with hESC research being heavily supported in some states and illegal in some others, with states weighing in with hESC funding programs of widely varying sizes. Competition between states is a good thing for hESC supporters — more governors and gubernatorial candidates may find it in their political interest to support state financing for this research if they can claim state support will keep their state from "falling behind." There will be increasingly vocal debates over royalties, product pricing, and other research management issues that will be resolved in a wide range of ways, and conflicts between the rules that apply to collaborating researchers located in different states. This system is less efficient and more administratively difficult than a single funding source and set of rules would be, but it's an accurate reflection of conflicting and diverse national public and political views about hESC that don't show any sign of going away anytime soon.

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23 Aaron D. Levine, "Research Policy and the Mobility of US Stem Cell Scientists," *Nature Biotechnology* 24 (July 2006): 865-866.

24 For an example of the coverage of the Singapore program see Terri Somers, "Singapore makes investment in its survival," *San Diego Union Leader*, December 18, 2006.