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**Policy Considerations for States Supporting Stem Cell Research:  
Evidence from a Survey of Stem Cell Scientists**

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## **Biographical Sketch**

Aaron Levine is a Ph.D. candidate in the Program in Science, Technology and Environmental Policy at Princeton University's Woodrow Wilson School where his research focuses on assessing the impact of public policy on biomedical research. Aaron holds an M.Phil. from the University of Cambridge, where he studied computational biology at the Sanger Centre. His undergraduate studies were in biology at the University of North Carolina at Chapel Hill.

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**Policy Considerations for States Supporting Stem Cell Research:  
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**Abstract**

Five states now provide funding for stem cell research and numerous states are developing or debating stem cell research policies. Yet despite this interest, few data exist to help policymakers design policies or forecast their impact. This article reports novel data from two surveys: one directed at those most affected by these policies – stem cell scientists themselves – and one at a group of biomedical researchers from less contentious fields. These data identified relatively high mobility among stem cell scientists, particularly those in states with restrictive policies, and a strong preference for states with permissive policies. These findings suggest state-specific policies may prove to be effective recruiting tools. They also suggest specific recruitment strategies and highlight the importance of first-mover advantage as several states compete to recruit from the same limited pool of mobile scientists. This research aims to provide a factual basis to support ongoing policy formulation in the area.

## **Policy Considerations for States Supporting Stem Cell Research: Evidence from a Survey of Stem Cell Scientists**

### **Introduction**

State-specific support for stem cell research has recently emerged as a new but controversial policy tool for state lawmakers. Following California's lead, where voters approved a \$3 billion proposition in November 2004, numerous states have developed stem cell research programs of their own or are actively debating such programs. State policymakers in Connecticut, for instance, approved a 10-year, \$100 million funding program in June 2005, and lawmakers in New Jersey, Illinois and Maryland have allocated state funds to support research in the field. All told, policymakers in at least 15 states have expressed interest in supporting stem cell research (Alliance for Stem Cell Research 2006).

These state policies have many goals. Firstly, they hope to counteract restrictions on federal funding for human embryonic stem cell research and accelerate potentially life-saving research. Concerned about the use of human embryos in research, President George W. Bush, on 9 August 2001, limited federal funding to research using human embryonic stem cell lines derived prior to his speech, where "the life or death decision has already been made" (Bush 2001). Federal money, from the U.S. National Institutes of Health (NIH), funds the majority of academic basic biomedical research in the United States (National Science Board 2006, Chapter 5). The president's policy, which cuts state of the art human embryonic stem cell research off from this funding source, has been criticized as too stringent (Daley 2004).

In addition to accelerating biomedical research, state policymakers hope that state-specific research support will yield economic benefits. In California, an economic impact study commissioned by supporters of the 2004 proposition concluded that the state might see direct

economic benefits between \$6.4 billion and \$12.6 billion, representing a potential return of 120 percent to 236 percent on the state's investment (Baker and Deal 2004, 2). Projected economic benefits included both increases in state tax revenues and reductions in state health care expenditures. A similar report found that a proposed \$380 million stem cell research initiative in New Jersey could have as much as \$1.4 billion in direct economic benefits for the state (Seneca and Irving 2005, i). These reports both suggest that state support for stem cell research will have a magnetic effect, increasing the appeal of the state to others in the life sciences industry, potentially leading new scientists and new companies to the state, and yielding additional economic benefits.

On the national level, policymakers have been worried for some time that stem cell scientists might leave the United States for more permissive countries. These concerns were particularly prevalent in mid-2001 when the President's policy announcement closely coincided with the highly-publicized departure of Roger Pedersen, a noted stem cell scientist who left the University of California at San Francisco for the United Kingdom. Pedersen, who decided to leave before the federal policy was enacted, cited political uncertainties that threatened his research as a key motivation for his departure (Abate 2001). Similar concerns frequently reappear in media coverage of major advances in embryonic stem cell biology, particularly when these advances are reported by research teams outside the United States. Quantitative evidence, looking at the geographic distribution of research publications, supports this idea that the United States is falling behind in research related to human embryonic stem cells, but does not link this finding to migration of stem cell researchers (Levine 2005; Owen-Smith and McCormick 2006).

Scientist mobility rapidly appeared as a state policy issue following passage of the California initiative. Unlike large-scale migration to the United Kingdom, which most policy

analysts deemed unlikely, California with its promised billions – not to mention its strong biotechnology industry and temperate climate – seemed a particularly appealing destination (Paarlberg 2005). This perception was reinforced when, just days after the proposition passed, prominent California scientists began to openly talk about their recruitment efforts (Cook 2004). Lawmakers suddenly envisioned a stampede of the country’s best scientists moving to California, in what has been termed a “stem cell gold rush” (Holden 2004). California’s progress has been hindered by ongoing litigation (Tansey 2006). Still, a recent analysis of another portion of the surveys reported here found that when compared with other biomedical researchers, U.S. stem cell scientists were disproportionately likely to have received job offers for positions in California (Levine 2006).

As biomedical research policy has traditionally been a federal responsibility, the rise of state-sponsored stem cell research has posed a host of challenges for state policymakers. Furthermore, only a limited literature on these state-specific challenges exists. One exception is work by Roger Noll, who outlined the political and economic challenges states must overcome to successfully fund this research (Noll 2006). A more substantial literature, including a report by the U.S. National Academy of Sciences (Committee on Guidelines for Human Embryonic Stem Cell Research 2005), addresses the regulation of stem cell research. Others have compared the diverse regulatory practices in existence today (Knowles 2004; Walters 2004) and examined potential state-specific regulatory frameworks (Knowles 2006).

One key concern is that policymakers possess little, if any, factual information on which to base stem cell research policies. Essentially no data exists on the future plans and mobility of stem cell researchers, and, thus, state policymakers are merely guessing that their policies will

prove appealing. Additionally, beyond a few anecdotes, only limited evidence exists to assess the impact of California's proposition.

This article reports novel survey data and aims to provide a factual basis for policymakers developing stem cell research policy. This survey represents one of the first attempts to examine the impact of stem cell policies on those most affected by the policies – stem cell scientists themselves. To help identify field-specific trends, these data are compared with results of a similar survey of biomedical researchers working in less contentious and less regulated fields. Together these data offer insights into the mobility of stem cell scientists at various stages in their careers and the factors, including public policies, influencing scientists' decisions to move. Additionally, scientists' preferred states for research and their awareness of the various state efforts to support stem cell research are examined.

The article is divided into four sections. The first provides an overview of stem cell science, providing sufficient detail for non-scientists to understand the issues at play in the policy debates. The second section examines the history of stem cell research policy in the United States and examines some of the state policies in place or under consideration. The third section presents the survey methodology and results. The article concludes with a fourth and final section that draws policy lessons from this analysis. This section offers tentative suggestions for state lawmakers developing stem cell policies.

## **Stem Cell Science**

The human body consists of countless individual cells. Some of these cells, such as neurons, are long-lived, while others, including skin and blood cells, have short life spans and must be replaced frequently. Stem cells are undifferentiated or partially differentiated cells that play a key role in the replenishment of mature cells throughout the body (U.S. Department of



Health and Human Services 2001, 1). All stem cells share at least two characteristics. First, they can divide repeatedly to create identical copies of themselves. Second, they can give rise to mature cell types. When these progenitor cells are found in differentiated tissues, they are referred to as adult stem cells. When they are found in early embryos, they are called embryonic stem cells.

### **Adult Stem Cells**

Stem cells have been identified in a variety of tissues, including bone marrow, peripheral blood, brain, spinal cord, dental pulp, blood vessels, skeletal muscle, epithelia of the skin and digestive system, cornea, retina, liver, and pancreas (U.S. Department of Health and Human Services 2001, 23-38). Although many of these adult stem cells are only poorly understood, one of their major roles is to replenish the supply of mature and differentiated adult cells in their respective tissues.

The hematopoietic, or blood-forming, stem cell found in bone marrow is the best understood stem cell. It forms the basis of the immensely successful bone marrow transplant therapies that have been developed over the last half century to treat various forms of leukemia and lymphoma. Immune rejection, a condition that results when a patient's immune system mobilizes to attack a transplant, is an important complication that these and other stem cell therapies must overcome. To minimize these complications, transplants are taken from genetically similar individuals. Cells derived from two different individuals are never completely compatible, however, unless the two individuals are identical twins. One advantage of adult stem cells is that, in some cases, it might be possible to use stem cells isolated from the patient – a strategy that greatly reduces immune rejection concerns.

Efforts to study hematopoietic stem cells since the 1960s illustrate both the promise and challenge of adult stem cell research. Knowledge of these cells has grown substantially over the years and the use of bone marrow transplantation has been expanded to treat not just leukemia and lymphoma but also a variety of other blood disorders. Hematopoietic stem cells have proven to be exceedingly rare, however, making up only one out of every 10,000 to 15,000 bone marrow cells, and difficult to grow outside of the body (U.S. Department of Health and Human Services 2001, 43-44).

### **Embryonic Stem Cells**

Human embryonic stem cells were successfully isolated in the late 1990s (Thomson et al. 1998), and scientific investigation of these cells remains in its early stages. Experiences with mouse embryonic stem cells, isolated in 1981 and now a key developmental biology research tool (Reviewed in Downing and Battey 2004), provide scientists with insights into the potential of the more recently-isolated human cells. In contrast to adult stem cells, human embryonic stem cells are relatively easy to isolate and can be maintained and grown in their undifferentiated state outside of the body. They exist only for a short period of time during development, however, and must be isolated during this time. This process typically requires the destruction of the embryo and is the primary source of the ethical controversy surrounding the field. Recent research shows that mouse embryonic stem cells can be derived without impacting development (Chung et al. 2006) and suggests that the same technique works with human cells as well (Klimanskaya et al. 2006). Although this technique reduces some ethical concerns, it raises other issues and has generated controversy (Weiss 2006).

Immune rejection may pose a problem with embryonic stem cell based therapies as it does with adult stem cell therapies, although some evidence suggests less-developed embryonic

cells will generate weaker immune responses (Drukker et al. 2006). One strategy to reduce these complications is to use patient-matched embryonic stem cells derived through somatic cell nuclear transfer, or cloning, technology. Although this technique remains controversial, research is advancing. Proof of principle work in mice has been completed (Rideout et al. 2002), and although dramatic advancements reported by a South Korean group have been deemed fraudulent (Wade and Sang-Hun 2006), numerous labs are actively pursuing research in the area (Vogel 2006). Scientists remain hopeful these cells may eventually prove be useful for treating patients with Parkinson's and type 1 diabetes, among other ailments.

## **Stem Cell Research Policy in the United States**

### **Federal Policy**

In the United States, the federal government is the major funding source for basic biomedical research at academic institutions (National Science Board 2006, Chapter 5). This funding is primarily awarded in the form of peer-reviewed grants from the NIH, which had a fiscal year 2005 R&D budget of approximately \$28 billion. This funding supports a wide range of biomedical research, with few significant restrictions on what types of projects qualify for funding. Adult stem cell research, for example, falls under this relatively unrestricted funding framework and this research has been largely exempt from the policy debates outlined below.

Federal funding of embryo-related research, on the other hand, has long been a controversial issue (For a review see Johnson and Williams 2004). Annually since fiscal year 1996, a rider, known as the Dickey Amendment, has been attached to the appropriations act for the Department of Health and Human Services, the NIH's parent agency. This rider forbids using appropriated funds for the creation of human embryos for research purposes or for "research in which a human embryo or embryos are destroyed, discarded, or knowingly

subjected to risk of injury or death greater than that allowed for research on fetuses in utero” (Pub. L. 109-149, 119 Stat 2880). Because of this rule, the initial research to derive human embryonic stem cells was funded by Geron Corporation rather than the federal government.<sup>1</sup>

The first federal guidelines specifically addressing human embryonic stem cell research were issued in August 2000 (Federal Register 65, no. 2 51976-81) (Wade 2000). These guidelines, issued by the NIH following consultation with the general counsel of the Department of Health and Human Services, indicated that federal funding would be available for research on existing human embryonic stem cell lines, but not for the derivation of new lines. Research on new lines derived with private money would be eligible for funding. The NIH began accepting grant applications immediately and planned to meet to review these applications on 25 April 2001 (Johnson and Williams 2004).

Just days before this meeting was scheduled to occur, it was cancelled by the NIH, pending a Bush administration review of the funding guidelines (Weiss 2001). A few months later, on 9 August 2001, President Bush announced his new policy (Bush 2001). Federal funding would be available for research on cell lines derived before his speech. However, funding would not be available for the derivation of new human embryonic stem cell lines nor, in contrast to the previous guidelines, for research using new lines derived with private funds.

The NIH has funded a number of research projects studying human embryonic stem cells since this announcement, but the policy has come under increasing criticism. Three major complaints have been voiced. The first relates to the limited number of approved cell lines. In 2001, President Bush stated that more than sixty lines would qualify for funding, but, more than five years later, only 21 human embryonic stem cell lines are currently approved.<sup>2</sup> The second complaint is that all of the approved lines were derived on mouse feeder cells, a now outdated

technique that complicates the process of transferring research discoveries into clinical settings (Gillis and Connolly 2001). The third complaint stems from research indicating that human embryonic stem cell lines decline in quality over time. Scientists originally believed these cell lines would prove essentially immortal, and, thus, that cell lines would remain useful for many years. A recent study of nine approved cell lines found that as these cells age, they exhibit serious abnormalities, calling the utility of older cell lines into question (Maitra et al. 2005).

This criticism, along with the political appeal<sup>3</sup> of stem cell research, has led to growing dissatisfaction with the federal funding policy among politicians. Most notably, on 24 May 2005 the U.S. House of Representatives passed The Stem Cell Research Enhancement Act (H.R. 810, 2005). This bill, known informally as the Castle-DeGette bill, was passed by the Senate on 18 July 2006 and vetoed by President Bush the next day. This veto suggests that states will continue to play an important role in funding stem cell research in the coming years. If it had become law, this act would have eliminated the current temporal restriction and permitted federal funding for research on new human embryonic stem cell lines derived from embryos leftover from fertility treatment (Pollack 2006).

### **State Policy**

A wide variety of state policies address stem cell research. As of October 2006, five states – California, Connecticut, New Jersey, Illinois and Maryland – have pledged financial support for stem cell research. These states have used different political strategies and financial mechanisms to provide this funding and are offering widely varying amounts. Massachusetts, while not providing funding, has passed legislation explicitly designed to foster regenerative medicine research, in part by clarifying the legality of embryonic stem cell research and the somatic cell nuclear transfer technique. These supportive policies are summarized in table 1. In

addition, Rhode Island's law banning human reproductive cloning explicitly indicates that it does not block somatic cell nuclear transfer for medical purposes, a legislative step some people believe gives Rhode Island's a permissive research environment.

Of these states, California dominates the policy debate. The California measure, known as Proposition 71, was developed by a coalition of medical groups, patient advocates and business leaders, who used California's initiative system to put it on the ballot. On 4 November 2004, as U.S. voters were reelecting President Bush, California voters approved the California Stem Cell Research and Cures Initiative by a 59-41 percent vote (Murphy 2004). The proposition calls for the state to support stem cell research for ten years with approximately \$300 million per year raised from the sale of tax-free bonds. Lawsuits challenging the proposition's constitutionality have held up the process of selling bonds and hindered implementation of the state's plans (Somers 2005). Despite these challenges, the state institute created by the proposition distributed its first grants – totaling \$12.1 million – in April 2006 (Allday 2006). Following a \$150 million loan from the state's treasury, the institute announced a second round of grants totaling \$151.5 million in August 2006 (Somers 2006).

In Connecticut, state support for stem cell research did not rely on a direct appeal to voters. Rather, it had its origins in a proposal by Governor M. Jodi Rell that was modified and expanded by the state's General Assembly. The bill that Governor Rell signed into law on 15 June 2005 calls for \$100 million in research support over 10 years (Conn. Gen. Stat. §19a-32d to 32g). The first \$20 million for fiscal years 2006 and 2007 will come from the state General Fund. Funding for fiscal years 2008 to 2015 will come from the state's tobacco settlement fund. More than 70 applications were received for the first round of grants and the state hopes to announce its initial funding decisions by December 2006 (Haigh 2006; Hathaway 2006).

New Jersey became the first state to award funding for stem cell research when it distributed 17 grants totaling \$5 million in December 2005 (Chen 2005). Including this funding, the state has allocated approximately \$20 million toward the research and the creation of the Stem Cell Institute of New Jersey since becoming the first state to commit public monies to the controversial field in June 2004 (Washburn 2004). Beyond this funding, New Jersey politicians have debated several larger proposals. One plan, proposed by then-Acting Governor Richard Codey in January 2005, called for a total of \$380 million in funding. Funding would come in two parts: \$150 million in unspent bond money to construct the stem cell institute and \$230 million from a bond referendum to support research grants (Mansnerus 2005). This plan and similar plans proposed more recently by Governor Jon Corzine have passed the State Senate but failed in the General Assembly.

Like New Jersey, Illinois has also promised limited funding while debating larger initiatives. The initial funding has come, rather controversially, through two executive orders by Governor Rod Blagojevich. The first, in July 2005, reassigned \$10 million originally allocated for “scientific research” specifically to stem cell research and the second, immediately following Bush’s veto, transferred \$5 million from an administrative budget to support research in the field (Yednak 2006). The state awarded \$10 million in grants to researchers at seven Illinois institutions in April 2006 (Ritter and Swartz 2006). The state legislature has debated several larger proposals, including a \$1 billion ten-year plan and a \$100 million five-year plan, but these have not been approved.

Maryland became the fifth state to commit state funding to stem cell research in April 2006 when Governor Robert Ehrlich signed a bill providing up to \$15 million to support academic institutions and private companies working in the field (Maryland Senate Bill 144,

2006 session). Future funding levels were left unspecified and the funding is permitted to be used for both adult and embryonic stem cell research (Wagner 2006).

A number of other states considered proposals to support stem cell research during their 2006 legislative sessions. Among these states are Florida and New York where legislation supported primarily, but not exclusively, by Democrats stalled in Republican-controlled legislative chambers and Missouri where a vote on a ballot initiative is scheduled for November 2006 (Stone 2006).

In contrast to these states actively supporting stem cell research, a number of states restrict various types of research. All told, twenty-six states have rules that could potentially hinder embryonic stem cell research (Vestal 2006). These laws vary in nature. In some states, including Louisiana and South Dakota, ethical concerns have led to restrictions on embryo research that prevent scientists from deriving new human embryonic stem cell lines. Other states, including Arkansas, Indiana and Iowa, don't explicitly address embryo research but prohibit somatic cell nuclear transfer, thus blocking the potential generation of patient-matched human embryonic stem cell lines. In still other states, laws aimed at restricting research on aborted fetal tissue, and passed before human embryonic stem cells were ever isolated, may incidentally restrict research in the field. This may be the case in Pennsylvania where a broadly-written 1989 law on fetal experimentation (18 Pa. Cons. Stat. § 3216), which makes it a felony to "knowingly perform any type of nontherapeutic experimentation...upon any unborn child," potentially blocks the derivation of new human embryonic stem cell lines. Still other states have chosen not to limit research explicitly but rather restrict use of state money in controversial research. Table 2 summarizes current state policies that explicitly limit or seem likely to restrict human embryonic stem cell research. States, where policies could potentially hinder research by,



for instance, restricting the purchase of human tissue for research, but do not clearly do so, are excluded. In addition, in 2006, at least ten states considered new restrictions, primarily aimed at blocking the somatic cell nuclear transfer technique (Stone 2006). Many of these bills died at the close of the legislative session, but may be introduced again next year. In Michigan a new law was enacted to explicitly clarify that economic growth incentives offered by the state did not apply to embryonic stem cell or somatic cell nuclear transfer research (Mich. Comp. Laws § 207.803).

[Table 1 / Table 2 Here]

## **Survey**

### **Methodology**

During September and October 2005, a survey was administered to stem cell scientists working at academic and non-profit medical research institutions in the United States. The survey was administered over the Internet, using the Princeton University web survey facility. The survey was pre-tested on a group of stem cell scientists, and, following revisions, sent to a larger sample of 1,033 stem cell scientists. This list of scientists was derived from three sources: *Who's Who in Stem Cell Research* (DataTrends Publications 2005), PubMed literature searches and the member directory of the International Society for Stem Cell Research. This participant list was designed to cover, as comprehensively as possible, the active U.S. population of stem

cell scientists and contained scientists working with both adult and embryonic stem cells. Each potential participant was contacted first by mail and then by email.

Responses were defined as usable if both an initial demographics section and at least a portion of a section on future plans were completed. A total of 365 responses met these minimal criteria, yielding an overall response rate of 35 percent. The actual number of responses varied by question as item non-response was permitted and a small number of respondents completed only a portion of the survey, but each question analyzed here was answered by at least 92 percent of these 365 respondents. Fifty seven percent of respondents were principal investigators and 35 percent were either post-doctoral researchers or advanced graduate students. Respondents came from 39 states and their distribution closely paralleled the distribution of academic biomedical research in the United States, as measured by the NIH's fiscal year 2004 extramural budget. Thirty-five percent of principal investigators and 58 percent of post-doctoral researchers and graduate students were born outside the United States. Nearly 35 percent of the respondents indicated that they had worked with human embryonic stem cells and 58 percent of those who had not worked with these cells believed they were likely (six or higher on a ten-point scale) to do so in the future. All told, a total of 265 respondents (73 percent) either used or were likely to use human embryonic stem cells. These respondents are categorized as human embryonic stem cell scientists in the analysis that follows.

A similar survey of other biomedical scientists working in less contentious fields was conducted in January 2006. The survey was also administered on the Internet, using the same university-based web survey facility. The survey was sent to a random sample of 1,847 regular academic members of the American Society for Biochemistry and Molecular Biology (ASBMB) and 1,904 regular academic members of the American Physiology Society (APS). Each potential

participant was contacted by email. These two societies were selected because together their members cover a wide range of biomedical research fields and it seemed unlikely that many of their members used stem cells in their research.

A total of 1,029 usable responses were received, yielding an overall response rate of 27 percent. The number of responses varied by question, but each question analyzed here was answered by at least 95 percent of these 1,029 respondents. 551 respondents were from the list of APS members and 478 were from the list of ASBMB members. Eighty seven percent of respondents were principal investigators. Respondents came from all fifty states and the District of Columbia. Twenty percent of principal investigators and 46 percent of post-doctoral researchers and graduate students were born outside the United States.

Both surveys included screening questions to ensure respondents were active researchers. The number of usable responses reported above only includes respondents who passed all relevant screening questions. For the stem cell survey, respondents were included in the final dataset only if they had, in the last six months, participated in a research project using or relating to stem cells. For the survey of non-stem-cell scientists, two screening questions were used. Respondents were included in the final dataset only if they had worked on a biomedical research project in the last six months and if they did not study or use stem cells of any type in their research. Both surveys contained both closed and open-ended questions, although the analysis reported here focuses on the closed-ended questions. Both survey protocols were approved by the Princeton University Institutional Review Panel for Human Subjects.

## **Results**

An important question for state policymakers seeking to recruit stem cell scientists is whether or not these researchers are considering leaving their current institutions to pursue

research elsewhere. For a variety of reasons, moving states may be a burden for many scientists. Figure 1 examines openness to a potential move and the potential destinations for stem cell scientists likely to move. Approximately 34 percent of principal investigators reported that they were likely (defined as six or higher on a ten point scale) to leave their current institution to study stem cell biology elsewhere within the next three to four years. In contrast, only 21 percent of principal investigators in other biomedical research fields indicated they were likely to leave their current institution within the same timeframe. This difference was statistically significant ( $P < .001$ , t-test,  $n=1,098$ ).

[Figure 1 here]

As post-doctoral researchers and graduate students are approaching natural transition points in their scientific careers, it is not surprising that nearly 73 percent of stem cell scientists and 79 percent of the other biomedical researchers indicated they were likely to leave their current institution within three to four years, but this result does confirm the high mobility of this group. A statistically significant difference was observed in the preferred destination of the junior scientists responding to this question with 21 percent of stem cell scientists and 7 percent of the other biomedical scientists indicating their preferred destination, if they were to move, was another country ( $P < .05$ , t-test,  $n=148$ ). As many of the respondents who selected another country as their preferred destination were born and trained outside the United States, this difference likely reflects the larger proportion of international scientists studying stem cells as compared to other biomedical research fields.

To further explore these differences in departure plans between the groups of scientists, a regression framework was utilized. In this analysis, which was restricted to principal investigators, the dependent variable was departure likelihood (one to ten scale, one = very unlikely, ten = very likely). A series of independent dummy variables were included to examine the impact of research field (stem cell research of any kind, human embryonic stem cell research or other biomedical research), demographic variables (age, tenure status, born in the United States, educated at undergraduate or graduate level in the United States) and state policy. For the policy dummy variables, all states in table 1 (except Maryland where the permissive policy was enacted after the survey) were considered permissive and all states listed in table 2 as restricting embryo research or somatic cell nuclear transfer research were considered restrictive. Interaction variables were added to specifically examine the effect of studying stem cells or human embryonic stem cells in a permissive or restrictive state. Table 3 contains the regression results as well as summary statistics for the principal investigator respondents. Although ordinary least squares regression results are presented to ease interpretation, results were similar when other frameworks were used, including an ordered probit framework designed for categorical dependent variables and a standard probit framework with the dependent variable collapsed to a binary indicator variable (data not shown).

[Table 3 here]

Three regression models are presented. The first (Model 1) excludes the interaction variables. Scientists holding tenure or exceeding 55 years in age were statistically significantly less likely to move. Interestingly, scientists, regardless of their individual fields, working in states with restrictive policies toward human embryonic stem cell research were, all else equal, statistically significantly more likely to move. This result may reflect a policy impact or a variety of other unobserved factors characteristic of restrictive states, such as relatively lower faculty salaries or underdeveloped biotechnology sectors. The point estimate of the impact of working in a permissive state was negative, suggesting these scientists were less likely to move, but this coefficient did not reach standard significance levels.

The addition of interaction variables between state policies and all stem cell scientists (Model 2) or state policies and human embryonic stem cell scientists (Model 3) permits a more nuanced assessment of the impact of state policy toward stem cell research. In these models, factors specific to permissive or restrictive states but affecting all biomedical scientists (e.g. salaries, collaboration opportunities) should be captured by the state policy indicator variables. Similarly, factors specific to stem cell research but not related to policy (e.g. newness of the field), should be captured by the field indicator variables. The influence of restrictive and permissive policies on stem cell scientists' departure likelihood should be indicated by the coefficient of the appropriate interaction variable. In both models, the coefficient on the interaction variable capturing the impact of restrictive state policies on stem cell scientists is positive (more likely to move) and differs significantly from zero. All else being equal, working in a state with restrictive stem cell research policies was associated with a departure likelihood that was 1.1 higher for all stem cell scientists and 1.2 higher for human embryonic stem cell scientists. Neither the state policy nor the field indicator variables reached standard significance

levels in either model. These results suggest that policy factors rather than field-specific or other unobserved state characteristics were a key factor leading to the overall higher departure likelihood for stem cell scientists seen in figure 1. Estimated coefficients for the interaction variables capturing the impact of state stem cell policies on stem cell scientists in permissive states were negative, as expected if these scientists were less likely to move, but the coefficients did not reach standard significance levels.

When recruiting scientists, policymakers developing stem cell research policies must decide how best to deploy their limited resources. Figure 2 illustrates how stem cell scientists presented with a set of eight factors that could potentially affect decisions to move ranked these influences. This list was not designed to be comprehensive but rather focused on factors state policymakers might potentially influence. The strength of the collaborator network and the quality of the facilities at the new institution received the highest average scores. In general, principal investigators and their more junior colleagues ranked the factors similarly. However, the differences between the two groups were statistically significant in three cases. Principal investigators considered both the collaborator network ( $p < .01$ , t-test,  $n=321$ ) and the quality of facilities more important ( $p < .05$ , t-test,  $n=321$ ), while post-docs and graduate students considered salary more important ( $p < .1$ , t-test,  $n=321$ ). When asked to identify the single most important factor, nearly 37 percent of principal investigators selected the strength of the collaborator network, while 35 percent of post-docs and graduate students chose the availability of tenure. State funding for stem cell research was relatively less important, selected by 15 percent and 11 percent of respondents in the two groups, respectively. Seven percent of principal investigators and 4 percent of their more junior colleagues wrote in factors not included in the list of eight factors. These ranged from family matters to intellectual property

considerations. Deciding between actively funding research or providing a regulatory framework encouraging research is a key question for states debating stem cell research policies. Although scientists ranked both forms of state support below a variety of other factors, principal investigators indicated that state funding was slightly more important than state legislation without funding ( $P = .1$ , t-test,  $n=198$ ).

[Figure 2 here]

Scientists' preferences are shaped by a variety of factors. Some of these, such as the quality of facilities, may be under the control of state policymakers, but others, such as a climate or proximity to family, are outside of their control. Table 4 examines scientists' preferred states. It compares the percentage of human embryonic stem cell scientists who ranked each state among their top three when asked in which states they would prefer to study human embryonic stem cells with the percentage of other biomedical researchers who ranked each state among their top three to pursue research in their respective fields. Clear differences were observed between the preferences of human embryonic stem cell scientists and the other biomedical researchers. These differences were particularly pronounced for states with permissive stem cell research policies, such as California, Massachusetts and New Jersey, which 42 percent, 35 percent and 11 percent more stem cell scientists ranked among their top three states, respectively ( $P < .001$ , t-test,  $n=1,233$ ). These field-specific differences are presumably due, at least in part, to differences or scientists' perceptions of differences in the research environment for various types of biomedical research in these states. As awareness of state efforts to support stem cell research may



influence the preferences of stem cell scientists, the percentage of all stem cell scientists who believed each state was attempting to support research in the field is also indicated in table 4.

[Table 4 here]

Although time constraints prohibited asking stem cell scientists detailed questions about each state, the survey did include a short section on New Jersey's plans. Figure 3 illustrates the potential effects of a comprehensive program including \$150 million for new facilities and \$230 million for research funding on the preferences of stem cell scientists. Scientists were asked to rank their interest in studying stem cell biology in New Jersey if the two proposals passed or if they failed. Excluding scientists already based in New Jersey, the average ranking on a one to ten scale increased from 3.0 to 6.9, in the hypothetical situation that both proposals passed. This difference is statistically significant ( $P < .001$ , paired t-test,  $n=327$ ).

[Figure 3 here]

## **Policy Implications**

The survey results presented here should be both useful and encouraging for states considering supportive stem cell research policies. Stem cells scientists appear sufficiently mobile that states with permissive research policies and appealing recruiting packages should

stand a chance of successfully attracting researchers. Particularly notable is the finding of mobility within the principal investigator population, as these laboratory directors play critical roles in attracting post-docs and graduate students to a research institution. Post-docs appear quite mobile and a promising strategy for states trying to increase their stem cell scientist population may be to target these younger researchers with offers of tenure-track positions.

The amount of international mobility observed among the post-doctoral and graduate student populations should interest and, perhaps, worry U.S. policymakers. Although the increased tendency for junior stem cell scientists to consider leaving the country reported here is likely due to the greater proportion of international scientists studying stem cells in the United States, this situation itself may be cause for some concern. Indeed, if policy uncertainties lead a substantial number of junior U.S. scientists to avoid human embryonic stem cell research and if their slots at U.S. institutions are filled by international students intending to return home, the United States may find itself short of trained scientists in the field in the future. Even if these results reflect an impact only on foreign-born scientists, they auger poorly for the development of stem cell research in the United States, given the important role the foreign-born and trained have historically played in the U.S. scientific community (Stephan and Levin 2001). This survey was completed before the South Korean fraud scandal broke (Wade and Sang-Hun 2006) and it is possible that scientists who considered South Korea an appealing destination have since reconsidered.

These results may also alarm policymakers in states that appear to be in danger of having their top researchers lured away. Given the link between restrictive policies and stem cell scientists' future plans reported here, states with large biomedical research communities but restrictive research policies may be at particular risk. In Pennsylvania, for instance, principal

investigators were more likely than not to expect to leave their current institution with the next three to four years. The situation appears similar in Michigan, where top scientists have reportedly already left for more permissive environments (Anstett and Bell 2005).

Although the estimated impact of working in restrictive states on the departure likelihood of stem cell scientists was statistically significant (see table 3), the multitude of factors, besides public policy, that influence scientists' future plans complicate interpretation of this analysis. Not all of the relevant factors could be included in the surveys and this limitation in the study may account for the relatively modest explanatory power of the departure likelihood regression analysis. Because scientists at different stages of their career have different mobility patterns, this analysis was limited to principal investigators. This restriction reduced the likelihood of finding statistically significant results from the departure likelihood analysis, particularly when compared with the analysis on preferred states presented in table 4, in which the preferences of scientists at all levels could be included.

The various factors influencing individual scientist's decisions to move suggest a few general lessons. First of all, due to the importance of collaborators, states with a strong stem cell research community, such as California or Massachusetts, are already at an advantage in the recruiting process. This finding poses particular challenges for states with a small number of principal investigators in the field. In these states, top scientists are both the key to new recruiting and likely targets of recruitment efforts themselves. Since losing one or two principal investigators could have a considerable effect, it seems crucial that these states first work to ensure their top scientists are satisfied, perhaps by providing research funding or upgrading facilities. Once retention is assured, states can then use these scientists to help recruit others.

As many states are competing over the same scientists and trying to build strong research networks, first-mover advantage is a crucial issue. States that lose scientists early on may have a harder time recruiting in the future, while states that gain scientists may, as long as more positions exist, have a relatively easier time recruiting. California, by virtue of its 2004 vote, has a first-mover advantage in the field. This position is evidenced by several recruiting successes announced by research institutions in the state (O'Brien 2005; Office of Communication and Public Affairs 2005). Still, ongoing litigation continues to hinder implementation of the state's plans, suggesting this advantage may not be insurmountable.

The data suggest that states should consider tailoring their recruiting efforts to the seniority level of the researchers targeted. Principal investigators focused on the collaborator network and should probably be approached and recruited, whenever possible, by their potential collaborators, the state's top scientists. Post-doctoral researchers, perhaps frustrated by lengthy post-doctoral fellowships and the continuing shortage of tenure-track jobs (Garrison, Gerbi, and Kincade 2003) may be lured effectively with the promise of tenure-track positions. Of course, this strategy should not be pursued in isolation, as collaborators and facilities remain important to this group. These more junior scientists also appeared more sensitive to salary concerns, a factor that policymakers may be able to control.

The identification of preferred states for human embryonic stem cell research, by respondents using or likely to use these cells, reflects a variety of considerations. California, the first choice of 57 percent of respondents and among the top three for 89 percent, topped the ranking. This may reflect the impact of Proposition 71 as well as the state's strong academic and biotechnology sectors, among other factors. Massachusetts, a long-term research leader with substantial private support for stem cell research, was a strong second. New York, though

popular, was ranked similarly by both groups of scientists. This result suggests the state's popularity reflects general characteristics of the state more so than stem cell policy considerations. Stem cell scientists' ranking of New Jersey immediately following New York, seems relatively high and might reflect the importance of New Jersey's supportive environment for this research. In open-ended questions, respondents who preferred New Jersey, pointed to several factors, including the "state's seriousness on stem cell research."

The relatively low ranking of both Connecticut and Illinois and the low awareness of research support in these states suggests that hurdles must be overcome before their efforts can be declared successful. These findings may reflect, in part, the limited time between the announcement of these efforts and the survey. Alternatively, policymakers may envision using state funding to retain scientists rather than recruiting others. Still, higher awareness could only be beneficial. Connecticut, which sent representatives to the annual conference of the International Society for Stem Cell Research in 2006, appears to be taking steps to improve visibility of its program.

Although New Jersey has, thus far, offered only modest support for stem cell research, its proposals have been high profile and enjoy high awareness among scientists. These proposals encompass new facilities and financial support for research. The state has a small nucleus of stem cell researchers that could form the core of a strong collaborator network, but research is fragmented among several institutions. Given this background, the interest stem cell scientists expressed in working in New Jersey offers evidence that state policy can have a substantial impact. Without the initiatives, only 11 percent of respondents ranked their interest in studying stem cell biology in New Jersey between seven and ten (on a one to ten scale). Assuming that both proposals passed, however, 65 percent of scientists ranked their interest at these levels.

Crafting policy in a fast-moving and controversial field, such as stem cell research, poses numerous challenges. Lawmakers must try first to understand the science. Then they must try to predict its future directions and assess the influence of potential funding and regulatory schemes. The analysis presented here should help policymakers understand the impact of state stem cell research policy and more effectively address these challenges.

## Notes

1. Geron Corporation, a public company headquartered in California, funded the academic research that led to the first successful derivation of human embryonic stem cell lines. In exchange, the company was granted exclusive commercial rights to certain follow-up research, including the use of these cells to produce neural cells, cardiomyocytes and pancreatic islet cells.
2. For an updated list of approved lines, see the NIH human embryonic stem cell registry at <http://stemcells.nih.gov/research/registry/>
3. Public opinion data in the United States has shown consistent broad-based support for human embryonic stem cell research. A recent survey found that 67 percent of all respondents and a majority of respondents of both sexes, all ages, education levels and political affiliations either strongly approved or approved of this research. (Hudson, Scott, and Faden 2005).

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Table 1 – State Funding and Support for Stem Cell Research

<b>State</b>	<b>Grants Announced</b>	<b>Total Pledged</b>
California	\$12 million (April 2006) \$150 million (August 2006)	\$3 billion over 10 years
Connecticut	\$20 million (Expected in December 2006)	\$100 million over 10 years
Illinois	\$10 million (April 2006)	\$15 million
Maryland	\$15 million (Timing to be determined)	\$15 million
Massachusetts	No funding provided. Legislation ensures research is legal	
New Jersey	\$5 million (December 2005)	\$20 million

Table 2 – State Policies Restricting Human Embryonic Stem Cell Research

	<b>Restricts Embryo Research</b>	<b>Restricts Somatic Cell Nuclear Transfer</b>	<b>Restricts State Funding</b>	<b>Relevant Statutes</b>
Arizona			X	Ariz. Rev. Stat. § 35-196.04
Arkansas		X		Ark. Code § 20-16-1001 to 1004
Indiana		X	X	Ind. Code § 16-18-2-56.5 Ind. Code § 16-34.5-1,2 Ind. Code § 35-46-5-2
Iowa		X		Iowa Code § 707B.1 to 4
Louisiana	X			La. Rev. Stat. § 9:121, 122
Michigan	X	X	X	Mich. Comp. Laws § 333.2685 to 2692 Mich. Comp. Laws § 333.16274,16275 Mich. Comp. Laws § 333.26401 to 26404
Minnesota	X			Minn. Stat. § 145.421, 422
Nebraska			X	Neb. Rev. Stat. § 71-7606
North Dakota		X		N.D. Cent. Code § 12.1-39
Pennsylvania	X			18 Pa. Cons. Stat. § 3203 18 Pa. Cons. Stat. § 3216
South Dakota	X	X		S.D. Codified Laws § 34-14-16,17,20 S.D. Codified Laws §34-14-27
Virginia		X		Va. Code Ann. § 32.1-162.21, 22

(Compiled from Andrews 2004; National Conference of State Legislatures; National Conference of State Legislatures)

Figure 1 – Future plans of U.S. stem cell scientists.

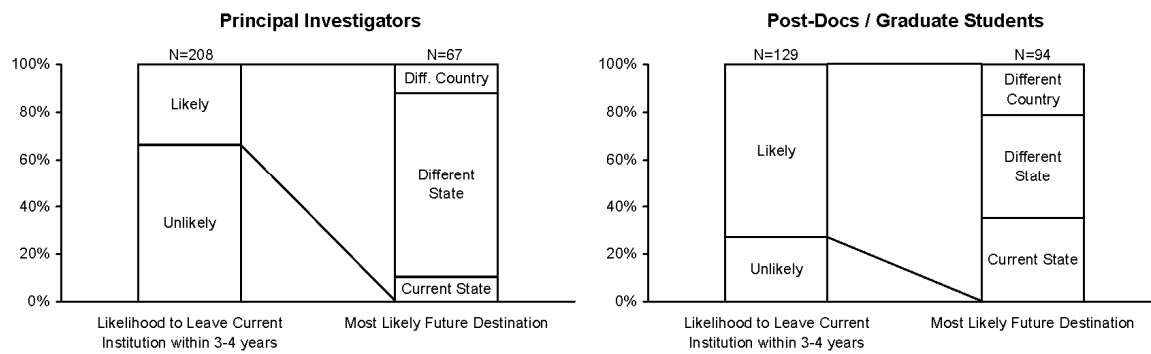


Table 3 –Regression Estimates Measuring Influences on Principal Investigator Departure Likelihood

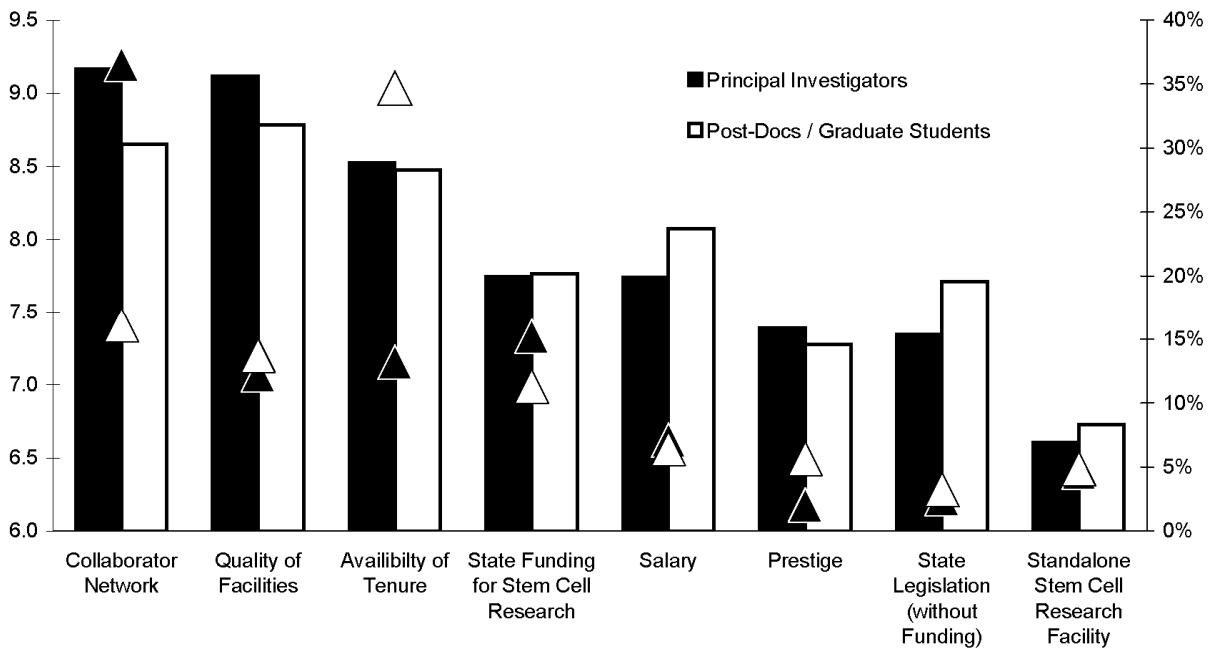
Independent Variable	Percent of Principal Investigator Respondents		Coefficient (Robust Standard Error)		
	Stem Cell	Other Biomedical	Model 1	Model 2	Model 3
Stem Cell Scientist	100	0	.1959 (.2197)	.0464 (.2894)	
Human Embryonic Stem Cell Scientist	71.3	0			0.2231 (0.3462)
Tenured	48.3	71.8	-.6251*** (.2036)	-.6462*** (.2039)	-.6506*** (.2038)
Restrictive State	21.1	21.4	.4328** (.2043)	.2510 (.2216)	.2948 (.2144)
Permissive State	30.6	19.6	-.1745 (.1961)	-.0852 (.2137)	-.0408 (.2094)
Born in US	64.7	80.1	-.3264 (.2762)	-.3300 (.2756)	-.3331 (.2751)
Educated in US	79.9	86.7	-.4314 (.3331)	-.4150 (.3321)	-.3838 (.3314)
Age 36 to 55	74.2	57.3	.4658 (.4087)	.4530 (.4026)	.4384 (.4024)
Age 56+	19.2	39.0	-1.1314*** (.4310)	-1.1481*** (.4260)	-1.1655*** (.4265)
Constant			4.5572*** (.4390)	4.5958*** (.4340)	4.5744*** (.4340)
Restrictive State * SC				1.1366** (.5453)	
Permissive State * SC				-.2927 (.5215)	
Restrictive State*hESC					1.1882* (.6474)
Permissive State*hESC					-.6424 (.5802)
R <sup>2</sup>			.1435	.1486	.1497
N			1020	1020	1020

\*Significant at the .10 level

\*\*Significant at the .05 level

\*\*\*Significant at the .01 level

Figure 2 – Factors Influencing Stem Cell Scientists’ Decisions to Move



Vertical bars (left axis) show the average ranking (on a one to ten scale) for each of eight factors and triangles (right axis) show the percentage of respondents who indicated that a specific factor was the single most important factor influencing their potential decision.

N=321 (197 principal investigators, 124 post-doctoral researchers / graduate students)

Table 4 – Preferred States for Research and Awareness of State Stem Cell Efforts

State	Percent of Scientists Ranking State in Top Three			Percent of All Stem Cell Scientists Aware of State Efforts to Support Stem Cell Research
	Human Embryonic Stem Cell	Other Biomedical	Difference	
California	89	47	42***	91
Massachusetts	62	27	35***	60
New York	22	18	4	29
New Jersey	15	4	11***	59
Maryland	13	11	2	13
Wisconsin	13	7	6**	28
Washington	11	16	-4	8
Connecticut	8	5	3	20
Colorado	6	14	-8***	2
Pennsylvania	5	11	-5**	6
North Carolina	5	13	-9***	3
Florida	4	9	-4**	7
Illinois	4	7	-3*	20
Oregon	4	10	-6***	4
Texas	3	10	-7***	3
Michigan	3	7	-4**	10
Georgia	2	4	-2*	1
N	250	983		344

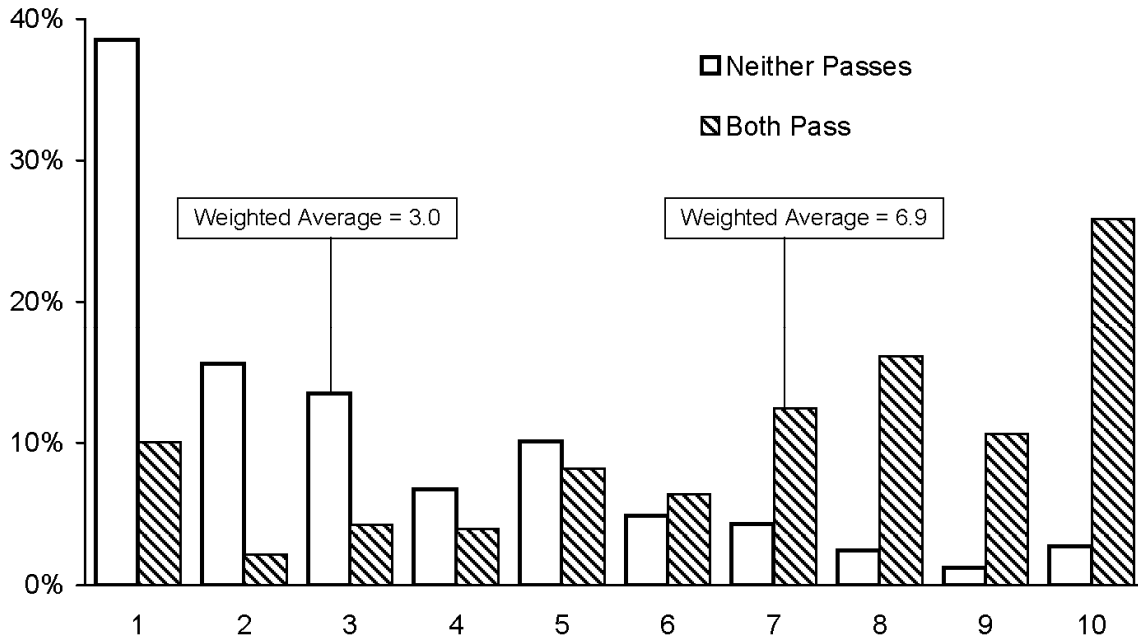
\*Significant at the .05 level

\*\*Significant at the .01 level

\*\*\*Significant at the .001 level



Figure 3 – Percent of Stem Cell Scientists Interested in Studying Stem Cells in New Jersey in Two Scenarios



(Interest Level, 1 = Very Uninterested, 10 = Very Interested)

N=327