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Impact of funding crunch on scientists' productivity: Evidence from the Bush stem cell policy experiment

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Abstract

In this study, I take advantage of a policy shock in the United States in 2001 that introduced restrictions on federal funding available for human embryonic stem cell (hESC) research to examine the impact of funding crunch on U.S. scientists' productivity and collaboration patterns. Employing difference-in-differences methodology, I find that this shock led to a decline in the research productivity of U.S. scientists in the hESC area relative to non-U.S. scientists. However, those U.S. scientists who had international ties prior to the shock experienced smaller impact relative to others. Moreover, I find that U.S. scientists expanded their cross-border ties following the policy shock, suggesting that they attempted to access funds and complementary resources outside the U.S. The results highlight the impact of funding shocks on research productivity and direction of individual scientists and also illustrate how scientists use international collaboration as a strategic tool to deal with negative shocks in their local institutional environments. The findings suggest that scientists actively engage in shaping their external institutional environment through their collaborative ties.

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ABSTRACT

In this study, I take advantage of a policy shock in the United States in 2001 that introduced restrictions on federal funding available for human embryonic stem cell (hESC) research to examine the impact of funding crunch on scientists' productivity and collaboration patterns. Employing difference-in-differences methodology, I find that this shock led to a decline in the research productivity of U.S. scientists in the hESC area relative to non-U.S. scientists. However, those U.S. scientists who had international ties prior to the shock experienced smaller impact relative to others. Moreover, I find that U.S. scientists expanded their cross-border ties following the policy shock, suggesting that they attempted to access funds and complementary resources outside the U.S. The results highlight the impact of funding shocks on research productivity and direction of individual scientists and also illustrate how scientists use international collaboration as a strategic tool to deal with negative shocks in their local institutional environments. The findings suggest that scientists actively engage in shaping their external institutional environment through their collaborative ties.

INTRODUCTION

Policy makers at organizational, regional, and national levels design numerous policies every year to shape the future of scientific and technological progress in the territories under their

control. Majority of these policies attempt to influence the level and direction of research by changing the distribution of available funds across research areas. Assuming that scientists actively and strategically respond to changes in their external environment (J. Furman, Murray, & Stern, 2012; Murray, 2010), the efficiency of such policies depends heavily on how accurately they take into account scientists' strategic reactions. However, there has been little empirical research investigating the impact of changes in the distribution of funds on scientists' research productivity and direction.

In this study, I attempt to address this gap by taking advantage of a policy shock in the U.S. that limited the research funds available to U.S. scientists for human embryonic stem cell (hESC) research. In 2001, the Bush administration placed severe restrictions on federal funding of hESC research due to ethical issues and instead increased funds for other subfields of embryonic stem cell research. This policy shock provides an excellent opportunity to investigate the impact of funding crunch on the productivity of U.S. scientists in the growing area of hESC research. It also enables me to explore how U.S. scientists reacted to the suppressed funding levels.

A passive view of scientists suggests that U.S. researchers would redirect their research away from hESC towards other areas of embryonic stem cell research where funding was more abundant. This was indeed a serious concern shared by both politicians and academics in response to the policy (Fletcher, 2001; Holden, 2005; S. Holland, Lebacqz, & Zoloth, 2001; Holm, 2002; A. Levine, 2004; A. D. Levine, 2006; McCormick, Owen-Smith, & Scott, 2009). Alternatively, to the extent that U.S. scientists were keen on pursuing their research in the growing hESC area, one would expect them to respond to this policy shock by actively seeking new funding sources. In particular, they could switch to the non-federal funds in the United States that emerged a few years after the introduction of the 2001 policy. At the same time, they could potentially seek more favorable and reliable hESC policies, financial resources and other

research materials outside the United States by expanding their international collaborative ties. These cross-border ties would not only help them access funds and research materials necessary for their research, but would also decrease their reliance on the uncertain and unfavorable institutional environment towards hESC research in the United States. Nevertheless, while these efforts towards finding new funding sources would partially address the decline in the available federal funding, I would expect them to negatively affect the productivity of U.S. scientists.

In order to empirically investigate these two views, I use longitudinal data on the research output of all the scientists in the Scopus database – the most extensive dataset on scientific publications – who have published at least one article in the field of stem cell research in the 15-year period from 1996 to 2010. Furthermore, I employ a difference-in-differences methodology to establish the causal impact of the 2001 policy on the research output, research direction and collaboration patterns of U.S. scientists compared to those of their counterparts in other developed countries with more permissive hESC policies.

My analysis provides a number of core findings. First, I find that the restrictions on federal funding of hESC research by the Bush administration in 2001 had a significant negative impact on the research output of U.S. scientists in the hESC area compared to that of scientists in other developed countries with more permissive policies towards hESC research. Second, I find little evidence of switch from hESC research to other embryonic stem cell research areas by the U.S. scientists. Third, I find that the impact of the policy was lessened after 2005 when large amounts of unconstrained hESC funding were introduced by several states. Fourth, I find an increase in the U.S. scientists' cross-border collaborations post-2001 in other countries with flexible hESC policies. Finally, the analysis also shows that those U.S. scientists who already had some cross-border collaborators prior to 2001 were affected less by the Bush policy.

The findings contribute to the growing literature on science policy by empirically examining the impact of changes in the funding levels on scientists' research productivity and direction. The results shed light on how scientists respond strategically to policies that influence their external institutional conditions (J. L. Furman & Stern, 2006; Jaffe, 2008; Lane, 2009; Lane & Bertuzzi, 2011; Murray, 2010). Furthermore, considering the growing globalized nature of science, the results underline how ignoring scientists' strategic responses can lead to international policy spillovers through cross-country collaborative ties (Vakili, McGahan, Rezaie, Mitchell, & Daar, 2013b). In addition, the paper contributes to the broad literature on scientific collaborations and provides further insights into the antecedents of international collaboration and its potential use as a risk aversion mechanism.

The paper is organized as follows: The next section summarizes the policy history of human embryonic stem cell research in the United States. Section 3 reviews the relevant prior research on this topic and presents the set of hypothesized predictions. Section 4 describes the empirical methodology to test them. Results and discussion follow.

HISTORY OF HESC RESEARCH AND POLICIES

Stem cells are undifferentiated biological cells that are capable of dividing and differentiating into specialized cell types such as skin cells, nerve cells, or muscle cells. There are two broad types of stem cells: adult stem cells, which can be found in any type of body tissues; and embryonic stem cells (ESC), which can only be derived from the inner cell mass of early-stage embryos. Adult stem cells are already successfully used in treating several severe conditions. However their big limitation is that they are lineage-restricted, meaning that they can only develop into particular forms of cells. A blood stem cell can differentiate into several types of blood cells, however, it cannot develop into nerve or brain cells. In contrast, embryonic stem

cells are known to be pluripotent, i.e., they can develop into any type of cell. Furthermore, they have the ability to self-propagate indefinitely under certain conditions.

Embryonic stem cells were first derived from mouse embryos in 1981 by two independent research teams. It took another 17 years before James Thomson and his research team at the University of Wisconsin-Madison made their breakthrough and developed a technique to grow and isolate human embryonic stem cells (Thomson et al., 1998). Because of their pluripotency and the fact that they are derived from human embryos, hESCs are acknowledged to have the highest potential among all types of stem cells to advance current clinical treatments and introduce novel therapies (Vogel, 1999). Yet, despite their scientific and economic importance, there have been ongoing political debates over hESC research (and, more broadly, ESC research) due to ethical concerns.

In the United States, the first laws prohibiting research on fetuses and embryos date back to 1973. However, these laws have not been rigorously enforced. In 1995, just a short while after the Clinton administration approved federal funding for research on leftover embryos created through in vitro fertility treatments, Congress passed the Dickey Amendment bill that prohibited any federal funds for use in research that could potentially result in the creation or destruction of a human embryo. It was during this period when Thomson made his breakthrough discovery of human embryonic stem cells in 1998 using private funding. Following Thomson's breakthrough and in recognition of the massive opportunities it opened up, in 1999, the Clinton administration loosened the policies governing federal funds available for embryonic research. Just a few months later, on August 9, 2001, the newly appointed President George W. Bush announced his administration's stem cell policy. Despite scientific community hoping for growing federal funds available for hESC research, the announced policy banned any federal funding for research on new hESC lines, while approving federal funding for existing hESC lines developed in the

United States or outside. The policy was later on repealed by President Obama through an executive order in March 2009.

THEORY

Prior Research on the Impact of the Bush Policy

Bush's stem cell policy act set off waves of concern in the scientific and regulatory communities (Fletcher, 2001; Holden, 2004; S. Holland et al., 2001; Holm, 2002; Johnson & Williams, 2007; Vogel, 2001). In April 2004, 206 members of Congress released a letter to President Bush urging him to relax embryonic stem cell research restrictions (Holden, 2005). Among other points, the letter highlights that "this promising field of research is moving overseas" and that "leadership in this area of research has shifted to the United Kingdom." Furthermore, the letter states that "it is increasingly difficult to attract new scientists to this area of research because of concerns that funding restrictions will keep this research from being successful." At a hearing by a Senate appropriations subcommittee in 2005, the then NIH Director, Elias Zerhouni, cited "mounting evidence" that numerous problems have been uncovered due to genetic instability of the aging 22 approved cell lines. In the same session, the Chair of the subcommittee, Arlen Specter, released several letters drafted by various institute directors warning that the NIH would fall behind other local and international institutions in the field due to restrictions (Holden, 2005).

In the wake of these concerns, several studies have attempted to document the impact of the Bush policy on the follow-on hESC research in the United States relative to other countries (J. Furman et al., 2012; A. Levine, 2004; Owen-Smith & McCormick, 2006; Scott, McCormick, & Owen-Smith, 2009; Vakili, McGahan, Rezaie, Mitchell, & Daar, 2013a). Using five less controversial biomedical research areas as the baseline, Levin (2004) reports that the share of hESC publications credited to U.S. scientists as a whole dropped considerably in 2003 and

remained at this lower level in 2004. Studying the same time period, Owen-Smith and McCormic (2006) also report a decline in the relative share of hESC publications by U.S. scientists compared to scientists elsewhere in the world at the national level. While both studies report a decline in the share of U.S. Stem Cell scientists, it is not clear whether this share is due to a decline in the productivity of U.S. scientists or rather an increase in the number of stem cell scientists in other regions of the world, particularly given the evidence of the growth in stem cell research in emerging markets such as China, South Korea, and Singapore (Vakili et al, 2013). Furthermore, both studies only examine the short-term impact of the Bush policy at the national level in the two years following the policy change due to data constraints. Looking at a much extended timespan, Vakili et al. (2013) find that the United States share of hESC publications stopped declining after 2003, increased slightly in 2004, and then remained consistently steady until 2010. Similarly, using a difference-in-differences methodology to analyze the causal impact of the 2001 policy, Furman, Stern and Murray (2012) also find that the United States' cumulative production of hESC research declined between 2001 and 2003 and rebounded in the subsequent years.

While these studies provide important insight into the impact of the Bush policy on the total share of the United States in hESC research, they do not report how these policies affected individual scientists' research productivity and direction. Moreover, these studies provide little explanation of how individual scientists responded strategically to the Bush policy intervention. Both Furman et al. (2012) and Vakili et al. (2013) provide evidence of an increase in the aggregate level of international collaborations involving U.S. scientists, suggesting that the recovery in the level of U.S. hESC publications might be related to the increased level of international collaboration. Yet their results are not fine-grained enough to establish a direct link between the quick recovery and increased amount of international collaboration.

Theoretical Development

Prior literature on incentives for innovation has largely focused on the appropriation mechanisms (Cohen et al., 2002; Gans & Stern, 2000; Gans & Stern, 2003), contractibility of outcomes (Gans & Stern, 2000), credit allocation (Merton, 1968; Azoulay, Stuart & Wang, 2014), and the problems associated with performance measurement (Holmstrom, 1989). More recently, Manso (2010) and Azoulay, Graff Zivin and Manso (2011) explored how the toleration of funding organizations for early failure would take the risk taking behavior of grant recipients. Both studies suggest that the higher toleration of early failure would spur move novel scientific inquiries and lead to the production of more high-impact publications. A few studies have also focused directly on the impact of receiving a grant on a scientist's productivity. Jacob and Lefgren (2011) estimated that receipt of an NIH grant with an average value of $1.7 million would lead to a 7% increase in the publication output of the recipient. Focusing on emerging economies, Benavente et al. (2012) report a positive effect from receiving FONDECYT grant (one of the major Chilean national funds) on the number of publications, but no significant effect on the quality of publications. While these studies all highlight the important role of funding organizations in incentivizing scientific research, few studies however have explored how changes in the distribution of funding available in a research domain would influence scientists' research output. In particular, we know little about how scientists would change their research direction and behavior in response to sudden funding crunches.

Faced with the 2001 Bush policy, U.S. researchers who had already invested or were planning to invest in hESC research suddenly found themselves in a new institutional setting with very limited funding available for research on new hESC lines. A passive view of scientists suggests that U.S. researchers who were mainly dependent on federal funding would shift their research

direction to either approved hESC lines or non-human ESC areas. This was indeed the intended purpose of the policy (Vogel, 2001).

However, there are several reasons to believe that such a shift in research direction was not in line with U.S. scientists' preferences and could thus potentially trigger their reactions to avoid this shift as much as possible. First, hESCs were considered to have the highest potential to cure severe human diseases (Vogel, 1999). Prior to 2001, when the Bush administration enacted their policy, hESC research had been growing faster than any other subfield of stem cell research. Furthermore, while U.S. scientists had the option to work on the approved hESC lines under the Bush policy, these lines had limited range of genetic diversity and many of them were contaminated with mouse embryonic feeder cultures by 2004 (Holden, 2004, 2005). Moreover, many new hESC lines with higher potential for therapeutic purposes were developed after the announcement of the Bush policy (Holden, 2004, 2005). Also, a more limited number of hESC lines mean higher competition among U.S. researchers to come up with new ideas and discoveries.

In order to partially circumvent the sudden drop of funding for hESC research in the United States, U.S. scientists could follow at least two strategies. First, they could replace federal funds with funds from non-federal agencies in the United States. This solution, of course, depends on the availability of such financial sources. About four years after the Bush policy announcement in 2001, many universities and private organizations started funding hESC research. For example, in 2005, Harvard University launched a fundraising campaign for hESC research focused on special therapeutic purposes. Several corporations such as WiCell, Inc., Geron, and BioTime had already invested in hESC research with financial interests in mind. Furthermore, the federal law did not impose any restrictions on whether states could invest in hESC research. While a few states such as Louisiana, Michigan, and Minnesota decided to re-enforce the

restrictive policies further at the state level, some other states took a completely opposite approach. The state of New Jersey became the first state to allocate funds for hESC research in 2005. Also, the State of California took out $3 billion in bond loans to fund hESC research in 2004, planning to invest $300 million per year for 10 years. Table 1 compares the yearly total amount of federal and state-level funds allocated to hESC research. While the first state-level funds did not materialize until four years after the Bush policy, they quickly surpassed the federal funds in just two years. To the extent that U.S. scientists were keen on continuing their research in hESC, they could seek funding from these non-federal sources as a strategic response to the Bush policy shock. There are reports indicating that the six states of California, Connecticut, Illinois, Maryland, New Jersey, and New York funded more hESC research than the federal government (Fossett, 2007).

One problem with this solution was that these alternative sources of funding were not abundantly available until four years after the introduction of the policy. Another major issue with this strategy was that, while it could resolve the lack of financial resources, it could not address the lack of other supplementary resources required for hESC research such as repositories for new hESC lines that were not abundantly available within the United States.

However, non-federal agencies were not the only sources from which U.S. scientists could seek financial resources for their hESC research. A second channel through which U.S. scientists could obtain both funds as well as other supplementary resources for their hESC research was by collaborating with funded scientists in countries with more flexible policies. Compared to the previous strategy, international collaboration is, on average, a more costly option. In a series of works, Cummings and his colleagues argue that the institutional, geographic, and temporal distances between collaborators in scientific or non-scientific environments leads to lower levels of productivity and output quality due to higher costs of coordination (Cummings, 2011;

Cummings, Espinosa, & Pickering, 2009; Cummings & Kiesler, 2005, 2007). In the case of hESC research, these cross-border collaborations were even more challenging due to different international policies governing the hESC research and the need for an appropriate division of labor that could allow such collaborations to take place (J. Furman et al., 2012).

Yet despite these costs, international collaboration had two important benefits over a switch to non-federal sources of funding within the United States. First, unlike the private- and state-level funds within the United States that emerged primarily with considerable delay, there were plenty of funds available outside the United States at the same time that the Bush policy was announced. In contrast to the United States several countries, including the United Kingdom, Sweden, Canada, China, Israel, and South Korea increased their legal support and funding for hESC research to gain a competitive advantage in this promising field. By expanding their collaborations overseas, U.S. scientists could potentially gain access to these funds immediately. In addition, international ties would not only help U.S. scientists access new financial sources, they would also offer a channel through which U.S. scientists could obtain other required inputs for their research, such as repositories for new hESC lines.

Furthermore, by crossing U.S. national boundaries, international collaboration could work as a diversification strategy through which U.S. scientists reduce their reliance on resources within the U.S. territory. Numerous studies on risk management have regarded diversification as an important strategic means to deal with uncertainties in the external environment (McNeil, Frey, & Embrechts, 2010). The same idea can be applied to scientists and the strategies they would pursue to deal with uncertain external environments. Hence, the high uncertainty in the U.S. policy environment regarding hESC research can arguably justify the higher cost associated with international collaborations.

While both of these strategies could help U.S. scientists circumvent the lack of federal funding for hESC research, pursuing them would necessarily require some time investment. Unlike the procedure for acquiring federal funding which is well organized and well known by scientists, accessing these two alternative sources of funding would not be as straightforward and hence require making new connections and searching through indirect ties with non-federal and foreign funding agencies. Hence, the investment in time and effort required for finding and accessing non-federal funds would essentially substitute the time and effort put into actual research, leading to a decline in the research productivity of U.S scientists, at least in the short-term. Also, since these alternative funds are not as abundant as federal grants, one would expect that only a fraction of U.S. scientists manage to successfully find alternative sources of funding.

In summary, I expect U.S. scientists to experience a decline in their research productivity in hESC in the short run. However, with the growth in the level of international collaborations and also the rise of state-level and private funds, I expect to see a bounce back in the U.S. scientists' research output. In particular, I expect an increase in U.S scientists' level of international collaborations with scientists in countries with flexible hESC policies post-2001. This also implies that those scientists who already had some cross-border collaborative ties pre-2001 could respond faster to the Bush policy shock by relying more heavily on the international sources and thus experienced less impact due to the policy shock.

EMPIRICAL METHODOLOGY

My empirical strategy includes two steps. The first step involves estimating the impact of the Bush policy shock on the subsequent research output of U.S. scientists in hESC and other embryonic stem cell areas. In order to capture the dynamic impact of the policy, I will measure the change in U.S. scientists' research output and direction in three time periods: the three years

following the policy (2002-2004), the three years following the rise of state and private funds (2005-2007), and finally the three years following the election of President Obama and the repeal of the policy (2008-2010). The main challenge to estimating the causal effects of these events is that we cannot observe what would have happened to U.S. scientists' research output should the Bush policy and the strategic responses it potentially triggered had not happened, i.e., we cannot observe the counterfactual. A change in the variables of interest can be driven by these events, or some other unobservable factors. For example, a possible decline in the hESC research output of U.S. scientists after the 2001 Bush policy could be driven by a general drop in hESC research at the global level. Alternatively, it could be driven by an increase in the global competition level in the field due to a sudden surge of scientists interested in this area.

In order to deal with this issue, I compare the changes in the research output of U.S. scientists (treated sample) after the Bush policy intervention (treatment) to those of another similar group of scientists (control sample) using a difference-in-differences methodology. The main underlying idea is that, under appropriate conditions, the trends for the control sample provides a proxy for the unobservable counterfactual trend for the treated sample (P. W. Holland, 1986; Imbens & Wooldridge, 2009). Thus, assuming that control and treated samples are in fact comparable and similar, any difference between their outcome trends after the treatment can be interpreted as the causal impact of the treatment on the treated sample. In the results section, I provide descriptive statistics to support the similarity assumption.

For this difference-in-differences estimation, I use the following equation:

(1) $$ResearchOutput_{it} = f(\beta_1 US_{researcher_i} * [2002-2004]_t + \beta_2 US\_researcher_i * [2005-2007]_t + \beta_3 US\_researcher_i * [2008-2010]_t + \mu_i + \gamma_t + \varepsilon_{it})$$

where $ResearchOutput_{it}$ stands for the quality adjusted publication count by scientist i in year t in hESC or non-human embryonic stem cell research, $US\_researcher_i$ is one if scientist i is a US-based researcher and is 0 otherwise, $[2002-2004]_t$, $[2005-2007]_t$ and $[2008-2010]_t$ are 1 within their respective time periods and are 0 otherwise, μ_i is a researcher fixed effect, and γ_t is a year fixed effect. β_1, β_2 and β_2 are the main coefficients of interest and capture the marginal difference between U.S. researchers and researchers in the control sample during each of the constructed time periods. Including researcher fixed effects control for idiosyncratic differences between different researchers. Also, including year fixed effects control for the macro time trends. To construct the quality adjusted measure of research output, each publication is weighted by the total number of citations it has received from subsequent publications. The model is estimated using a conditional fixed-effects Poisson model with cluster-robust standard errors. The clustering is at the individual scientist level.

I use the same estimation model to examine whether those U.S. scientists who already had access to more diversified sources of funding through international ties pre-2001 were less affected by the 2001 policy shock or not. To test this idea, I repeat the estimation only for the groups of U.S. scientists who had one or more publications with non-U.S. co-authors in the four years before the policy announcement (from 1996 to 2000). The control sample would also include only those non-U.S. scientists in the developed countries with flexible hESC policies who had one or more international collaborations during the same period. The estimating equation is essentially the same as equation (1).

In the second step, my goal is to examine the two hypothesized strategic responses by U.S. scientists after the Bush policy in 2001. For the change in the amount of U.S. scientists' international collaborations in response to the policy, I use the following linear difference-in-differences estimations:

(2) $share\ of\ internaional\ collaborations\ in\ hESC_{it} = \beta_1 US_{researcher_i} * [2002-2004]_t + \beta_2 US\_researcher_i * [2005-2007]_t + \beta_3 US\_researcher_i * [2008-2010]_t + \mu_i + \gamma_t + \varepsilon_{it})$

where $share\ of\ internaional\ collaborations\ in\ hESC_{it}$ is the ratio of hESC publications by scientist i in year t that involves at least one international collaborator from a country with a flexible hESC policy over her total number of hESC publications. β_1, β_2 and β_2 again capture the change in the level of international collaboration of U.S. scientists within each of the time periods respectively.

Data

The data for this study is collected by searching the Scopus on-line database from 1980 to 2012 for all articles that mention keywords relevant to Stem Cell in their title or abstract. With more than 47 million records from about 18,500 peer-reviewed scientific journals, Scopus is currently the most comprehensive and encompassing database of scientific publications. More than 20 percent of the articles recorded in Scopus are in languages other than English and more than half of them are assigned to scientists outside the United States.[1] For the purpose of this study, I excluded all the conference proceedings, reviews, and reports as well as all publications before 1995 and after 2010. This resulted in 65,759 articles in the stem cell area. Next, all the articles were categorized into different subclasses based on particular word combinations (such as "human embryonic stem cell," "hESC," "stem cell," etc.) in their title and abstract. This resulted in 1,658 articles on hESC and 3,896 articles on non-human embryonic stem cell (ESC excluding hESC). In order to assess the reliability of the classification, an expert in the field reviewed 200 randomly selected articles in detail and manually categorized them. Comparing the automatic

[1] Every article in Scopus has an English abstract.

categorization based on keywords to results from the manual categorization by the expert revealed more than 90 percent accuracy.[2]

In the next step, for each article I identified the list of authors and their affiliations. Scopus assigns a unique identifier to each author in the database. Taking advantage of these unique identifiers, I created longitudinal yearly records of all the publications in each research category for each unique scientist in the sample. In less than 5 percent of the total sample, some author data was missing or could not be extracted successfully and, hence, was dropped. Furthermore, Scopus reports the number of citations that each publication has received from subsequent works published until the time of data collection. Following prior research in this stream, I created a yearly citation-weighted publication count in each research category for each scientist in the sample. I use this weighted publication count as the measure of scientists' research output. The issue with the simple publication count is that it does not account for the heterogeneity in the quality of different publications. Assuming that the number of citations that a publication receives from subsequent research is a reliable proxy of its quality, this weighting scheme can therefore account for quality differences in the publications sample (J. Furman et al., 2012; J. L. Furman & Stern, 2006; Harhoff, Narin, Scherer, & Vopel, 1999; Trajtenberg, 1990).

Subsequently, I identified the country of affiliation for each author on each article by analyzing the text of the affiliation. In cases that multiple affiliations were assigned to an author on a particular article (about 19 percent of the time), only the first affiliation was used. Next, using the country data, I determined the location of each author in each year from 1995 to 2010. Each country in the sample is then categorized as either "constrained" or "flexible" in its policy regime with regards to hESC research based on an analysis of the public records on regulations,

2 Both the false positive rate and false negative rate were below 10 percent.

laws, and policies implemented in each country between 1995 and 2010. Countries classified as "constrained" include the United States, Austria, Colombia, France, Germany, Italy, Norway, Poland, Slovakia, and Tunisia. Countries in the "flexible" category are Argentina, Australia, Belgium, Brazil, Canada, Chile, China, the Czech Republic, Denmark, Finland, Greece, Hong Kong, Hungary, Iceland, India, Iran, Israel, Mexico, the Netherlands, New Zealand, Portugal, Russia, Singapore, South Africa, South Korea, Spain, Sweden, Switzerland, Taiwan, Turkey, and the United Kingdom.

Also, each country is further labeled as "developed market" or "emerging market" according to its status in the UN database. Countries marked as "developed market" include the United States, Canada, Japan, countries of Western Europe (the United Kingdom, Germany, the Netherlands, Sweden, France, Italy, Spain, Austria, and others), and the Antipodes (Australia and New Zealand). Countries in the "emerging market" category with active RM scholars are those in Asia (China, South Korea, Singapore, Taiwan, India, Malaysia, Hong Kong, Thailand, and others), Latin America (Brazil, Mexico, Argentina, and others), the Middle East (Israel, Turkey, Iran, Saudi Arabia, and others), Eastern and Central Europe (Russia, Czech Republic, Hungary, Poland, Romania, and others), and Africa (Egypt, Tunisia, South Africa, and others).

Using the above categorizations for the countries in the sample and also the co-authorship data on each article, for each author I calculated the yearly average number of international co-authors as well as the yearly number of publications that involves at least one cross-border collaborator from emerging countries with flexible hESC policies.

EMPIRICAL ANALYSES

Descriptive Statistics

Table 2 presents some summary statistics for the research outputs and collaboration patterns of hESC scientists in the treated and control samples in 2000. Both samples include those scientists who were active in SC in 2000 and later started publishing in hESC. The difference between the two samples and the calculated t-stats are reported in the third columns. There is no significant difference in the mean publication counts, mean weighted publication counts, and mean number of co-authors between the treated and control samples in the year prior to the policy change. Overall, the equality-of-distributions tests and summary statistics suggest that treated and control samples were quite similar before the Bush policy shock and thus satisfy the second assumption for the DID estimation.

As mentioned in the empirical methodology section, one of the conditions for a reliable DID estimation is the similarity between treated and control samples pre-treatment. Figure 1 shows the estimated density function of publication counts in SC for the treated and control samples in 2000. The graphs suggest that the treated and control samples were quite similar in terms of research productivity in SC. I further performed a Kolmogorov-Smirnov equality-of-distributions test to compare the distribution of SC and ESC researchers within the United States to those in other developed countries with flexible policies in 2000. All three tests rejected a significant difference between the distribution of U.S. and non-U.S. researchers in terms of research output in these areas of research in 2000.

Estimation results

The results from estimating equation 1 are presented in Table 3. All models are estimated using a conditional fixed-effects Poisson model. Model 1 estimates the year-by-year change in the research output of U.S. scientists relative to that of other scientists in developed countries with flexible hESC policies. The model only includes scientists who had at least one publication in the broader field of stem cell research pre-2001. Each scientist enters into the sample on the year of her first stem cell publication. The sample structure and the inclusion of scientist fixed effects guarantee that the estimated coefficients solely reflect the changes in each scientist's research output. The estimates show a significant decline in U.S. scientists' hESC publications in the three years following the policy announcement. The insignificant, yet negative, coefficients for the subsequent time periods show some recovery and growth in their research output. The results support the hypothesized predictions. They are also consistent with reported findings in previous studies (J. Furman et al., 2012; A. Levine, 2004; McCormick et al., 2009; Vakili et al., 2013a).

In order to test a potential short-term switch from human to non-human embryonic stem cell research post-2001, in model 2, I estimate the relative change in the U.S. scientists' research output in non-human embryonic stem cell research. The results show no significant change in U.S. scientists' non-human embryonic stem cell publications during any of the time periods following the policy announcement. The results suggest that U.S. scientists did not switch their research direction to other embryonic areas with more abundant funding.

Model 3 repeats the estimation in model 1 only for the scientists who had one or more international collaborations prior to the policy shock. The control sample includes those non-U.S. researchers in developed countries with flexible hESC policies who also had international ties in pre-2001. Estimated coefficients are negative but none of them are significant. The results

suggest that U.S. researchers with some prior international ties were less affected by the Bush policy. These results together suggest that the 2001 Bush policy indeed had a short-term negative impact on the U.S. scientists' research output in hESC. Furthermore, the results suggest that, consistent with the prediction, U.S. scientists managed to recover their hESC research output subsequently, despite the fact that the policy was still in effect until 2009.

Table 4 illustrates the results for the impact of the 2001 policy on the collaboration patterns of U.S. researchers and the research productivity of their collaborators. Model 1 shows the impact of the policy on the share of U.S. scientists' hESC publications with at least one cross-border collaborator. Consistent with the prediction, the results suggest that U.S. scientists significantly increased their cross-border publications with non-U.S. scientists from countries with flexible hESC policies in the three years following the Bush policy. With the emergence of state-level and private funds, the difference in the international collaboration levels of U.S. and non-U.S. scientists disappear. Model 2 presents the estimation results for the impact of the 2001 policy on the share of U.S. scientists' internationally collaboration publications in non-human embryonic stem cell research. The estimated coefficients are either small and insignificant or negative, suggesting no increase in the level of international collaboration of U.S. scientists in other embryonic research areas.

DISCUSSION AND CONCLUSION

This paper provides a detailed analysis of the impact of the restrictions put on the federal funding of hESC research in the United States in 2001 on U.S. scientists' research output and behavior in hESC. The results show that U.S. hESC researchers experienced a decline in their research output for a while after the 2001 policy, but recovered to some extent subsequently. The paper also presents an in-depth analysis of how U.S. scientists responded strategically to the changes in

the policy environment by switching to expanding their international collaborative ties post-2001 policy. The results contribute to the literature on scientific collaboration by highlighting how scientists engage in strategic behavior in order to mitigate negative policy shocks that affect the resources they require for their research. The results suggest that scientists do not easily conform to the restrictive policies that are imposed on them, rather that they actively seek strategies to maintain their research agenda in the global community (Bozeman & Corley, 2004; Murray, 2010). The results particularly call into question the efficiency of restrictive policies governing the funds in shaping scientists' research direction and portfolio. The findings illustrate how scientists' strategic choices in response to the introduced policies can undermine the intended purpose of these policies and lead further to unintended consequences.

This issue is particularly important when we consider the current globalized nature of science. A new policy that limits access to a particular resource in one country can easily become ineffective due to an unintended increase in cross-country collaborations that facilitates access to that resource in other countries. This can potentially lead to knowledge spillovers and persuade scientists to engage in collaborations that would otherwise not be planned or desired. On the flipside, facilitating access to a particular resource for a group of scientists can attract new collaborators seeking to take advantage of new opportunities. Considering the longevity of collaborative ties, encouraging international collaborations can lead to long-term positive impacts on national scientific progress and technological advancement. There is large evidence that collaboration is an important channel through which tacit knowledge and research capabilities can be transferred (Inkpen & Pien, 2006; Jones, 2009; Mowery et al., 1996; Powell, 1998; Singh, 2005). Hence, understanding how scientists actually shape and alter their collaborative ties not only helps better anticipate the impacts of policies, but also provides new levers for policy makers to advance local scientific and technological capabilities through

attracting international collaborators. There is anecdotal and qualitative evidence that several emerging markets such as China, South Korea, and Singapore have boosted their scientific and technological progress by providing supportive institutional environments for international collaboration and complementing that with a considerable amount of resources for research in several areas of science including stem cell, nanotechnology, and biotechnology (Fox, 2007; Greenwood et al., 2006; Hwang, 2005; Xin, 2007).

The paper also provides a new potential explanation for why scientists engage in international collaborations. Previous studies have mentioned incentives such as sharing ideas, exchanging data, tackling global societal challenges, and improving national competitiveness as possible drivers of cross-border collaborations. The results from this study suggest that scientists may expand their international ties in order to diversify their research resources and shield themselves against uncertainties in their national legal environment.

The findings in this paper also point to several opportunities for future research. First, this study looks at only one of the U.S. scientists' strategic responses to the introduced hESC policy in 2001. Studying other potential reactions, for instance, moving to states or countries with more supportive policies or quitting institutions that are more heavily dependent on federal funding (such as public universities) and joining more independent private institutions, provide further insight into scientists' strategic behavior. Furthermore, this study mainly focuses on the impact of the 2001 Bush policy on the productivity and collaboration patterns of U.S. scientists. As the results suggest, a considerable amount of cross-border policy spillovers have occurred through international collaborative ties. Studying these policy spillovers in a broader context provides another avenue to better understand the impact of national policies on the global scientific progress. Finally, the growth of cross-border collaborative ties with scientists outside the United States, particularly in emerging markets, as a response to the 2001 U.S. policy provides an

excellent context to study how internationalization of knowledge production impacts the knowledge commercialization and use further down the value chain.

Figure 1: Estimated density function of Stem Cell publications by U.S. hESC scientists versus hESC scientists in other developed countries with flexible hESC policies in 2000

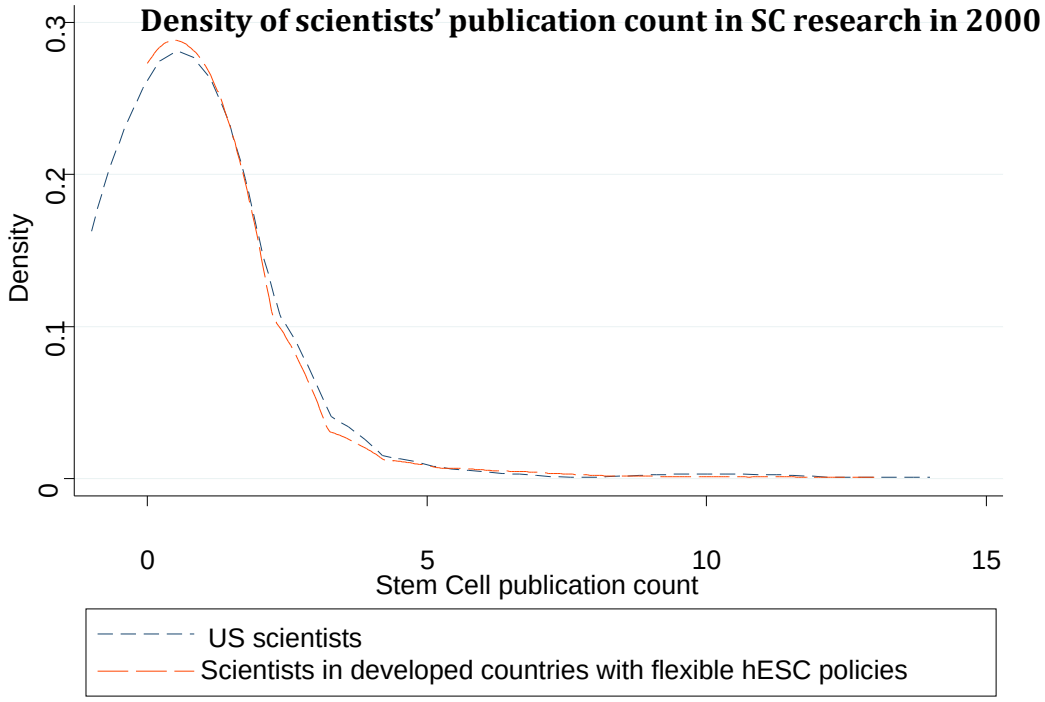

Table 1: Annual federal and state-level grants for hESC research

year	Total federal grants for hESC research	Total state-level grants for hESC research
1999	0	0
2000	0	0
2001	0	0
2002	10.1 m$	0
2003	20.3 m$	0
2004	24.3 m$	0
2005	39.6 m$	5.1 m$
2006	37.8 m$	73.2 m$
2007	88.1 m$	246.2 m$
2008	142.6 m$	426.1 m$
2009	165.2 m$	519.5 m$
2010	123.0 m$	214.3 m$

Table 2: Summary statistics

Variable	U.S. scientists with at least one hESC publication	Scientists in developed countries with flexible hESC policies with at least one hESC publication	Difference
Number of scientists	315	258	57
Stem cell publication count	0.860 (1.539)	0.705 (1.377)	0.155 (p= 0.210)
Weighted stem cell publication count	113.492 (341.578) [n= 315]	95.604 (273.900) [n= 258]	-17.887 (p= 0.496)
Embryonic stem cell publication count	0.063 (0.244)	0.039 (0.213)	-0.024 (p=0.202)
Weighted embryonic stem cell publication count	17.062 (151.684)	16.797 (102.729)	16.916 (p= 0.980)
Number of stem cell publications with international collaborators	0.146 (0.442)	0.190 (0.490)	-0.044 (p=0.260)

Table 3: The impact of Bush policy on U.S. scientists' research output in hESC and other embryonic research areas

Model:	**(1)**	**(2)**	**(3)**
Sample:	scientists with at least one pre-2001 publication	scientists with at least one pre-2001 publication	scientists with at least one pre-2001 publication with international collaborators
Dependent Variable:	weighted hESC publication count	weighted non-human embryonic stem cell publication count	weighted hESC publication count
Regression:	Conditional fixed-effects Poisson with robust standard errors	Conditional fixed-effects Poisson with robust standard errors	Conditional fixed-effects Poisson with robust standard errors
US Scientist × [2002-2004]	-1.741* (0.934)	-0.030 (0.348)	-0.550 (0.852)
US Scientist × [2005-2007]	-1.141 (0.968)	0.166 (0.316)	-0.712 (1.004)
US Scientist × [2008-2010]	-0.948 (0.983)	0.186 (0.313)	-0.679 (1.048)
Scientist fixed effects	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes
Observations	3,601	7,440	1,527
N. of Scientists	489	1191	194
Chi-squared	212.77**	279.66**	127.36**

Table 4: The impact of Bush policy on U.S. scientists' cross-border collaborations

Model:	**(1)**	**(2)**
Sample:	scientists with at least one pre-2001 publication	scientists with at least one pre-2001 publication
Dependent Variable:	Share of hESC publications with international collaborators from countries with flexible hESC policies	Share of other embryonic publications with international collaborators from countries with flexible hESC policies
Regression:	Panel OLS with fixed effects	Panel OLS with fixed effects
US Scientist × [2002-2004]	0.523**	0.041
	(0.179)	(0.065)
US Scientist × [2005-2007]	0.069	0.000
	(0.105)	(0.044)
US Scientist × [2008-2010]	0.117	-0.171**
	(0.108)	(0.036)
Scientist fixed effects	Yes	Yes
Year fixed effects	Yes	Yes
Observations	896	2,082
N. of Scientists	539	1,345

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