Public Research, Technology Licensing, and IP Commercialization; Mapping Interdependencies in the Cell Therapy Field

by

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Abstract
We examine interdependencies between public funding for science, corporate R&D, and IP commercialisation. We use the US federal funding moratorium on specific types of Human Embryonic Stem Cell (hESC) research over the period 2001 and 2009 as a case study to examine these interdependencies. Our data show that the US funding moratorium not only slowed down scientific progress, but also reduced the number of R&D projects initiated by US companies in the cell therapy field, and increased failure rates for R&D projects that did get underway. These effects were specific to the US, and negatively affected the international competitive position of the US cell therapy sector. Our findings provide important new insights into the role of science funding in supporting technology commercialization in R&D-intensive sectors.

INTRODUCTION

The creation of intellectual property (IP) in technology-intensive industries such as the bio-, nano-, and clean- technology industries draws on resources from across the realms of science, industry, and the state (e.g. Kenney 1986; Pisano 2006; Powell et al. 2005; Zucker et al. 1998). While existing scholarship has expanded our appreciation of the dynamics governing the interplay between scientific and industrial research communities in product innovation processes, our appreciation of the role of the state as the chief patron of public research in shaping these dynamics remains less well developed. Accordingly, we will focus in this paper on uncovering interdependencies that link science policies emanating from the realm of the state, to the development of novel IP by scientific and industry research communities.

Policy levers that control public funding for basic and applied research have been particularly potent as a mechanism through which the state asserts itself in the development of R&D in high-tech industries. For example, in Silicon Valley, the US region with the largest amount of early stage funding for biotechnology firms, private venture capitalists provided US$ 104 Million in seed and start-up funding for biotechnology firms in 2012 (Thomson Reuters 2014). In contrast, federal spending on biomedical research at the region's three research universities through the National Institutes of Health (NIH) alone for 2012 was US$ 258 Million (NIH 2014a). In addition, the same NIH distributed US$ 41 Million to Silicon Valley start-up firms through its Small Business Innovation Research (SBIR) grant scheme during that year (NIH 2014b). Although the social and economic impact on industrial activity has always formed a critical political rationale for public funding support for science, the mechanisms through which public funding support for science shapes new product development activities and the broader R&D environment in industry deserve further exploration.

We will map interdependencies between public funding for science, technology licensing, and IP commercialisation in science-based industries. We will highlight how the funding environment in a field of scientific scholarship does not only play an important role in supporting the scientific output of universities in terms of publications; It is also critical in regulating the flow of commercial knowhow from universities to industry. Also, we show how the scientific funding environment plays an important role in shaping decisions by managers about which IP commercialisation projects to focus on, and the ability of managers to bring these projects to a successful conclusion. Finally, our results indicate that the negative effects on industrial R&D of scientific funding restrictions most affect the geographic localities where these funding restrictions are enacted and that spill-over effects to other localities are limited.

We will assess the outlined interdependencies by examining the impact of a geographically localised policy shock restricting scientific funding for a specific line of scholarly enquiry. Specifically, we examine changes in the commercial R&D landscape in the nascent global cell therapy industry following the imposition of a federal funding moratorium on research involving new human embryonic stem cell (hESC) lines in the US in 2001. Comparing the impact of this moratorium in the US with the situation in other countries where no moratorium was put in place has proven to be a fruitful 'natural experiment' setting for examining the impact of scientific funding cuts on the advancement of science (Furman et al. 2012; Owen-Smith 2006), and on the regional mobility of scientists (Levine 2008; 2012).

In our study, we examine the impact of the US federal hESC research funding moratorium on the environment for commercialising IP in the global cell therapy sector. To this end, we created a unique dataset with information about 868 worldwide university-industry deals in the cell therapy field from 1986 until 2013, and the advancement of 633 IP commercialisation

projects involving new cell therapies initiated by life sciences companies from across the globe over the period 1989 until 2013. We use these data to analyse the impact of the hESC research funding moratorium on the US cell therapy sector and contrast the development of this sector with that of cell therapy sectors of countries not affected by this moratorium. We find that apart from diminishing the role of universities in commercial markets for ideas in the cell therapy field, the US hESC research funding moratorium reduced the propensity of US firms to initiate novel IP commercialisation projects in the cell therapy field as compared to firms elsewhere. Moreover, firms that did initiate novel cell therapy projects experienced a diminished ability to bring these projects to a successful completion. Using comparative data on the number of IP commercialisation projects in the cell therapy projects started and completed by overseas firms we highlight that the scientific funding moratorium undermined the competitive position of the US cell therapy industry. Finally, we find evidence of spill-over effects that suggest that the detrimental consequences for the development of commercial IP by US firms in the cell therapy sector reached beyond the hESC sub-fields targeted by the federal funding moratorium.

We will proceed as follows. First, we will specify the interdependencies between public funding for science, technology transfer, and successful IP commercialisation that are the focus of our paper. We then introduce the global cell therapy sector, and US federal funding restrictions on hESC research as the empirical context in which to test our hypotheses. After presenting our results, we will discuss limitations, implications, and avenues for further research.

THEORY

Public research and its role in spawning novel R&D projects in industry

Over the past decades, academic institutions have moved to the forefront as a critical source of innovative input for product development activities in key sectors of contemporary

economies (Cohen et al. 2002; Laursen and Salter 2004; Liebeskind et al. 1996; Mansfield 1998; 1991; Mowery et al. 2004). The number of university patents increased 15-fold, while the overall number of patents increased by less than 50% over the period 1965-1992 (Henderson et al. 1998). Moreover, universities have accumulated significant patent portfolios in fields such as biotechnology: Over the period 1990-1994, the proportion of biotechnology patenting by universities and government entities increased from 15% to 20% (Adelman and DeAngelis 2007). Thus, the transfer of university-owned IP to industry now constitutes a key mechanism through, which publicly funded research is transferred to industry in the life sciences.

In assessing the impact of restrictions on public research, on commercial downstream R&D, economists have long recognized the difficulty for private actors to take over the role of public research in sustaining innovation and economic performance in technology-intensive industries (Arrow 1959; Nelson 1959). Albeit socially (and economically) valuable, risks and uncertainties associated with scientific research and difficulties to *ex ante* determine its applications, are seen as preventing private business to take on this role. Accordingly, there is a clear expectation in the economics and management of innovation literature that if the state withdraws its support for public research, this will be detrimental to the development of commercial markets for IP. We are interested in examining more closely the detrimental effect of funding restrictions on the R&D environment in industry.

First, a weakening of support for public research will diminish the flow of ideas from universities to firms, around which novel IP commercialization projects are organized. Previous work highlights the importance of this flow in supporting corporate R&D pipelines. One survey published in the 1990s highlights that 15% of new products developed by industry over the period 1986-1994 could not have been developed without recent advances in academic research,

and that this number was substantially higher in industries such as the life sciences industry, where 31% of new drugs and medical products were tied to recent advances in academic research (Mansfield 1996). Another 1994 survey finds that 41,4% of pharmaceutical drugs R&D builds on findings from public research, 12,3% of pharmaceutical drugs R&D relied on prototypes that were the result of public research, and 35,4% of pharmaceutical drugs R&D relied on instruments and techniques developed through public research (Cohen et al. 2002). Therefore, a reduced availability of ideas that could support the development of new projects will likely have a negative impact on the initiation of new corporate R&D projects in a field where funding is restricted.

Second, reduced support for public research will make existing ideas for new R&D projects less attractive to pursue. Public research contributes to ideas for new IP commercialization projects and to the completion of existing projects in equal measure (Cohen et al. 2002). Technological challenges that firms encounter along IP commercialization pathways and the knowhow they need to tackle these challenges are often difficult to predict *ex ante*, especially in the development of more radically innovative projects such as those pursued in science-intensive industries. As a result, firms in these industries rely to an important extent on external knowledge in product development activities (Ahuja and Lampert, 2001; Katz and Tushman, 1981; Lee and Allen, 1982; Phene et al. 2006). Scientific knowledge is often seen as a particularly important source of external knowledge for firms in science-intensive industries (Fleming and Sorensen 2004; Jong and Slavova 2014). We argue that scientific funding restrictions negatively affect confidence about the availability of critical scientific knowhow along the IP commercialization pathway among R&D managers, investors, and others whose

support is key, By undermining this confidence, scientific funding restrictions diminish the attractiveness of such projects as investment options.

Third, the development of absorptive capabilities that firms require to search for and assimilate external scientific knowledge requires significant investments in internal R&D organizations (Cohen and Levinthal, 1990, Fabrizio, 2009 and Fleming and Sorenson, 2004), and collaborations with academic laboratories (Liebeskind et al. 1996; Zucker et al. 1998). An extensive literature has emerged that examines the organizational models (Chesbrough 2006; Powell and Sandholz 2012), and the institutional practices and strategies (Jong and Slavova 2014; Stern 2004; Gittelman and Kogut 2002) for interacting with academic communities that optimize these absorptive capabilities. Investments associated with the development of absorptive capabilities become more attractive as scientific fields these organizations are tied into expand, and firms are able to exploit economies of scale and scope in interactions with external academic expert groups (Katz and Martin 1997; George et al. 2002). We argue investments in internal R&D organizations become less attractive as the base of external public research these organizations are expected to draw on is diminished through funding restrictions.

Taken together, the outlined dynamics suggest that science funding restrictions diminish firms' propensity to make investments in new IP commercialization projects, and we therefore hypothesize a negative effect of funding restrictions in a scientific field on the number of novel IP commercialization projects that are initiated that build on scholarship in that specific field:

Hypothesis 1a: *The enactment of scientific funding restrictions in a scientific field has a negative impact on the propensity of firms to launch new IP commercialization projects that build on research in that field.*

In addition, we argue that the negative impact of funding restrictions on commercial R&D is an impact that is geographically concentrated. The emphasis in scholarship on the role of scholarly knowhow in driving industry innovation over the past decades has shifted from examinations of knowledge flowing from public research as a public good characterized by non-excludability (e.g. Arrow 1959; Nelson 1959), towards examinations that highlight the tacit and excludable nature of such knowledge (e.g. Thursby and Thursby 2000; Liebeskind et al. 1996). As the transfer of such tacitly held knowledge requires personal interactions, commercial and academic R&D in science-intensive industries such as the biotechnology industry tends to be geographically co-located (e.g. Zucker et al. 1998). As a result, we expect that negative effects on firms' propensity to launch novel IP commercialization projects as a result of deteriorations of the funding environment for public research are larger within the geographic areas where these funding restrictions are concentrated and our hypothesis 1b posits that:

Hypothesis 1b: *The negative impact of the enactment of scientific funding restrictions on the propensity of firms to launch new IP commercialization projects in a field is larger for firms that are geographically located in the country where these restrictions are enacted.*

Public research and corporate R&D performance

The resource environment, in which novel IP commercialization projects are initiated create path dependencies that shape these projects' subsequent development. For example, the literature on new technology firms, which are often constituted around new IP commercialization projects, highlights the importance of various factors relating to the composition of founding teams for the development and success of these firms (Beckman 2006; Eesley et al. 2013; Eisenhardt and Schoonhoven, 1990; Klepper 2001). Similarly, the financing environment for

new technology firms is important in determining subsequent success; 'hot' financing environments during periods when venture capital is abundant produce firms that are more innovative than firms that receive their initial venture capital investments in financing environments that are less 'hot' (Nanda and Rhodes-Kropf 2013). We argue that a resource environment within which public research support is comparatively weak will hamper the success of IP commercialization projects that are conceived in this environment for several reasons.

First, we argue that funding restrictions undermine firms' ability to successfully move IP commercialization projects along their development trajectories. External public research not only plays an important role in science-intensive industries at the inception stage of novel IP commercialization projects, but also in supporting R&D processes once these projects are underway. In fact, the development of corporate R&D projects in science-intensive industries such as the biotechnology industry has been linked to the research environment at academic laboratories, from which firms are spun-off and the quality of the scientific networks founders bring into firms (Jong 2006; Murray 2004; Powell and Sandholtz 2012). Moreover, academic collaborations and publishing in high-quality scientific journals have been linked to increased R&D productivity of biotechnology firms (Jong and Slavova 2014). Accordingly, we expect the relative dearth of quality scientific resources in less favorable public research environments to undermine the success of commercial IP commercialization projects.

Second, indirect effects are likely to undermine firms' ability to successfully complete IP commercialization projects in fields, for which funding for public research is restricted. Product innovation in science-intensive sectors is generally organized within collaboration networks that involve webs of multiple partners such as investors, contract manufacturers, and licensing

partners, which possess different competencies that are critical to a project's success (Powell et al. 1996; 2005; Stuart et al. 2007). In deciding whether or not to commit resources to a field, firms that are potential development partners in a field are likely to be more inclined not to if funding for public research in a sector is restricted. Even if individual firms are willing to commit resources to projects if the scientific funding environment becomes less favourable, managers of these firms will likely find it more difficult to mobilise other key actors around these projects, increasing these projects' chances of failure.

Similarly, firms' ability to attract high-quality researchers might be negatively affected in a public research environment where academic career prospects are diminished as a result of reduced funding. Prospects to build up their stature in broader scientific communities is an important factor determining career decisions by researchers; This has been shown in the context of researchers pursuing careers in corporate research environments (Stern 2004) as well as in academic research environments (Anstett and Bell 2005; Levine 2006, 2008, 2012). Thus, we expect it to be more difficult for firms to assemble the teams of high-quality researchers necessary to turn IP commercialization projects into a success in fields where public research faces restrictions.

Taken together, we posit the following hypothesis regarding the propensity of IP commercialization projects to be successful in a field where funding for public research is restricted:

Hypothesis 2a: *IP commercialization projects that are initiated after the enactment of scientific funding restrictions are less likely to be successful.*

Finally, we argue that the negative impact of funding restrictions on firms' capabilities to bring IP commercialization projects to a successful conclusion is an impact that is geographically

concentrated in the country where these restrictions are enacted. Like for the effect of funding restrictions on firms' propensity to initiate IP commercialization projects, we argue that the negative effect on firms' propensity to successfully complete projects is especially strong for firms that are in the same country as the public research institutions that are hit by funding cuts.

Hypothesis 2b: *IP commercialization projects that are initiated in a country where scientific funding is restricted are less likely to be successful.*

SETTING AND METHODS

Research setting

The US hESC research funding restrictions as an interesting case study

The US federal funding moratorium covering research on new hESC lines that was enacted in 2001 provides a good context, in which to examine the impact of scientific funding restrictions. The scope of the moratorium was limited; hESC research was a nascent field in 2001 and still today represents a fraction of scholarly activities in the stem cell research field. In 2012, three years after the moratorium had been largely reversed by Presidential order, US$146 Million of the US$1.4 Billion NIH funding for stem cell research was used for hESC research (NIH 2013). The hESC funding moratorium also spanned a period that offered an otherwise favourable funding environment for biomedical research. For example, the annual NIH budget roughly doubled over the 1995-2005 period.

Moreover, because the 2001 moratorium on federally funded hESC research was US-specific, we are able to present our comparison of the US case with that of countries where no moratorium was in place, as a unique controlled research setting to examine the impact of changes in the funding environment for public research on the development of commercial IP in science-intensive industries. Accordingly, by pitting the development of corporate R&D

activities in the cell therapy field in the US and corporate R&D activities in countries where no moratorium was in place to control for other institutional factors that are typically associated with support for innovation in science-intensive industries such as those relating to venture capital, or the broader entrepreneurial ecosystem of regions such as Silicon Valley.

Impact of hESC research funding moratorium on US scientific contributions

The impact of the federal hESC research moratorium on scientific work in the hESC field has been well documented. Assessments of the impact of the 2001 federal hESC research funding moratorium find a sizable, short-term drop in the research productivity of US-based researchers in hESC research as compared to researchers based elsewhere (Furman et al. 2012; Moon and Cho 2014; Owen-Smith and McCormick 2006). In fact, US knowledge production in the hESC field was 35 to 40 per cent below anticipated levels in the aftermath of the 2001 policy, and measured in terms of forward citations to core research publications in the hESC field, US-based hESC follow-on work declines by nearly 59 per cent relative to non-US-based research over the period 2001-2003 (Furman et al. 2012). The federal hESC research moratorium affected the career mobility of researchers in the hESC field as well: Researchers at both state and national levels moved to places with more favourable funding environments following the enactment of the moratorium (Anstett and Bell 2005; Levine 2006, 2008, 2012; NIH 2013).

Work that examines the long-term impact of restrictive hESC funding finds a gradual recovery from the outlined deterioration of the hESC research environment in the US. Furman et al. (2012) highlight a narrowing of the gap in research productivity between non-US- and US-based hESC researchers after 2004: Over the period 2004-2007 the production of US hESC follow-on papers was only 29 per cent lower than the production of non-US follow-on papers. The gradual improvement in the scientific landscape for hESC research in the US can be

attributed to three factors. First, US researchers forged collaborative ties with international research groups that operated in a less restrictive regulatory environment (Furman et al. 2012). Second, public funding initiatives were launched at the state level to offset the funding gap in the hESC research field that had been caused by federal policies. The most notable of these initiatives was California Proposition 71, which was enacted through a referendum by Californian voters in 2004 to issue state bonds of a total value of US$3 billion to fund stem cell research. Third, the federal hESC research moratorium was completely abolished in 2009, removing barriers to hESC research that had held back US-based researchers in the first place.

Data and analyses

To examine changes in R&D activity in the cell therapy field, we first collected data on the flow of intellectual property from academic institutions to industry in the field. To this end we obtained information on the numbers of technology transfer deals between academic institutions and commercial firms for different timeframes over the period 1986-2011 from the Thomson Reuters Recombinant Capital database. The Recap database is an industry-leading business intelligence database on commercial biopharma deals and has been widely used in studies on collaborations in the life sciences sector (e.g. Rothaermel and Hess 2007; Padgett and Powell 2012; Powell 1998). We collected data on a total of 6,079 university-industry deals, of which 864 deals were in the cell therapy field.

Second, we used the number of new cell therapies entering clinical trials within a specific timeframe as a proxy for product development activity in the cell therapy field. Clinical trials data have been widely used as a proxy for innovation activity in studies on the life sciences sector. Moreover, the focus on products in development as a proxy for innovative performance is appropriate given the importance of development-stage products in this industry as a driver of

company value for industry practitioners. To obtain information on the number of clinical trials in the cell therapy field, we used the Citeline Pharmaprojects database, which is an industry-leading database that tracks clinical trials in the life sciences industry. We identified a total number of 521 cell therapy projects that entered clinical trials over the period 1986-2011.

To examine variations in firms' ability to successfully complete the R&D performance of firms that are linked to whether a project was initiated during a period of funding restrictions, we run a series of logit regressions with *project failure*, which is a binary variable, as the dependent variable. We consider a project a failure if the company that originated the project ceases its development and does not find a licensee for the project. Independent variables consist of various project level measures (i.e. the source material for the cell therapy, numbers of clinical trials conducted, numbers of patient enrollment in the trials, and the therapeutic class of the project), as well as various organizational level measures (i.e. firm size, firm age, and numbers of university deals in our study period).

RESULTS

Impact of hESC research funding moratorium on R&D activity

Our data show that the hESC research-funding moratorium not only impeded academic work, but also had an impact on commercial markets for IP that academic institutions participate in. Table 1 outlines a drop in the share of technology commercialization deals US universities were involved in, in the cell therapy field following the 2001 policy intervention in hESC research Moreover, the diminished position of US universities in commercial markets for ideas in the cell therapy field was particularly pronounced in the immediate aftermath of the enactment of the federal hESC research moratorium over the 2001-2003 period. Reflecting a broader uptick in scientific activities in the cell therapy field by universities for this period, we observe that US

universities regained their lost share in the market for commercial technologies in the cell therapy field in the periods following 2004.

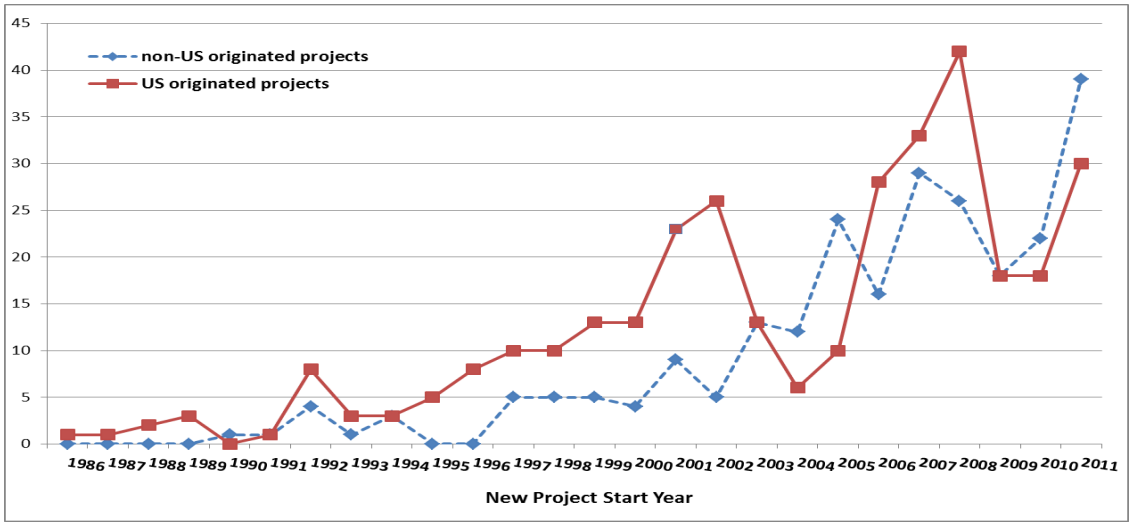
Table 1: Share of university deals in cell therapy and overall biotechnology fields

	No. cell therapy deals (N = 864)	Percentage of cell therapy deals that are with universities	Percentage of cell therapy deals that are with US universities	No. university-industry deals in biotechnology
1986-97	128	35%	34%	299
1998-00	63	17.4%	15.8%	804
2001-03	107	10.3%	10.3%	1056
2004-07	254	21.6 %	16.1%	1369
2008-11	312	21.1%	15%	2551

Source: Data collected and compiled from Reap IQ Series (*8*).

We find a significant decrease in the numbers of cell therapy products moved into (pre-) clinical trials by US firms following the enactment of the hESC research funding moratorium while numbers of products moved into trials by non-US firms increased. Figure 1 is based on data from the Pharmaprojects Citeline database; It highlights that whereas in 2002, twenty-six new cell therapy projects originated by US companies and five new cell therapy projects originated by non-US companies entered development, this situation had reversed by 2005. In that year ten new cell therapy projects originated by US companies, as compared to twenty-four new cell therapy projects originated by non-US companies, entered development. However, the graph also highlights that the pipelines of US firms gradually recovered as state initiatives aimed at filling up the federal funding gap kicked in during subsequent years. One of the most noted of these initiatives was the US$3 billion Proposition 71, the California Stem Cell Research and Cures Act, which Californians passed in 2004. By 2006, US originators again were leading in terms of numbers of new cell therapy projects these firms moved into (pre-) clinical trials.

Figure 1: Number of cell therapy projects entering clinical trials by originator country



Source: Compiled from Citeline Pharmaprojects database

Impact of hESC research funding moratorium on R&D performance

For the purposes of our logit regression analyses, we extracted from our sample of 521 cell therapy projects, only projects with starting years ranging between 1997 and 2011, leaving us with a sample of 483 projects. Our descriptive statistics on this sample suggest that the sub-samples of US- and non-US- projects are similar in many respects. Projects for example have similar failure rates (65.3% for US projects versus 58% otherwise) and the percentage of projects initiated by large firms is similar for US- and non-US- projects (10% for US projects versus 9% for non-US projects). We also find that over half of the projects were conducted by smaller firms with less than 50 employees (57% for US projects versus 56.4% for non-US projects). The only significant difference between US and non-US cell therapy project we find is that projects initiated by non-US firms are more likely to be autologous projects than projects initiated by US firms (36.6% of projects initiated by US firms versus 49.5% of projects initiated by non-US firms).

Table 2: Descriptive statistics cell therapy projects initiated between 1997 and 2011

	US	Non-US	chisq. test	Total
Failed projects	164 (65.3%)	135 (58.2%)	Chisq = 2.61 P = 0.106	299 (61.9%)
Autologous	92 (36.6%)	115 (49.5%)	Chisq = 8.21 P = 0.004	207 (42.8%)
Large firm (emp >= 500)	25 (9.96%)	21 (9.05%)	Not significant	46 (9.52%)
Small firm (emp <= 50)	144 (57.4%)	131 (56.5%)	Not significant	275 (56.9%)
Project start 1997 – 2000	41 (16.3%)	19 (8.2%)	Chisq (3)=20.8 P = 0.000	60 (12.4%))
Project start 2001 – 2003	52 (23.5%)	27 (14.4%)		79 (16.4%)
Project start 2004 – 2008	106 (42.2%)	107 (46.1%)		213 (44.1%)
Project start 2009 – 2011	52 (20.7%)	79 (34.1%)		131 (27.1%)

Chi-square test is used to test the significance level of the comparison of us and non-us group among the variables in our analysis: * denotes p<.05, ** denotes p <.01, and *** denotes p<.001

Table 3 presents the comparison of project failure rates for different time periods. We find roughly similar failure rates for US and non-US cell therapy projects during the period preceding the enactment of the US hESC research-funding moratorium. Of those projects that were launched before 2001, 75% of US projects failed and around 79% of non-US projects failed. However, we observe a drop in the success rates for projects initiated by US-based firms in comparison to success rates for projects initiated by non-US-based firms following the enactment of the US hESC research funding moratorium; Failure rates for IP commercialization projects launched between 2001 and 2003 are 92% for US projects and 85% for non-US projects. This divergence is again reversed once US state initiatives supporting stem cell research kick in from 2004 and projects initiated by US firms over the period 2004-2008 are again more successful than projects initiated by their non-US counterparts (75% for non-US projects versus 67% for US projects). For the final cohort projects initiated during the period 2009-2011, the difference between failure rates between the US projects and non-US projects becomes insignificant again.

Table 3: Average failure rates of projects launched in different time-window

	No. Projects	Failure rates US projects	Failure rates Non-US projects	Diff (US minus non-US)
Before 2001	60	75.6%	78.6%	-3%
2001 – 2003	79	92.3%	85.2%	7.1%
2004 - 2008	213	66.9%	74.8%	-7.9%
2009 - 2011	131	26.9%	24.1%	2.8%

To further examine the impact of public funding restrictions in a field of scientific research on the success prospects of IP commercialization projects in that field, which are launched when these restrictions are in place, tables 4 and 5 present a number of logit regression models. In Table 4 we examine factors affecting the termination of US cell therapy projects and exclude from our sample non-US projects. We use the first three models to investigate whether the fact that a US project was initiated before or after the enactment of the US hESC research funding moratorium affected the chances of failure of that project. Accordingly, we use a binary variable in these models, *post2001*, to indicate whether a US project was launched before or after 2001. Model 1 is the base model, model 2 adds variables that control for characteristics of the organizations that conduct clinical trials for cell therapy projects, and model 3 adds variables that control for project characteristics in determining project failure. The fact that a project was initiated before or after the enactment of the 2001 hESC research funding does not have a significant effect on the propensity of the project to fail in any of the three models. Our results do indicate that projects initiated by smaller firms (with fewer than 50 employees) and projects that run larger clinical trials are more successful. Therefore, models 1-3 suggest that there is not a statistically significant long-term impact of temporarily concentrated funding restrictions in a field of study on the failure rates of projects in the R&D field that is linked into this field.

In order to examine the short-term impact of hESC funding restrictions on the corporate R&D environment in the cell therapy sector, we examine more closely how the timing of the inception of new IP commercialization projects in the cell therapy field before or after the enactment of the hESC research funding moratorium affected the propensity of these projects to fail. Specifically, instead of using the binary variable *post2001*, in models 4-6 we use four different variables that localize the inception of cell therapy projects in one of four consecutive time-windows (*1997-2000*, *2001-2003*, *2004-2008*, and *2009-2011*), to examine the effect of the hESC research funding moratorium on R&D project failure rates. The cutting points of different time-windows are determined based on several policy events. The first event is the 2001 enactment of the federal funding moratorium for research on new hESC lines. The second event was the 2004 passage of Proposition 71 by California voters, and smaller similar state initiatives that were enacted around the same time, that created alternative public funding streams for research in the hESC field, on which a federal funding moratorium was in place. The third event was the 2009 signing of the executive order 'Removing Barriers to Responsible Scientific Research Involving Human Stem Cells,' that reversed the 2001 federal funding moratorium on specific types of hESC research. These three policy events represented important watershed moments in the development of the funding environment for hESC research in the US, and we therefore chose these three events to delineate the different time-windows for our analyses.

Confirming results of models 1-3, models 4-6 indicate that projects initiated by smaller firms and projects that involve larger clinical trials are less likely to fail. In addition, we find that projects launched by US firms during the years 2001-2003, which covers the period immediately following the enactment of hESC research funding restrictions are more likely to fail than those launched during the period before the enactment of these restrictions. Models 4-6 also highlight a

significant drop in failure rates over the period 2009-2011 after the enactment of various state initiatives in support of cell therapy research and the rescinding of restrictions on federally funded hESC research.

Table 4: Results of logistic regression models (US projects only)

	Logit regression DV = Project failed and not licensed out to other firm					
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Post2001	-0.585 (.392)	-0.502 (.418)	0.655 (.554)			
2001-2003				1.351* (.636)	1.199+ (.632)	1.382+ (.752)
2004-2008				-0.424 (.419)	-0.443 (.469)	-0.534 (.604)
2009-2010				-2.129*** (.480)	-2.339*** (.533)	-2.805*** (.675)
Large firms (>= 500 emp)		-0.303 (.561)	-0.139 (.719)		-0.892 (.570)	-0.924 (.706)
Small firms (<= 50 emp)		-0.895*** (.329)	-1.162* (.507)		-0.843* (.386)	-1.368* (.565)
Company age		-0.039 (.036)	-0.028 (.049)		-0.011 (.038)	-0.0033 (.042)
Company age^2		0.0003 (.00024)	0.00026 (.0003)		0.00022 (0.00025)	0.0001 (.00028)
A startup firm		0.278 (.421)	0.429 (.533)		0.117 (.444)	0.236 (.539)
Autologous			-0.101 (.477)			-0.287 (.395)
No. enrollments			-0.0013* (0.0006)			-0.0027* (.0011)
No. clinical trials conducted			-0.172 (.125)			-0.220 (.143)
No. university deals			-0.097 (.123)			-0.192 (.135)
Therapeutic class fixed effects	No	No	Yes	No	No	Yes
Observations	251	237	235	251	237	235
Pseudo R^2	0.007	0.044	0.136	0.170	0.202	0.306
Log likelihood	-160.78	-145.44	-130.17	-134.4	-121.41	-104.56

Chi-square test is used to test the significance level of the comparison of us and non-us group among the variables in our analysis: + denotes p<.10, * denotes p<.05, ** denotes p <.01, and *** denotes p<.001

To assess the specificity of the short-term effect of hESC research funding restrictions on project failure rates, and any spillover effects of these restrictions beyond the US we employ difference-in-difference techniques in analyzing our entire sample of US- and non-US- R&D projects. Results of our logit regression analyses, which include *USfirms* and *Post2001* as interaction terms are presented in Table 5.

Table 5: Results of logistic regression models (Full sample)

	Logit regression DV = Project failure		
	Model 1	Model 2	Model 3
US projects	0.151 (.183)	0.262 (.191)	0.207 (.222)
Before 2001	1.923*** (.401)	1.949*** (.472)	4.261*** (.697)
2001-2003	2.899*** (.346)	3.013*** (.348)	3.729*** (.289)
2004-2008	2.236*** (.298)	2.263*** (.333)	3.064*** (.378)
US x Before 2001	0.207 (.401)	0.402 (.418)	0.390 (.623)
US x 2001-2003	0.584+ (.346)	0.487 (.352)	1.429*** (.334)
US x 2004 - 2008	-0.530+ (.298)	-0.518 (.332)	-0.394 (.323)
Large firms (>= 500 emp)		-0.486 (.327)	-0.732 (.622)
Small firms (<= 50 emp)		-0.212 (.427)	-0.289 (.451)
Firm age		0.020*** (.005)	0.026*** (.008)
Firm age^2		-0.00008*** (.00002)	-0.00009*** (-0.00003)
A startup firm		0.120 (.249)	-0.028 (.187)
Project duration			-0.306*** (.037)
Autologous			-0.258 (.167)
No. enrollments			0.00013 (0.0002)
No. trials conducted			-0.448* (.222)

No. university deals			-0.132*** (.020)
Observations	483	455	453
Pseudo R^2	0.185	0.195	0.304
Log likelihood	-261.6	-244.09	-210.04

Chi-square test is used to test the significance level of the comparison of us and non-us group among the variables in our analysis: * denotes p<.05, ** denotes p <.01, and *** denotes p<.001

We find that older firms are associated with higher failure rates than younger firms. Also, IP commercialization projects are less likely to fail as these progress and complete subsequent development stages. Numbers of university deals also have a positive impact of the decreasing of log odds in failure, reemphasizing the importance of university knowledge in the industrial world.

Finally, model 3 indicates a positive and significant coefficient of the interaction term, highlighting a short-term increase in failure rates over the period 2001-2003 that is specific to projects initiated by US firms in the immediate aftermath of the enactment of the hESC research funding moratorium in the US. To deal with the fact that coefficients and their significance might not represent accurate relationships in non-linear logistic models, such as logit models, we also estimated the marginal effects of the interaction terms (Ai and Norton 2003).

Figure 2: Predicted failure rates for projects initiated by US and non-US firms

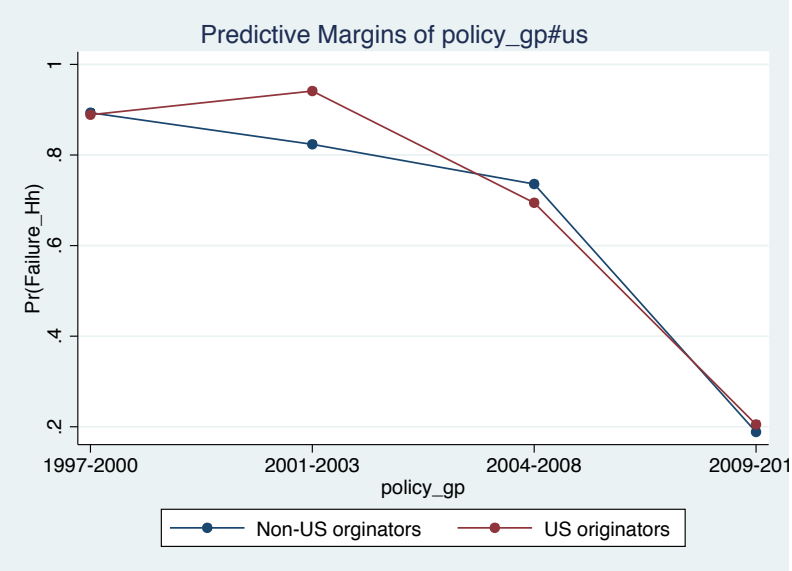


Figure 2 illustrates our estimates and highlights that IP commercialization projects initiated by US firms had a higher predicted marginal probability of failure (94%) than projects initiated by non-US firms (82%) over the 2001-2003 period. In estimating these effects, results of the difference-in-difference test are strong, both in magnitude and statistical significance. This finding supports the contention that negative effects of scientific funding restrictions are not only confined to the time period within which funding restrictions are in place, but also to the geographic location where these restrictions are enacted.

Concluding remarks

Our study represents an important advance in our appreciation of interdependencies between public funding for science, technology transfer, and IP commercialisation. Existing scholarship highlights the importance of science in product development processes in industry (e.g. Cohen et al. 2002; Zucker et al. 1998). Our analyses that outline how changes in the scientific funding environment affect the inception and success prospects of novel IP commercialisation projects build on this scholarship and provide new insights into the pathways through which scientific work supports corporate R&D, and how funding levers science that policy makers control, shape innovation processes in industry.

In addition, our results inform more practical debates surrounding science policy in an environment, in which funding for basic research is increasingly contested. Specifically, the presented historical case study provides new insights into the negative effects of scientific funding restrictions beyond the effects of such restrictions on the academic work of directly affected scientists, on technological innovation and industry competitiveness. Proponents of the 2001 hESC funding moratorium asserted that because of its limited scope (the moratorium neither completely banned hESC research, nor restricted private and state-level funding), effects

on corporate R&D activities and industry competitiveness would be minor and manageable. Our evidence suggests that this assertion did not turn out to be entirely correct. First of all, we showed a drop of licensing activity by US universities in the cell therapy field and a drop in the number of IP commercialisation projects initiated by US companies in the cell therapy field, in the aftermath of the enactment of the hESC moratorium in 2001. Second, our results highlighted a worsening of the R&D environment for cell therapy projects. Our analyses did not suggest a long-term effect on firms' ability to successfully complete cell therapy projects that outlasted the period of reduced funding for hESC research in the US. However, our analyses did indicate that while funding was reduced, cell therapy projects originated by US companies were more likely to fail, and that the international competitive position of US companies in the cell therapy sector was weakened.

Future research will be able to provide a systematic examination of underlying drivers of the effects we highlighted. Specifically, anecdotal evidence we encountered in conducting this research and existing scholarship in the finance literature highlight that investment decisions in high-tech sectors are influenced by how investors perceive the sentiment of other investors. For example, investors in 'hot markets' fund companies that are riskier and more innovative (Nanda and Rhodes-Kropf 2013). As the most important single source of funding for biomedical research, the federal government supposedly plays an important role in shaping investor sentiment in specific R&D fields. Further scholarship will be able to shed a light on the processes, by which managers and investors take cues from changes in science policies in decisions about which R&D projects to pursue. In addition, studies that highlight the importance of firms' ties to scholarly communities in the development of absorptive capabilities in science-intensive industries suggest that changes in the scholarly environment in a field affect the

effectiveness of firms' search efforts for external knowhow that is a critical input in the R&D process. Future studies will be able to explore how firms adapt R&D organizations and search strategies to such changes in the external scholarly environment.

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