Public Funds and Local Biotechnology Firm Creation

Published in Research Policy

Christos Kolympiris [b]
Management Studies, Wageningen University and Research Center
Hollandseweg 1, 6706 KN, Wageningen (Building 201), De Leeuwenborch, Room 5063, Netherlands
christos.kolympiris@wur.nl

Nicholas Kalaitzandonakes
Department of Agricultural and Applied Economics, University of Missouri, 125 A Mumford Hall, Columbia, MO 65211, USA
kalaitzandonakesn@missouri.edu

Douglas Miller
New Analytics LLC and Hutton School of Business
University of the Cumberlands, Williamsburg, KY 40769 USA
douglas.miller@ucumberlands.edu

[b] Corresponding author: Please send communication to Christos Kolympiris, Assistant Professor, Management Studies and Business Administration, Hollandseweg 1, 6706 KN, Wageningen (Building 201), De Leeuwenborch, Room 5063, Wageningen UR, Netherlands. Email: christos.kolympiris@wur.nl Phone: +31 (0) 317 482372

1. Introduction

Following the Great Recession and recognizing the robustness of the US knowledge economy, which sustained high employment and wages amid broad economic weakness,[1] in 2009 the U.S. government made a strategic decision to substantially increase federal funding for research and development (R&D) in high technology industries such as biotechnology (Hand, 2009; Mervis, 2009). In 2011 Ben Bernanke, the chairman of the Federal Reserve, publicly outlined the rationale and the influential role of government investments in R&D (Bernanke, 2011). Not surprisingly, interest in measuring the returns to public R&D investments quickly followed, not only in the U.S. (Basken, 2012) but also, in Europe, Australia, New Zealand and elsewhere (pg. 137 Stephan, 2012). These recent developments have revitalized a general interest towards the relationship between government funded R&D and economic growth. This relationship has been the focus of a long stream of research that has stressed the contribution of public R&D to increased innovation and productivity and has concluded that the social rate of return to public R&D investment is typically high (e.g. Beise and Stahl, 1999; Mansfield, 1991, 1995, 1997; Narin et al., 1997; Salter and Martin, 2001; Tijssen, 2002; Toole, 2012). Such findings have, in turn, supported continuing public R&D spending over time.

The conceptual underpinnings of such work are also strong. Investments in R&D tend to be risky, mainly due to limited knowledge appropriability and uncertainty of outcomes (Arrow, 1971). Such characteristics can discourage private parties from investing in R&D because the expected private rate of return is low. In fact, the social rate of return from R&D investments

[1] We subscribe to the definition of the knowledge economy in Powell and Snellman (2004): "production and services based on knowledge-intensive activities that contribute to an accelerated pace of technological and scientific advance as well as equally rapid obsolescence"

often outweighs the private rate (Griliches, 1992; Hall, 1996). Consequently, governments may be able to correct this market failure by funding R&D and increase the odds of socially desirable outcomes (Arrow, 1962; Nelson, 1959).[2]

This sort of argument for government intervention relies heavily on a complete understanding and accounting of the benefits from public R&D funding. Yet, one potential benefit from public R&D funding, firm creation, has received relatively limited attention in the academic literature despite the strong link between firm creation and economic growth (Van Praag and Versloot, 2007; Wennekers and Thurik, 1999). Indeed, there are good theoretical reasons to expect that public R&D funding may encourage firm creation. For instance, increased R&D expenditures can expand the knowledge base developed in universities and other research institutions and a part of it can be commercially exploited through firm spinoffs (Chachamidou and Logothetidis, 2008; Lockett and Wright, 2005).[3] New firms may also be formed to capitalize on non-appropriated knowledge (e.g. Acs et al., 2009; Audretsch and Keilbach, 2007).

In this study we focus on the question of whether publicly funded R&D expenditures lead to firm births in knowledge-intensive industries and in particular in biotechnology. A number of studies have examined the relationship between R&D expenditures and firm births but most have not delineated the sources of funds that support R&D (Bade and Nerlinger, 2000; Goetz and Morgan, 1995; Karlsson and Nyström, 2011; Kim et al., 2011; Kirchhoff et al., 2007; Woodward et al., 2006). Accordingly, our knowledge on the impact of public R&D funding on firm creation is limited.

[2] Salter and Martin (2001) and Chaminade and Edquist (2006) elaborate that additional considerations, besides the market failure arguments, are often in place before the government intervenes in the market place.
[3] Data from the Association of University Technology Managers (AUTM) suggest that over the last twenty years more than 9,000 university spinoff firms were created based on knowledge and intellectual property developed at major research universities in the US.

In our review of the literature we have identified only two studies that have focused on the impact of public R&D funding on the creation of biotechnology startups: Chen and Marchioni (2008) and Zucker et al. (1998). Both studies find a positive relationship between indicators of publicly funded R&D activity and local biotechnology firm births. Our study adds to the findings of these two studies and introduces a number of methodological and measurement improvements. For instance, these previous studies do not distinguish between the type of organization that receives the public funding and performs the R&D. Here, we recognize the potential for differential efficiencies between industrial and academic R&D organizations on the rate of firm creation (Bade and Nerlinger, 2000; Karlsson and Nyström, 2011) and examine the impacts of public R&D funds directed to universities, private firms, research institutes and research hospitals separately. The two previous studies have also measured the impact of federal R&D outlays on firm creation in the biotechnology industry for rather short periods of time (up to two years). Here, we extend the period of analysis to 18 years (1992 to 2010) recognizing the inherent long cycles involved in R&D funding, knowledge development and potential firm creation from such new knowledge. As well, instead of proxies of R&D intensity employed in the two previous studies (a life sciences index and a count of faculty members with grants) we use a more direct and sharper measure of R&D activity, namely, the dollar amount of R&D funding awarded to universities, private firms, research institutes and research hospitals.

We focus on firm births in the biotechnology industry for several reasons. First and foremost, because the biotechnology industry is a core part of the knowledge economy and understanding how it grows is important. Second, because the industry is a heavy recipient of

federal research funds (Lazonick and Tulum, 2011), it is a fertile ground for our investigation.[4] Third, because of the close linkage between basic biotechnology research and commercial applications, there is potential for a strong relationship between the level of R&D activity and firm births (Argyres and Liebeskind, 1998; McMillan and Narin, 2000). Fourth, because the biotechnology industry exhibits a strong tendency to cluster in narrow geographies (Audretsch and Stephan, 1996; Powell et al., 2002; Zucker et al., 1998), biotechnology firm births tend to concentrate in regions with large venture capital pools, specialized labor pools, and anchor institutions, like large biotechnology firms and universities (Audretsch and Stephan, 1996; Powell et al., 1996; Powell et al., 2012; Zucker et al., 1998). These are exactly the types of institutions and geographies that a large share of public biotechnology R&D investment is typically directed to. For these and other reasons, we expect that if a relationship between public funding of R&D and firm creation exists, it should be possible to detect in the biotechnology industry.

For our empirical analysis we construct a rich dataset that includes all R&D funds from the largest funding source, the National Institutes of Health (NIH), directed towards biotechnology research from 1992 up to 2010. We complement this dataset with information about biotechnology firm births, venture capital investments and other relevant variables from Thomson's Financial SDC Platinum Database and other sources.

We organize the rest of the paper as follows: In the next section we briefly discuss the biotechnology industry and some of its characteristics that make it attractive for our analysis. In sections 3 and 4 we review the relevant literature and develop our theoretical expectations on the effects of federal R&D monies on biotechnology firm births. In section 5 we describe

[4] Biotechnology is not a heavy recipient of public R&D investments only in the US, but across the world (for instance see Dohse (2000).

our econometric model and estimation procedures, and in section 6 we review the data we use. In section 7 we present the estimation results and in section 8 we discuss how we test the robustness of those results. Finally, in section 9 we offer concluding comments, implications for policy and suggestions for further research.

2. The Biotechnology Industry

The scientific origins of biotechnology can be traced back to the advancements of molecular biology and related fields in the 1950s (Kenney, 1986). However, biotechnology as an industry began to develop after the discovery of the basic technique for recombinant DNA in 1973 from Stanley Cohen of Stanford University and Herbert Boyer of University of California – San Francisco.

The fundamental discoveries in genetic engineering led to an ever-increasing rate of innovation. By the mid-1980s, a large number of novel products and processes were being pursued in a variety of industries (Mowery and Nelson, 1999). For instance, in the pharmaceutical industry regulatory proteins (e.g. human insulin and growth hormone), vaccines, antibiotics and monoclonal antibodies for diagnostic and therapeutic uses, were early targets. In agriculture, animal health products and growth promotants, and genetically engineered plants (e.g. plants resistant to herbicides, insects, diseases, and drought), were also broadly pursued. Improved amino acids, enzymes, vitamins, lipids, were the main targets in the specialty chemicals industry. And, R&D activities extended in various other industries, from food processing to environmental remediation.

The development of waves of biotechnology innovations and associated competencies, such as genetic engineering, bioprocessing, genomics, proteomics, metabolomics and others,

has since continued and has led to an ever-expanding range of potential commercial applications and in the scope of the industry (Orsenigo et al., 2001). In parallel, scores of scholarly works have documented the industry's growth, its reliance on scientific talent and new knowledge development and transmission as well as its emergence at the core of the knowledge economy (e.g. Audretsch and Stephan, 1996; Liebeskind et al., 1996; Whittington et al., 2009; Zucker et al., 1998).

Since its initial emergence, an important feature of biotechnology has been that new knowledge development in the lab has found immediate commercial applications in the market place. As such, biotechnology has continued to blur the distinction between basic and applied research. This feature, has led to its lasting success in attracting risk capital and in firm creation (Ernst&Young, 2012). It has also proved a good fit and a catalyst for the emergence of the entrepreneurial university (Renault, 2006). With regard to science, biotechnology has promoted interdisciplinary research, largely because it draws upon a number of diverse knowledge bases and housing all relevant knowledge under one roof is increasingly difficult (Pisano, 2006). Furthermore, it has promoted intense university-industry collaboration and commercialization of university research as well as firm creation.[5]

In sum, the biotechnology industry is at the center of the knowledge economy, it is heavily supported through government R&D funds, and many of its features make it an important industry to analyze the relationship between public funding of R&D activities, knowledge development and firm creation.

[5] It is not clear how many of the university spinoffs in the US are biotechnology firms as AUTM does not provide details about the industrial focus of these new firms. However, from the few universities that do provide such details as well as from survey results, biotechnology startups appear to constitute a large majority (Wobbekind et al., 2012; Zhang, 2009)

3. How Can Federal R&D Expenditures Lead to Firm Births?

Except, perhaps, in exceptional cases, there are inherent measurement difficulties with establishing a direct causal relationship between specific government R&D funds, ensuing new knowledge outcomes and resulting firm births by tracing some sort of lineage. In this study, we instead ask the question whether an increase in the amount of public R&D investment in some location leads to a parallel and measurable increase in firm births within some distance from the location where the R&D activity takes place. In principle, there are, at least, two mechanisms that public R&D spending may lead to firm creation. First, government R&D expenditures can lead to firm births because they can expand the level of knowledge that can be pursued commercially by research organizations with voluntary firm spinoffs and other forms of ventures that have formal ties to these organizations (e.g. joint ventures, subsidiaries, etc.).[6] Second, they can strengthen localization economies, which can attract and support the creation of new firms in a given region.

The first mechanism is straightforward. Federal funds can expand R&D outlays which, in turn, would tend to yield more knowledge (Cohen and Levinthal, 1989). As Klevorick et al. (1995) demonstrate, public R&D expenditures can expand the scope of opportunities that can be pursued commercially. As such, voluntary spinoffs, which rely on the research and knowledge flows of research organizations, could materialize (Garvin, 1983; Ndonzuau et al., 2002). Indeed, in knowledge industries, such as biotechnology, voluntarily spinoffs from incumbent firms as well as from public research institutions are common (Chachamidou and Logothetidis, 2008; Lockett and Wright, 2005). For example, the first ever biotechnology

[6] Often, in the literature on the determinants of firm births there is a distinction between startups which are defined as new firms without a specific scientific origin, and between spinoffs/spinouts which refer to firms that spawn from particular institutions such as universities and private firms. In order to develop our theoretical expectations we consult with research that uses both terms.

firm, Genentech, was a spinoff from the University of California, San Francisco. Similarly, Intermune Pharmaceuticals was a spin out of Connetics Corporation and Guidant of Eli Lilly (Ledbetter and Zipkin, 2002).

The second mechanism that can encourage firm births through the strengthening of localization economies is more indirect. Localization economies are typically defined as gains from the co-location of similar firms. They can be partitioned to gains in the knowledge base of firms (knowledge spillovers, network externalities and the like) and gains from efficiencies in the costs of doing business (access to a skilled labor pool and specialized suppliers, availability of firms in complementary industries) (Döring and Schnellenbach, 2006). An increase in the level of R&D expenditures in a particular location can lead to improvements in localization economies and, hence, in the odds of local firm creation.[7]

More specifically, confronted with substantial research expenditures, long research cycles, scientific complexities and a strict regulatory environment (DiMasi and Grabowski, 2007; Haussler and Zademach, 2007) firms in high technology industries often leverage the imperfect appropriability of knowledge (Arrow, 1962; Nelson, 1959) and its inherent difficulty of transfer over physical space (Audretsch, 1998) by sourcing knowledge and know-how from nearby research-intensive institutions. This happens via interpersonal interactions of economic actors working in similar problems, collaboration between nearby firms, participation in local professional networks and labor mobility of highly trained employees (Bathelt et al., 2004;

[7] As we discuss in this section, a significant body of research demonstrates the existence and strength of knowledge spillovers between closely located actors. Nevertheless, other contributions, including Breschi and Lissoni (2001), have questioned the relevance of knowledge spillovers. Similarly, physical proximity among actors may also increase the chances that one's ideas can be appropriated by others (Shaver and Flyer, 2000) perhaps due to increased local competition. For an opposing view see Feldman and Kelley (2006) and Audretsch and Stephan (1999).

Dahl and Pedersen, 2004; Kolympiris and Kalaitzandonakes, 2013; Liebeskind et al., 1996; Saxenian, 1991).

As the knowledge base of research organizations increases with their R&D investment (Cohen and Levinthal, 1989), the opportunity for knowledge acquisition by closely located firms should increase as well. Indeed, especially young firms located in proximity to research intensive institutions often achieve higher innovative outcomes potentially due to such knowledge acquisition effects (Acs et al., 1994; Anselin et al., 1997, 2000; Fischer and Varga, 2003; Jaffe, 1989). Accordingly, the potential for knowledge acquisition can provide strong incentives for newly founded firms to locate in proximity to sources of knowledge that can be exploited (Grossman and Helpman, 1992).

A somewhat different form of localization economies that is almost unique to the biotechnology industry, has been described by a stream of research developed by Powell and his colleagues (e.g. Powell, 1996; Powell et al., 2002; Powell et al., 1996; Powell et al., 2012; Whittington et al., 2009). [8] As they explain, the diversity of local organizations (e.g. firms, universities etc.) in a region can boost the local biotechnology birth rate. When there is diversity in the local environment, communities can more easily overcome declines and increased competition can create different standards, practices, rules and strategies that are most relevant for success. This is particularly relevant for biotechnology perhaps because its broad knowledge base favors numerous competing experimentations before reaching the most desired outcome. Among the diverse organizations, Powell and his colleagues highlighted the

[8] These studies have also noted that networks across relevant actors are an important source of innovation in biotechnology. Such networks can potentially influence the startup rate of a region as long as new startups are attracted to them. To capture such ties we would need access to the formal and, potentially, informal linkages of the biotechnology firms, universities and research institutes in our dataset. Such information is not available to us. However, insofar as organizations that receive more funds tend to engage more heavily in networks, concerns of the impact of this data limitation on our work should be alleviated.

importance of a local anchor entity (e.g. large firm, research university, etc.) that "...becomes a scaffolding that, either intentionally or unexpectedly, assists subsequent connections.." (Powell et al., 2012). In this context of the biotechnology industry, federal R&D funds are allocated to different types of research institutions and might increase the diversity of local research organizations. At the same time, the bulk of such funding goes to large research universities that may act as anchor organizations in various regions. As such, public R&D funding might increase firm births in the biotechnology industry through the location effects described by Powell and his colleagues. Indeed, there is significant evidence that most early biotechnology startups were founded around universities, where major breakthroughs took place (Audretsch and Stephan, 1996; Owen-Smith and Powell, 2004).

Investments in R&D can augment knowledge spillovers among proximate firms but can also induce efficiencies in the costs of doing business of knowledge industries by enhancing specialized and localized labor pools and encouraging the presence of firms in complementary industries. Specifically in biotechnology, service providers and other suppliers such as firms with expertise in biological materials and advanced laboratory equipment tend to locate in regions with high research intensity (Stuart and Sorenson, 2003a). Insofar as newly founded biotechnology firms are attracted by the resource endowment of a given region (Stuart and Sorenson, 2003b) an increase in the availability of research dollars can boost the attractiveness of the region as a potential startup location.

Along the same lines, an increase in R&D spending, especially through government grants to universities that train new scientists through research, can enhance the talent in the local labor pool and accordingly boost the local availability of highly-skilled labor (Pouder and St. John, 1996). Employee turnover from incumbent firms can also enhance the local labor

pool (Kim and Marschke, 2005). A region with ample highly-skilled labor could therefore attract and encourage the creation of new local firms.

Regions rich in knowledge base may also lead to firm births through a mechanism described under the Knowledge Spillover Theory of Entrepreneurship (KSTE). Knowledge originally developed at incumbent organizations may be commercially pursued by alert individuals, often previous employees, who recognize the potential of these projects and mobilize local networks and other means towards the development of their firm (Acs et al., 2009; Audretsch and Keilbach, 2007).[9] [10]

4. Empirical Evidence on Federal R&D Expenditures and Firm Births

Empirical evidence in the literature is generally consistent with the arguments in the previous section and suggests a positive relationship between R&D expenditures and firm creation. A stream of research has documented a consistent positive association between proxies of R&D intensity, such as the number of R&D employees in a region, and the rate of local firm births (Bade and Nerlinger, 2000; Goetz and Morgan, 1995; Karlsson and Nyström, 2011; Kim et al., 2011; Kirchhoff et al., 2007; Woodward et al., 2006).[11]

Importantly, several studies in this stream of research have sought to distinguish the relative impact of academic and industrial R&D on firm creation. These studies have found

[9] Previous employers can guard against the use of knowledge acquired internally (Kim and Marschke, 2005), but significant evidence of firm spinoffs without formal ties with the parent company (Agarwal et al., 2004; Klepper and Sleeper, 2005) suggests that such protection schemes are often bypassed.

[10] Bhide (1994) provides indirect evidence towards such effects by reporting that 71 percent of firm founders in his sample stated that their business originating idea came either through replication or modification of an idea encountered through previous employment.

[11] Indirect evidence is also provided by studies that examine the relationship between the density of institutions that conduct R&D in a region and the rate of new firm births at that region as well as from studies that analyze the rate that academic institutions and private organizations spawn startups (e.g. Baptista and Mendonça, 2010; Klepper and Sleeper, 2005; Steffensen and Rogers, 2000; Stuart and Sorenson, 2003a).

that who conducts the R&D matters to the rate of firm creation and there appears to be a stronger linkage between the creation of new firms with R&D activity occurring in firms rather than with R&D taking place in academic institutions (Bade and Nerlinger, 2000; Karlsson and Nyström, 2011). What is difficult to infer from all these previous studies, however, is the impact of federally funded R&D on firm creation because they measure R&D activity without any reference to its funding source.

A handful of studies have examined directly the relationship between government R&D funding and firm creation and here the evidence is more limited and nuanced. Kim et al. (2011) examined the factors that influence the annual rate of firm births and deaths in the US (without any specific industry focus) and found that industrial R&D expenditures had a positive effect on firm births but government R&D investments had no distinguishable effect. Samila and Sorenson (2010) also studied the relationship between federally funded R&D grants to academic institutions and the annual rate of firm births in the US (again without a specific industry focus). Samila and Sorenson (2010) concluded that while in isolation federal R&D funding to academic institutions did not affect the firm birth rate in the regions where the R&D activity occurs, in regions rich in venture capital it did exhibit a positive effect. The authors then concluded that the local availability of venture capital acted as a catalyst to firm creation.

Two more studies, Chen and Marchioni (2008) and Zucker et al. (1998), have examined the linkage between federally-funded R&D and biotechnology firm births and both have documented a positive relationship. More specifically, Chen and Marchioni (2008) examined the impact of federal research funds given to an MSA over the 2003-2005 period on the number of venture capital-backed biotechnology firms in an MSA in 2006. The level of federal funds given to an MSA was used in a principal component analysis along with other

indicators, such as the number of life scientists, universities, institutes and hospitals in an MSA, in order to construct a composite index of biotechnology research intensity in an MSA. In turn, this index was found to have a strong explanatory power in the number of MSA biotechnology firm births. Hence, Chen and Marchioni (2008) provide indirect empirical evidence for a positive impact of public R&D funding on biotechnology firm creation but the marginal effect of such funding could not be computed. Zucker et. al (1998) studied the births of biotechnology firms in a given U.S. Functional Economic Area in 1990. They evaluated the impact of federal funding on firm creation by examining the relationship between the number of faculty members in local universities that have received federal grants between 1979 and 1980 and biotechnology firms ten years later. They found that federal R&D funding had a positive impact on biotechnology firm births but, as in the case of Chen and Marchioni (2008), the marginal impact of such federal investments on local firm creation was not part of the analysis.

In broad strokes then, existing empirical evidence indicates that: (a) more R&D spending tends to increase firm creation; (b) who performs the R&D matters and firm R&D activities appear to have a higher marginal impact than university R&D activities on firm births; and (c) increased government R&D spending may have a positive effect on firm creation under some conditions, especially in the biotechnology industry. The existing literature and empirical evidence, however, leave a number of questions unanswered, including the most basic one –just how many more firm births might one expect from, say, an additional $1 million in public R&D funding in a given region? This is the principle question we address in this study within the context of the US biotechnology industry. To answer this question, we

make a number of methodological improvements in what we consider to be potential limitations in previous studies.

Specifically, the cycles of R&D grant acquisition, performance of R&D, creation of new knowledge, and application of the new knowledge through the creation of new firms can be long and variable in length from one year to another. As such, we propose that the relationship between public R&D funding and firm creation must be examined over a long period of time in order to allow for sufficient lags in the process and year-to-year variations in the flows of funds and firms.[12] Since the capacity of different types of research institutions to translate knowledge into firm births might be different, we also propose that the effects of public R&D expenditures on firm creation should be considered separately by the type of recipient. Finally, we propose that instead of various indirect indicators of publicly funded R&D intensity, a direct measure of public R&D funding (dollars spent) should be used in this analysis so that the marginal effects on such spending can be calculated.[13]

We implement the proposed improvements in the analysis that follows. More specifically, we use a direct measure of public R&D spending; we extend the period of analysis to 18 years (1992 to 2010) to ensure adequate consideration of lags and year to year variations in R&D investments and firm births; and we partition public R&D funds to those directed to universities, private firms and research institutes and hospitals.

[12] For instance, in Chen and Marchioni (2008) and Zucker et al. (1998) the time span of public R&D outlays measured and the lags between outlays and the new firm counts are rather limited. Chen and Marchioni (2008) measure federal R&D spending for a two year period and Zucker et al. (1998) for a one year period. It is therefore possible, that the results could weaken or strengthen if their period of analyses were lengthened allowing for multiple funding cycles, potential longer lags between funding and firm creation as well as natural variations in external conditions that may also affect firm births over time (e.g. overall business climate and conditions in financial markets).

[13] Previous measures of public R&D activity have been somewhat crude. In addition to making difficult the derivation of a direct measure of the marginal effect of public R&D spending on firm creation, they may also distort the potential relationship. For example, the count of faculty members supported by federal grants used in Zucker et al. (1998) may mask important differences across the size of grants and accordingly the level of knowledge generated and firm created from public R&D funding.

Consistent with previous work that finds the impact of R&D activities on firm creation to materialize within a narrow geographic scope, we measure the number of firm births at the same MSA where federal funds are allocated (Karlsson and Nyström, 2011; Samila and Sorenson, 2010). The MSA is used as the unit of analysis because it is small enough to capture the spatially bounded nature of localization economies and the tendency of spinoffs to locate close to parent organizations but it is large enough to exhibit independent economic activity (Abel and Deitz, 2012; Samila and Sorenson, 2011). Further, MSAs are generally more homogeneous across U.S. states[14] than cities or other geographic units which allows us to provide more meaningful comparisons across MSAs of rural and urban regions.

5. Methods and Procedures

We specify a two-way fixed effects model in which the dependent variable y_{it} is the number of biotechnology firm births in Metropolitan Statistical Area i and year t. Given that the dependent variable is an observed count, the general form of the expected count is formulated as follows:

$$E(y_{it}|X_{it}, A_i, \Gamma_t) = m\left(X_{it}\beta + \sum_i a_i A_i + \sum_t \gamma_t \Gamma_t\right) \qquad (1)$$

where X_{it} is the 1×13 row vector that contains thirteen non-constant explanatory variables, which we describe later in this section. Function m is a link function that maps the linear combination of the explanatory variables into an expected count that is non-negative.[15]

[14] The MSAs are U.S. population centers and exhibit less economic and geographic heterogeneity than the component spatial units (e.g., cities, towns, suburbs, villages, neighborhoods, and boroughs).

[15] To estimate the model in (1) we use the Poisson maximum likelihood estimator. Following earlier contributions to this literature, the standard Poisson variance assumption of equal conditional means and variances may be too restrictive for much of the economic count data encountered in practice, so we relax this condition in our

The two-way unobserved components in our model are represented with the second and third terms in equation (1). In particular, A_i equals 1 for MSA i and is 0 otherwise, and Γ_t equals 1 for year t and is zero otherwise. The year dummies can capture time-varying effects, such as favorable or unfavorable environments in financial markets on firm births (e.g. a "hot IPO market" (Lowry and Schwert, 2002)). The MSA dummy variables are used to capture time-constant factors that may affect firm location choice for a wide range of industries, including biotechnology. For example, the MSA dummies can approximate the local effect of taxes (Bartik, 1985, 1989; Rathelot and Sillard, 2008) and economic initiatives (Woolley and Rottner, 2008), which despite potential deviations from year to year are expected to be largely time constant.[16] [17]

The set of explanatory variables in equation (1) includes the lagged dependent variable (i.e., the firm birth rate in each MSA at time $t-1$) in order to capture potentially dynamic relationships in firm births. Regions conducive to new firm creation are expected to show a historical pattern of firm births (Andersson and Koster, 2011), so we expect a positive sign for the coefficient of the lagged dependent variable. We also use the estimate of this coefficient to

---

estimated model. When relaxed, the computed standard errors are not sensitive to any conditional variance assumption and allow for arbitrary serial correlation (Wooldridge, 1999).

[16] We should note that because some MSAs cross state borders, local taxes and economic initiatives may vary within an MSA. Accordingly, the interpretation of the region-specific dummy variable as a true fixed effect may be limited. As a robustness check, whenever the analysis is limited to the MSAs that do not cross state borders the results remain qualitatively similar to those reported in Table 3.

[17] We have also run fixed effects models using procedures that are included in popular statistical software, such as SAS and STATA, (e.g. TCOUNTREG). Unfortunately, some of these procedures are still experimental and as such they only report limited fit statistics. Furthermore, the available routines are suitable mainly for one-way count panel models but in our application we need to estimate a restricted or partial-two-way model (some cross-sectional effects are restricted to zero) because some cross-sectional observations have limited variability. In addition, in all the procedures we used, the number of observations drops drastically because the standard FE Poisson model as described in Wooldridge (2002) drops all observed zeros from the log-likelihood. As a result, the sample of such models is quite different from the base model and as such the results are not directly comparable. Given all these problems as well as the findings of Greene (2002) that the fixed effects estimator in different families of nonlinear models is biased, we opted to not present fixed effects estimates here.

distinguish between the short and long run effects of federal funds on the local firm birth rate (Wooldridge, 2009).

Since the lagged count variable in X_{it} is a function of the cross-sectional unobserved component (represented by the time-invariant dummy variable A_i in (1)), the presence of lagged dependent variables in panel models generally causes bias and inconsistency problems in the standard estimators for panel models (Wooldridge, 2002). For one-way panel models of count data, the potential inconsistency problem may be resolved by using quasi-differenced data or an instrumental variables estimator. Given that our data may have two-way unobserved components, we use the dummy variable approach, which is roughly comparable to the within estimator. Although the within estimator is also biased for data sets with a fixed temporal dimension, the bias converges to zero as the number of time series observations becomes large. Our data set has 18 years of time-series observations, so the potential bias in the two-way ML estimator of equation (1) may be small for this relatively large data set, and we present alternative versions of the estimated model in order to evaluate the evidence of potential bias in the estimator.

To test whether federal funds relate to local firm births and whether the type of the recipient mediates that effect, we include the average total amount of federal grants awarded at MSA i's universities, private firms and institutes/hospitals from $t-1$ to $t-5$ [18] in linear and quadratic form. The amount of funds that each MSA receives from NIH within a five year window is fairly stable due to the common multiyear nature of grants awards. Due to the similarity across adjacent observations of the lagged variables, strong correlations exist among

[18] In order to include early years in the empirical analysis, we use a 5 year average for available observations. For example, the observation for 1995 is the average value of years 1992 to 1994, which is a 3 year average. Thus, the empirical analysis only omits data on the dependent variable for 1992. As we show in section 8, this empirical choice did not have a noticeable impact on our results.

yearly lagged observations, and we employ an average value versus separate year lags in the empirical model. We use a five year lag average because the period up to five years before firm birth is perhaps the most relevant in capturing the true effects of federal funds because a large number of grants expire after the five year window.[19] The quadratic form of the variables in question is included in the analysis in order to account for potential nonlinearities in the relationship between federal R&D monies and firm births at the MSA level.

In line with our theoretical expectation, we anticipate an overall positive contribution of NIH funds to firm births, and the rate may be increasing at an increasing rate (i.e., the quadratic coefficient is positive) or increasing at a decreasing rate (i.e., the quadratic coefficient is negative). Also in line with our theoretical expectations, we expect the magnitude of each variable that measures the amount of funds provided to a given type of institution to vary among types of institutions which would signal that different types of recipients have distinct effect on the generation of new firms from federally-funded research. As well, we include three interaction terms (university funds*private firm funds, university funds*research institute funds, research institute funds*private firms funds) to account for potential synergies (positive sign of the interaction terms) or congestion effects (negative sign of the interaction terms) that may arise when funds are allocated to different recipient types/organizational forms in the same MSA.

To account for time-varying factors that can influence the yearly birth rate of a given region we add three relevant control factors in the analysis. The first control variable is the average GDP of the MSA in the five years prior to a firm birth. The variable is used to capture

[19] Previous research has found 5-year windows for lag structures to be appropriate (e.g. Aharonson et al., 2008; Baum et al., 2000). As shown in Table 5, to test the robustness of our findings to the specification of the year lag structure we specified the relevant variables with different lag structures and found nearly identical results to those reported in Table 3.

the effect of overall economic conditions on the yearly firm birth rate. These conditions are expected to arise from factors such as regional cost advantages, amenities and a region's prestige (Bartik and Gray, 2002; Frenkel, 2001; Stuart and Sorenson, 2003b). Given the highly localized nature of venture capital investments in biotechnology (Kolympiris et al., 2011; Powell et al., 2002) and the contribution of venture capital to regional firm birth rate (Samila and Sorenson, 2010, 2011) the second control variable is the average total venture capital funds invested in biotechnology firms in the MSA in the five years prior to a firm birth. We expect a positive sign for the variable in question. Note that the two aforementioned control variables are specified as 5-year averages so that we could compare them with the corresponding variables that measure the 5-year average inflow of NIH dollars at a given MSA. To ensure that our empirical analysis is robust to the size of the MSA, we also include a control variable for the population of the MSA at year t.

6. Data Sources and Presentation

The data used to construct the variables that measure the yearly federal funds allocated to universities, private firms, and research institutes/hospitals (and the associated interaction and quadratic terms) were obtained from NIH's Research Portfolio Online Reporting Tools (RePORT). We collected data from 1992[20] to 2010 on the amount awarded by NIH to every principal investigator (PI) as well as each funded project's title and each PI's affiliation at the

[20] The effect of NIH money on local firm births could have been larger in the early years because the industry may have not attained complete maturity during these years. Accordingly, firm births prior to 1992 would also be of interest to the present study. Unfortunately, 1992 is the first year for which NIH data are available. Further, the boom in the biotechnology industry occurred some years later than 1992, so 1992 is still among the early years.

time the project was funded.[21] In order to identify biotechnology grants, a keyword search was performed for all project titles[22]. After we sorted out the biotechnology grants, we adjusted the nominal award money to 2007 values using the CPI and classified each project's PI affiliation to universities, private firms and research institutes/ hospitals after consulting with the categorization of each institution as private firm, university and so on provided by RePORT. Whenever in doubt, we visited each institution's website. Then, we constructed the MSA-specific explanatory variables by adding the inflation adjusted award monies for each type of institution[23].

Figure 1 presents the historical real NIH funding levels for biotechnology by institution type. Biotechnology funds increased through the 1990s, flattened-out between 2003 and 2004, and stabilized starting in 2005. The proportion of funds directed to the different types of institutions remained stable over time mainly because most grants are multiyear awards. Universities attract the largest share of the funds while private firms receive the least amount of

[21] NIH's RePORT reports the PI and the institution that each project is awarded. It is possible that the PI may have more than one affiliation. Nevertheless, this does not present a problem as we allocate the funds to the institution reported in the NIH grant. NIH grants are made, principally, to an institution rather than a PI and as such the research is expected to occur in the recipient institution listed in the award. While no official statistics exist, information provided by the Office of Statistical Analysis and Reporting (OSAR) of NIH, indicates that the majority of NIH grants are individually allocated to a single institution and a single PI. As such, we allocate all awarded monies in each grant to the location of the primary recipient institution and PI. For the small number of NIH grants involving multiple institutions, this attribution scheme might lead to misallocation of funding among institutions and locations but we do not expect this type of error to be significant. We indirectly tested for the significance of such a potential error by taking advantage of a recent change in NIH grant awards. Specifically, since the beginning of 2007, NIH has allowed grants to have multiple investigators (Brainard, 2006). When we re-estimated our base model on a limited data set for the 1992-2007 period, we found the results to be qualitatively similar to the results of Table 3, where the analysis extended to 2010.

[22] The list of biotechnology keywords was constructed after consulting with biotechnology researchers employed at the authors' institutions. Almost 400 keywords were used but 155 of them characterized 99% of all grants in our dataset. The abbreviated list is presented in Appendix Table 1. It should be noted that medical and biotechnology research often overlap. There are, however, many cases of medical research that is different from biotechnology. Examples include research on clinical diagnostics, clinical test kits, infectious diseases and magnetic resonance imaging (MRI).

[23] Starting in 2007, NIH implemented a new system to measure the amount of funds for biotechnology. Our measure of biotechnology funds, which is comparable to the updated NIH system, is conservative when compared to the original NIH estimate; the 2007 real total biotechnology amount estimate of NIH is about 5 billion dollars while our estimate for the same year is about 3 billion dollars.

grants from NIH[24]. Interestingly, as seen in Table 1, the correlation coefficients between monies for the different types of institutions on a per-MSA-year base are moderate, ranging from 0.52 to 0.57. The magnitude of those correlations suggests that there is variation in funding levels across the different types of institutions within the MSAs, and this should help us to estimate the separate effects of the funds on firm births.

[Figure 1 about here]

[Table 1 about here]

We used the Thomson's Financial SDC Platinum Database, the Zoominfo web-based database, and the web-based Moneytree report to identify biotechnology firm births and to construct the dependent variable and the time lag variable. Each firm's location and founding date were generally available in all three data sources, but missing observations were gathered from the websites of the individual firms. All three data-sources report firms that during their lifetime received funds from venture capital firms. Perhaps due to the highly selective nature of venture capital investments, venture capital-backed firms are often overperforming and generate substantial revenues and associated increases in value added and jobs; they are then precisely the type of firms that Shane (2009) argues public policy should focus on.[25] By extension, venture capital-backed firms appear a suitable sample for our study.[26] [27] Figure 2

[24] NIH is currently required to set aside 2.5 percent of its extramural R&D budget exclusively for grants of the Small Business Innovation Research (SBIR) program (Wessner (ed.), 2009) which mainly go to private firms. The required percentage has slightly fluctuated over time but some of the NIH funds issued to private firms are SBIR grants. Also note that the majority of funds for private firms do not come from the federal government but from other sources like venture capital funds. Hence, the overall firm-generation capacity of private firms will be underestimated here because we do not include the total research amount received by private firms (besides NIH funds).

[25] Shane (2009) even suggests that the criteria used by venture capitalists in choosing the firms they invest in should be adopted by federal agencies, such as NIH, that provide funds.

[26] Approximately 80 percent of the firms were common in all three databases but SDC was more comprehensive in reporting the foundation date of each firm as well as its address, which were the two main pieces of information we sought from these data sources in order to assign the birth of each firm to an MSA at a certain year.

presents the number of firm births by year, which exhibit an increasing trend over time even though year to year variations are substantial. Firm births peaked in 2000 with 102 new biotechnology firms and declined after 2005.

[Figure 2 about here]

To illustrate the spatial character of firm births, Figure 3 presents the cumulative amount of NIH grants collected from 1992 to 2010 for all MSAs in the U.S. along with their cumulative firm births for the same period. Each MSA is represented by its principal city as defined by the U.S. Census Bureau; for those MSAs with two principal cities, the more geographically central city in the MSA is depicted in the map. MSAs are classified according to their NIH fund accumulations, and larger symbols in the figure indicate MSAs with more biotechnology firm births. The general pattern observed from Figure 3 is that the MSAs that host institutions that have attracted large amounts from NIH have also experienced more firm births. Only 12 percent of the MSAs (9 of 75) with the highest NIH fund accumulations did not have any firm births while the corresponding percentage for MSAs with lower or no NIH fund accumulations was 76 percent (107 of the 140) and 97 percent (151 of the 156), respectively. For example, Boston's MSA had 181 firm births and the largest funds accumulation of all MSAs with more than $4.1 billion from 1992 to 2010. Also, San Francisco

---

Importantly, for about 90 percent of the firms we used to construct our dependent variable SDC provided the status of each firm as of the end of 2010, which is the year our analysis ends. The large majority of the firms were in business for at least 7 years after their births and some were merged or acquired.

[27] Although venture capital–backed firms often locate where venture capital investments occur, because of our focus on firms of this kind we may have overlooked some firms in regions with less venture capital activity, which could lead to a potential bias in our estimates. In general, we do not expect this issue to be important as 60 percent of the firms in our sample were founded outside the three traditional venture capital hubs of San Francisco, Boston and San Diego. Furthermore, existing empirical evidence from a broad set of industries indicates that the effect of regional venture capital activity *per se* on firm foundings is not particularly strong (Samila and Sorenson, 2010, 2011). Empirical evidence from the biotechnology industry suggests that the impact of venture capital activity on firm births is either weakly positive and lessens even more when other factors (e.g. university presence) are explicitly considered (Stuart and Sorenson, 2003a) or it is negative, potentially due to the fact that venture capital activity favors the creation of a small number of large firms (Zucker et al., 1998).

had 201 firm births while having the 6th highest total NIH fund accumulation. In contrast, Los Angeles had only 27 firm births while having received the 3rd total largest amount from NIH with more than $2 billion from 1992 to 2010. While Figure 3 implies a positive association between firm births and total NIH funds, it does not provide a comprehensive picture of the relationship under consideration because it does not account for temporal, spatial, and other structural effects that might shape firm firms in various locations. The estimated count data model is therefore expected to provide more specific evidence on the conditional impact of NIH funds on firm births across the U.S.

For the remaining variables, we used data from the U.S. Bureau of Economic Analysis to construct the GDP for each MSA and we transformed the nominal GDP values to 2007 dollars using the CPI. Data available at the U.S. Census Bureau was employed to form the MSA population variable. Finally, the variable that measured the venture capital investments at a given MSA was built with data from the SDC Platinum database. SDC provided the nominal venture capital amounts awarded to biotechnology firms per year. In order to construct the variable in question, we converted these amounts to 2007 dollars using the CPI and summed up the values for all firms located in each MSA.

[Figure 3 about here]

Table 2 presents descriptive statistics for the dependent variable and selected independent variables. The average number of firm births per MSA year is 0.18 with a standard deviation of 1. The dependent variable is right-skewed because most of the MSAs did not have any firm births in a given year. On average, universities receive about $3.69 million per MSA year, research institutes receive about $1 million per MSA year, and private firms attract about $0.12 million per MSA year. Note that regardless of the type of the institution, the standard

deviation of NIH funds is greater than the variable mean, which indicates the wide range of values in the observed funding levels. As with the dependent variable, these explanatory variables exhibit strong right skewness because most observations in a given year equal zero. Most MSAs did not receive biotechnology-related funds from venture capitalists but the relative size of the standard deviation of the average venture capital invested as compared with its mean (36.8 versus 4.9) indicates that when (and where) venture capital investments occurred, they were of significant magnitude. Finally, the average GDP for a given MSA was almost $19 billion with most MSAs having a GDP of more than $2.4 billion.

[Table 2 about here]

7. Estimation Results

The fit statistics reported at the bottom of Table 3 come from a maximum likelihood (ML) estimation of the previously described Poisson count model which was based on an exponential specification for the conditional mean[28]. Note, however, that there might be unobserved or difficult to measure time-varying regional characteristics (for instance, the quality of support towards entrepreneurship provided in the MSA) that can boost or hinder the firm birth rate in a given MSA across years. If such unobserved factors do exist, they may lead to a violation in the assumption of independence across observations (Nichols and Schaffer, 2007; Stimson, 1985). For this reason we compute standard errors clustered at the MSA level using generalized estimating equations (GEE).[29] This practice accounts for potential clustering

[28]For the cross-sectional fixed effects, the ML estimators of these parameters are only identified when the associated dependent variable exhibits changes during the sample period (Allison, 2008). Accordingly, the set of MSA-specific dummies was defined as the set of 104 MSAs that over the sample period had at least one firm birth, and we use a partial or restricted form of the fixed effects specification.

[29] GEE is a method to estimate the standard errors which first estimates the variability within the defined cluster and then sums across all clusters (Zorn, 2006).

effects and yields identical estimates to ML. These last estimates of the fitted Poisson count model are reported in the first column of Table 3. As we discuss in detail in Section 8, a number of robustness checks suggest that our estimates are generally consistent across different estimators, sets of regressors, lag structures, and model specifications.

To evaluate the potential bias due to the presence of the fixed effects and the lagged dependent variables in (1), we estimate an alternative model and report the results in the second column of Table 3. The second model includes all the independent variables previously discussed except the temporal lag. The small differences between the estimates of the two models suggest that the temporal lag does not induce substantial bias in the ML parameter estimators. Accordingly, in the following discussion we refer only to the estimates of the full model in the first column.

[Table 3 about here]

The joint significance tests reported at the bottom of Table 3 indicate strong significance for the MSA-specific and the year-specific variables[30] [31]. As well, the condition number for the set of explanatory variables (39.67) reduces inference concerns that relate to multicollinearity because it is within the range of the generally regarded as safe level of 30 and well below the worrisome condition number of 100 (Belsley et al., 1980).

[30] We also estimated models with one-way (only MSA-specific) fixed effects, and these have largely similar results with those reported in Table 3.

[31] Separate year-specific and MSA-specific fixed effects were mostly statistically significant as well and are not reported in Table 3 for ease of exposition. Importantly, the significance of the MSA-specific dummy variables suggests that time-invariant characteristics such as fiscal policies at the regional level have an impact on the location patterns of biotechnology firm births.

[Table 4 about here]

The estimated coefficients for the NIH variables are largely positive and provide empirical support to the proposition that federal R&D spending contributes to local biotechnology firm births. Because the NIH funding variables for the recipient institutions appear in multiple terms (i.e., linear, quadratic, and cross-product terms), we have to combine the individual marginal effects to evaluate the overall marginal effect from NIH funding on firm births. The semi-elasticities for the three recipient types are reported for the two estimated Poisson models in Table 4. For research universities, the results of Table 4 indicate that, on average, an additional $1 million of public R&D funding awarded to universities over a 5 year period is expected to generate in the following year an increase of 5.93 percent in local firm births per MSA. Regarding the short run and long run effects of federal money on local firm births[32], the estimated long-run effect is close to 2 percent higher than the short-run effect (0.0612 and 0.0623 respectively).

With regard to the marginal effect of federal R&D funds awarded to private firms on the regional firm birth rate, the estimated semi-elasticity reported in Table 4 implies that, on average, an additional $1 million of federal R&D funds awarded to private firms over a 5 year period is expected to increase the number of local firm births in the following year by 58.11 percent per MSA. This finding provides empirical support to the proposition that the impact of federal R&D funding on firm creation is sensitive to the recipient type. What makes this finding striking is the sheer difference in magnitude. Federal R&D funding directed to private firms is found to have an impact on firm creation that is almost ten times larger than that directed to research universities. This difference is consistent with the findings of previous

[32] The long run effect is estimated with $\beta \; / \; 1 - \gamma$ where β is the short run effect and γ is the estimated coefficient of the lagged births variable (Wooldridge, 2009).

studies that document differential effects between industrial and academic R&D on firm births (Bade and Nerlinger, 2000; Karlsson and Nyström, 2011). Similar to the results for universities, the estimated short-run and long-run multipliers for private firms are nearly identical, and the marginal effects do not exhibit a higher order relationship that is economically relevant.

With regards to federal R&D funds awarded to research institutes and hospitals we find that the impact of such funds on local biotechnology firm creation is slightly lower than that of research universities but substantially lower than that of private firms. In particular, our results show that, on average, an additional $1 million of federal R&D funds awarded to research institutes/hospitals in a five year period is expected to increase the number of biotechnology firm births in the following year by about 5 percent for the MSA of interest. Given that unlike private firms, universities and research institutes are not driven mainly by profit maximization, a possible impetus of the observed difference may be the potential tendency of private firms to direct their efforts mainly towards the end of research with higher commercial value. It may also be the result of diminishing returns of public R&D funding to firm creation (note the difference in the relative size of public R&D spending in universities and private firms), or some other factor.

The statistical insignificance of the lagged dependent variable suggests that prior local firm births do not have strong explanatory power in the rate of local firm formation and the same holds for venture capital investments, the size of the MSA and its economic growth.

8. Sensitivity Analysis

In order to evaluate the robustness of our findings we performed a number of tests and we present the results in Table 5.

[Table 5 about here]

First, we tested for the case under which our results are influenced by a "virtuous cycle" where funds go to regions that already host many firms and in turn (mainly due to the enhanced capacity of firms to generate new firms from federal funds) these regions end up with more firms. To address the issue, we computed the annual NIH funds towards private firms in the same MSA measuring only those funds that went to firms that were at least seven years old[33]. As shown in Model 1 in Table 5, the results once again indicate that federal funds towards incumbent firms promote local firm births and imply that the estimates reported in Table 3 may represent a lower bound on the impact of such funds on the local startup rate. The estimates of the university and institutes impacts are in the same range with the estimates of Table 3 but the institute impact is no longer statistically significant.

The estimated scale parameter for the Poisson model reported in Table 3 indicates under-dispersion in the variance of the dependent variable (i.e., the observed variance is less than a standard Poisson random variable), which may be due to the large number of observations with a zero count[34]. Due to this potential under-dispersion, we also constructed a Generalized Poisson model (Famoye, 1993; Famoye and Singh, 2003) which has properties that are appropriate for under-dispersed data (Hilbe, 2011). The results of this model are

[33] We are grateful to two anonymous reviewers for pointing this potential issue and for suggesting ways to address it.

[34] The Poisson model with the variance equal to the mean is not reported in Table 3 because the Poisson variance assumption was not supported by the data.

presented as Model 2 in Table 5 and are qualitatively similar[35] with the results presented in Table 3.

In Model 3 we present estimates of a linear probability model that tests the sensitivity of our results to the exclusion of MSAs without firm births across years from the analysis that relates to the Maximum Likelihood estimator we used for the count models. In Model 3, those MSAs are included in the analysis. Although OLS ignores the count feature of the dependent variable, the estimates largely corroborate our previous findings that funds directed towards private firms have a much stronger marginal effect on local firm births than funds directed towards universities and research institutes/hospitals.

Another estimator that ignores the count feature of our data but addresses potential endogeneity between the dependent and the independent variables is the Arellano-Bond estimator (Arellano and Bond, 1991)[36]. In our application, in Model 4, we use it to test the possibility that our estimates are plagued by the potential endogeneity of the lagged dependent variable. The estimated coefficients do not provide evidence that such an issue is present in our models.

Models 5 to 8 test the sensitivity of our estimates to the model specification. In particular, we build models that include each funding category separately and then a model that does not include the interaction terms. The estimates of these models are largely comparable with the estimates presented in Table 3.

[35] The main difference is the statistical significance of the quadratic terms. But, their magnitude is so small that it suggests a nearly nonexistent economic impact from these higher-order terms.

[36] To construct the instruments we use a one year lag of the independent variables, which we model as weakly exogenous implying that we allow for the case that they are correlated both with "past and...possibly current realization of the error" (pg. 86 Roodman, 2009). Different configurations of the set of variables we use to construct the instruments yield qualitatively similar results to those reported in Table 5. The estimates presented in Model 4 of Table 5 are derived from the Arellano -Bond system estimator, which, in our application, yields similar estimates to the difference estimator.

Models 9 and 10 are built to test the robustness of our estimates to the construction of the time lag we used to estimate the effect of federal funds (5 year average). In model 9, the 5 year average lag is replaced by a one year lag and in model 10 the 5 year average lag is replaced by a 3 year average lag. Both models suggest that the choice of the lag structure does not significantly impact the results.

Finally, as we note at the bottom of Table 3 in order to include early years in the empirical analysis, we use a 5 year average for available observations where for example, the observation for 1995 is the average value of years 1992 to 1994, which is a 3 year average. In model 11 we test the potential influence of that choice in our estimates and build models that use observations only after 1997. The results are nearly identical to those presented in Table 3.

In conclusion, the tests we conducted support the overall conclusions we have drawn from our main results reported in Table 3 and indicate that our findings are robust to alternative model specifications and data constructions.

9. Summary, Discussion and Concluding Comments

Partly due to a strategic decision of the U.S. government to substantially increase funding towards R&D in order to boost the U.S. economy during the severe downturn of the late 2000s, interest in the relationship between public R&D spending and economic growth has been revitalized. A longstanding academic literature has established that public funding matters for economic growth as it increases innovation, productivity and the like. Nevertheless, the impact of public R&D funding on the creation of new firms has received little attention despite strong theoretical constructs that support the association. Indeed, empirical evidence on the relationship between public R&D funding and firm creation has been scant and indirect.

In this study, we have analyzed the relationship between federal R&D funds and local firm births in the U.S. biotechnology industry and our findings suggest that government R&D spending has a positive impact on firm creation. Our results, therefore, corroborate the empirical evidence that has been provided by a handful of previous studies that have also found a positive relationship between public R&D funds and regional firm births, especially in the biotechnology industry. Our analysis focused on biotechnology because it is central to the knowledge economy; it is a heavy recipient of federal research funds; it displays a close linkage between basic research and commercial application; and it tends to cluster around geographies and institutions that receive significant government R&D funding. As such, we presumed that if a positive relationship between public R&D spending and firm creation exists, it should be evident in the biotechnology industry.

By developing separate measures of the effect of federal R&D funds awarded to different types of recipient research institutions, we find that public funds dispensed for R&D to existing firms have, proportionally, a much stronger positive impact on local firm births than funds directed to universities and research institutes/hospitals. We also find that temporal and spatial factors in our analysis (two-way fixed effects) explain part of the variation in the birth rate of biotechnology firms across different Metropolitan Statistical Areas in the U.S. Hence, year-to-year variation in market conditions (e.g. “hot IPO” markets) as well as regional differences in infrastructure, business climate, taxes, initiatives and other factors tend to condition the overall impact of public R&D funding on firm creation. These findings reinforce our view that analysis of the relationship between public R&D spending and firm creation must be done over a long period of time and across large geographies to allow for lags as well as spatial and temporal variation that are inherent in such a relationship.

The specific quantitative results in our study are of particular interest. We find that, depending on the recipient of funds, a $1 million increase in the average amount of federal R&D funding associates with an increase of 5 to 58 percent in the number of local biotechnology firm births a few years later. Therefore, the magnitude of the effect has a considerable range. The specific size of this marginal effect is important because it relates to the job-creation process and other direct economic benefits associated with entrepreneurship and firm creation (Van Praag and Versloot, 2007). Given that such marginal effects have not been produced in other studies, it is important that future studies confirm and refine them. Having a deeper understanding of such marginal effects across sectors and geographies as well as of the conditions that determine them could boost the overall impact of public R&D funding on economic growth and employment. It could also provide a more accurate accounting of the extent public R&D funding corrects market failures in certain knowledge sectors.

Measurement of the marginal effects of public R&D on firm creation, like those we provide in this study, may also offer useful insights in the debate about the gradual emergence of the entrepreneurial university, which in addition to its teaching and research mission, promotes local firm births and economic development (Etzkowitz, 1998). Our empirical estimates suggest that publicly funded R&D in universities and research institutes has a positive impact on local firm creation. Characterizing the differences in such marginal effects between universities and private firms as well as across locations and sectors may help identify their sources and improve the efficiency of the entrepreneurial universities and their impact on local economies through the creation of new ventures.

Before closing, we note that our empirical models contain some unexplained variance. This variance can be reduced in a number of ways. We have discussed a number of

mechanisms that have been identified in the literature and could explain the differences in the marginal effects of public R&D spending we found in this study. However, we have not tested the relevance of such mechanisms in our analysis. Explicitly accounting for the mechanisms that shape the differential impact of government R&D spending on firm creation across recipient institutions, is an important area for further investigation. Also, we treat all institutions in our three fund recipient categories (university, private firm, and research institute or hospital) as homogeneous (aside from MSA-specific difference), but there are distinct types of academic institutions (Di Gregorio and Shane, 2003) or private firms that may affect the local rate of associated firm births differently. Future research can determine if these within-group differences are significant and how the different types of subgroups perform. Finally, data limitations do not allow us to directly account for the network ties in the biotechnology industry that have been noted in previous work. Testing whether federal funds influence the creation of such ties, which can promote local firm creation, could yield important insights.

Acknowledgements

Research funding provided by the Ewing Marion Kauffman Foundation Strategic Grant #20050176 is gratefully acknowledged. An earlier version of the paper was presented at the 35th DRUID Celebration Conference at ESADE Business School in Barcelona, Spain. We thank Peter Klein and James Kaufman for valuable inputs during the development of the paper and Sebastian Hoenen and Lifeng Tu for assistance in data collection.

References

Abel, J., Deitz, R., 2012. Do Colleges and Universities Increase Their Region's Human Capital? Journal of Economic Geography 12, 667-691.

Acs, Z.J., Audretsch, D.B., Feldman, M.P., 1994. R&D spillovers and innovative activity. Managerial and Decision Economics 15, 131-138.

Acs, Z.J., Braunerhjelm, P., Audretsch, D.B., Carlsson, B., 2009. The knowledge spillover theory of entrepreneurship. Small Business Economics 32, 15-30.

Agarwal, R., Echambadi, R., Franco, A.M., Sarkar, M.B., 2004. Knowledge Transfer Through Inheritance: Spin-out Generation, Development, and Survival. Academy of Management Journal 47, 501-522.

Aharonson, B.S., Baum, J.A.C., Plunket, A., 2008. Inventive and uninventive clusters: The case of Canadian biotechnology. Research Policy 37, 1108-1131.

Allison, P.D., 2008. Convergence failures in logistic regression, p. 2008.

Andersson, M., Koster, S., 2011. Sources of persistence in regional start-up rates—evidence from Sweden. Journal of Economic Geography 11, 179.

Anselin, L., Varga, A., Acs, Z.J., 1997. Local geographic spillovers between university research and high technology innovations. Journal of Urban Economics 42, 422-448.

Anselin, L., Varga, A., Acs, Z.J., 2000. Geographic and sectoral characteristics of academic knowledge externalities. Papers in Regional Science 79, 435-443.

Arellano, M., Bond, S., 1991. Some tests of specification for panel data: Monte Carlo evidence and an application to employment equations. The Review of Economic Studies 58, 277-297.

Argyres, N.S., Liebeskind, J.P., 1998. Privatizing the intellecutal commons: Universities and the commercialization of biotechnology. Journal of Economic Behavior & Organization 35, 427.

Arrow, K., 1962. Economic welfare and the allocation of resources for invention, in: Nelson, R.R. (Ed.), The Rate and Direction of Inventive Activity. Princeton University Press, Prinveton, NJ.

Arrow, K., 1971. Economic Welfare and the Allocation of Resources for R&D, in: Arrow, K. (Ed.), Essays in the Theory of Risk Bearing. American Elsevier, New York.

Audretsch, D.B., 1998. Agglomeration and the location of innovative activity. Oxford Review of Economic Policy 14, 18.

Audretsch, D.B., Keilbach, M., 2007. The Theory of Knowledge Spillover Entrepreneurship. Journal of Management Studies 44, 1242-1254.

Audretsch, D.B., Stephan, P.E., 1996. Company-Scientist Locational Links: The Case of Biotechnology. American Economic Review 86, 641-652.

Audretsch, D.B., Stephan, P.E., 1999. Knowledge spillovers in biotechnology: sources and incentives. Journal of Evolutionary Economics 9, 97-107.
Bade, F.-J., Nerlinger, E.A., 2000. The Spatial Distribution of New Technology-Based Firms: Empirical Results for West-Germany. Papers in Regional Science 79, 155-176.
Baptista, R., Mendonça, J., 2010. Proximity to knowledge sources and the location of knowledge-based start-ups. Annals of Regional Science 45, 5-29.
Bartik, T.J., 1985. Business Location Decisions in the United States: Estimates of the Effects of Unionization, Taxes, and Other Characteristics of States. Journal of Business and Economic Statistics 3, 14-22.
Bartik, T.J., 1989. Small Business Start-Ups in the United States: Estimates of the Effects of Characteristics of States. Southern Economic Journal 55, 1004-1018.
Bartik, T.J., Gray, W.B., 2002. The Effects of Environmental Regulation on Business Location in the United States, Economic costs and consequences of environmental regulation. International Library of Environmental Economics and Policy.Aldershot, U.K. and Burlington, Vt.:Ashgate, Dartmouth, pp. 129-151.
Basken, P., 2012. In Budget Battle, Science Faces New Pressures to Prove It Delivers, The Chronicle of Higher Education.
Bathelt, H., Malmberg, A., Maskell, P., 2004. Clusters and knowledge: local buzz, global pipelines and the process of knowledge creation. Progress in Human Geography, 31-56.
Baum, J.A.C., Calabrese, T., Silverman, B.S., 2000. Don't go it alone: Alliance network composition and startups' performance in Canadian biotechnology. Strategic Management Journal 21, 267-294.
Beise, M., Stahl, H., 1999. Public research and industrial innovations in Germany. Research Policy 28, 397-422.
Belsley, D.A., Kuh, E., Welsch, R.E., 1980. Regression diagnostics. Wiley Online Library.
Bernanke, B., 2011. Promoting Research and Development: The Government's Role, Speech at the Conference on "New Building Blocks for Jobs and Economic Growth." Washington, D.C.
Bhide, A., 1994. How Entrepreneurs Craft Strategies That Work. Harvard Business Review 72, 150-161.
Brainard, J., 2006. NIH Allows Multiple Principal Investigators on Grants and Stops Compiling Departmental Rankings, The Chronicle of Higher Education.
Breschi, S., Lissoni, F., 2001. Localised knowledge spillovers vs. innovative milieux: Knowledge "tacitness" reconsidered. Papers in Regional Science 80, 255-273.
Chachamidou, M., Logothetidis, S., 2008. Spin-off creation behaviour of universities and research institutions: an initial approach for nanotechnology. International Journal of Technology Transfer & Commercialisation 7, 384-397.
Chaminade, C., Edquist, C., 2006. Rationales for public policy intervention in the innovation process: A systems of innovation approach, in: Smits, E.R., Kuhlmann, S., Shapira, P. (Eds.), The Theory and Practice of Innovation Policy. An International Research Handbook. . Edward Elgar, Cheltenham, UK & Northampton, MA, USA, pp. 95-114.
Chen, K., Marchioni, M., 2008. Spatial Clustering of Venture Capital-Financed Biotechnology Firms in the U.S. Industrial Geographer 5, 19-38.
Cohen, W.M., Levinthal, D.A., 1989. Innovation and learning: the two faces of R & D. Economic Journal 99, 569-596.

Dahl, M.S., Pedersen, C.Ø.R., 2004. Knowledge flows through informal contacts in industrial clusters: myth or reality? Research Policy 33, 1673-1686.
Di Gregorio, D., Shane, S., 2003. Why Do Some Universities Generate More Start-Ups Than Others? Research Policy 32, 209-227.
DiMasi, J.A., Grabowski, H.G., 2007. The cost of biopharmaceutical R&D: Is biotech different? Managerial and Decision Economics 28, 469-479.
Dohse, D., 2000. Technology policy and the regions—the case of the BioRegio contest. Research Policy 29, 1111-1133.
Döring, T., Schnellenbach, J., 2006. What do we know about geographical knowledge spillovers and regional growth?: A survey of the literature. Regional Studies 40, 375-395.
Ernst&Young, 2012. Beyond Borders: Global Biotechnology Report 2012.
Etzkowitz, H., 1998. The norms of entrepreneurial science: cognitive effects of the new university-industry linkages. Research Policy 27, 823.
Famoye, F., 1993. Restricted generalized Poisson regression model. Communications in statistics. Theory and methods 22, 1335-1354.
Famoye, F., Singh, K., 2003. On Inflated Generalized Poisson Regression Models. Advances and Applications in Statistics 3, 13.
Feldman, M.P., Kelley, M.R., 2006. The ex ante assessment of knowledge spillovers: Government R&D policy, economic incentives and private firm behavior. Research Policy 35, 1509-1521.
Fischer, M.M., Varga, A., 2003. Spatial knowledge spillovers and university research: evidence from Austria. Annals of Regional Science 37, 303-322.
Frenkel, A., 2001. Why High-technology Firms Choose to Locate in or near Metropolitan Areas. Urban Studies 38, 1083-1102.
Garvin, D.A., 1983. Spin-Offs and the New Firm Formation Process. California Management Review 25, 3-20.
Goetz, S.J., Morgan, R.S., 1995. State-level locational determinants of biotechnology firms. Economic Development Quarterly 9, 174.
Greene, W., 2002. The bias of the fixed effects estimator in nonlinear models. Unpublished manuscript.
Griliches, Z., 1992. The search for R&D spillovers. Scandinavian Journal of Economics 94, 29-47.
Grossman, G.M., Helpman, E., 1992. Innovation and growth in the global economy. MIT press.
Hall, B.H., 1996. The private and social returns to research and development, in: Smith, B.L.R., Barefield, C.E. (Eds.), Technology, R&D, and the Economy. Brookings Institution and the American Enterprise Institute, Washington, DC., pp. 140-183.
Hand, E., 2009. Science grants rise with stimulus spending, Nature.
Haussler, C., Zademach, H.-M., 2007. Cluster performance reconsidered: Structure, linkages and paths in the German biotechnology industry, 1996-2003. Schmalenbach Business Review (SBR) 59, 261-281.
Hilbe, J.M., 2011. Negative binomial regression. Cambridge Univ Pr.
Jaffe, A.B., 1989. Real effects of academic research. American Economic Review, 957-970.
Karlsson, C., Nyström, K., 2011. Knowledge accessibility and new firm formation, in: Desai, S., Nijkamp, P., Stough, R.R. (Eds.), NEW DIRECTIONS IN REGIONAL

ECONOMIC DEVELOPMENT. Edward Elgar Publishing, Inc., Northampton, Massachusetts, pp. 174-197.
Kenney, M., 1986. Biotechnology: The university industrial complex. Yale University Press.
Kim, J., Marschke, G., 2005. Labor Mobility of Scientists, Technological Diffusion, and the Firm's Patenting Decision. RAND Journal of Economics 36, 298-317.
Kim, Y., Kim, W., Yang, T., 2011. The effect of the triple helix system and habitat on regional entrepreneurship: Empirical evidence from the US. Research Policy 41, 154-166.
Kirchhoff, B.A., Newbert, S.L., Hasan, I., Armington, C., 2007. The Influence of University R & D Expenditures on New Business Formations and Employment Growth. Entrepreneurship: Theory & Practice 31, 543-559.
Klepper, S., Sleeper, S., 2005. Entry by Spinoffs. Management Science 51, 1291-1306.
Klevorick, A.K., Levin, R.C., Nelson, R.R., Winter, S.G., 1995. On the sources and significance of interindustry differences in technological opportunities. Research Policy 24, 185-205.
Kolympiris, C., Kalaitzandonakes, N., 2013. Geographic scope of proximity effects among small life sciences firms. Small Business Economics 40, 1059-1086.
Kolympiris, C., Kalaitzandonakes, N., Miller, D., 2011. Spatial collocation and venture capital in the US biotechnology industry. Research Policy 40, 1188-1199.
Lazonick, W., Tulum, Ö., 2011. US biopharmaceutical finance and the sustainability of the biotech business model. Research Policy 40, 1170-1187.
Ledbetter, A., Zipkin, I., 2002. Achieving venture returns through corporate spinouts. Journal of Commercial Biotechnology 8, 339.
Liebeskind, J.P., Oliver, A.L., Zucker, L.G., Brewer, M.B., 1996. Social networks, learning, and flexibility: Sourcing scientific knowledge in new biotechnology firms. Organization Science, 428-443.
Lockett, A., Wright, M., 2005. Resources, Capabilities, Risk Capital and the Creation of University Spin-Out Companies. Research Policy 34, 1043-1057.
Lowry, M., Schwert, G., 2002. IPO market cycles: Bubbles or sequential learning? Journal of Finance 57, 1171-1200.
Mansfield, E., 1991. Academic research and industrial innovation. Research Policy 20, 1-12.
Mansfield, E., 1995. Academic research underlying industrial innovations: sources, characteristics, and financing. Review of Economics and Statistics, 55-65.
Mansfield, E., 1997. Academic research and industrial innovation: An update of empirical findings. Research Policy 26, 773-776.
McMillan, G.S., Narin, F., 2000. An analysis of the critical role of public science in innovation: the case of biotechnology. Research Policy 29, 1.
Mervis, J., 2009. Amid the Gloom, Researchers Prepare for a Boom in Funding. Science 323, 1274-1275.
Narin, F., Hamilton, K.S., Olivastro, D., 1997. The increasing linkage between US technology and public science. Research Policy 26, 317-330.
Ndonzuau, F.N., Pirnay, F., Surlemont, B., 2002. A stage model of academic spin-off creation. Technovation 22, 281.
Nelson, R.R., 1959. The simple economics of basic scientific research. The Journal of Political Economy 67, 297-306.
Nichols, A., Schaffer, M.E., 2007. Clustered standard errors in Stata, United Kingdom Stata Users' Group Meetings 2007. Stata Users Group.

Orsenigo, L., Pammolli, F., Riccaboni, M., 2001. Technological change and network dynamics - Lessons from the pharmaceutical industry. Research Policy 30, 485-508.
Owen-Smith, J., Powell, W.W., 2004. Knowledge networks as channels and conduits: The effects of spillovers in the Boston biotechnology community. Organization Science 15, 5-21.
Pisano, G., 2006. Can science be a business? Harvard Business Review 10, 1-12.
Pouder, R., St. John, C.H., 1996. Hot spots and blind spots; geographic clusters of firms and innovation. Academy of Management Review 21, 1192-1225.
Powell, W.W., 1996. Inter-organizational collaboration in the biotechnology industry. Journal of Institutional and Theoretical Economics (JITE), 197-215.
Powell, W.W., Koput, K.W., Bowie, J.I., Smith-Doerr, L., 2002. The spatial clustering of science and capital: Accounting for biotech firm-venture capital relationships. Regional Studies 36, 291-305.
Powell, W.W., Koput, K.W., Smith-Doerr, L., 1996. Interorganizational collaboration and the locus of innovation: Networks of learning in biotechnology. Administrative Science Quarterly, 116-145.
Powell, W.W., Packalen, K.A., Whittington, K., 2012. Organizational and institutional genesis: The emergence of high-tech clusters in the life sciences, in: Padgett, J., Powell, W.W. (Eds.), The emergence of Organizations and Markets. Princeton University Press, Princeton & Oxford.
Powell, W.W., Snellman, K., 2004. The knowledge economy. Annual review of sociology, 199-220.
Rathelot, R., Sillard, P., 2008. The Importance of Local Corporate Taxes in Business Location Decisions: Evidence from French Micro Data. Economic Journal 118, 499-514.
Renault, C.S., 2006. Academic capitalism and university incentives for faculty entrepreneurship. The Journal of Technology Transfer 31, 227-239.
Roodman, D., 2009. How to do xtabond2: An introduction to difference and system GMM in Stata. The Stata Journal 9, 86-136.
Salter, A.J., Martin, B.R., 2001. The economic benefits of publicly funded basic research: a critical review. Research Policy 30, 509-532.
Samila, S., Sorenson, O., 2010. Venture capital as a catalyst to commercialization. Research Policy 39, 1348 - 1360.
Samila, S., Sorenson, O., 2011. Venture capital, entrepreneurship and economic growth. Review of Economics and Statistics 93, 338-349.
Saxenian, A.L., 1991. The origins and dynamics of production networks in Silicon Valley. Research Policy 20, 423-437.
Shane, S., 2009. Why encouraging more people to become entrepreneurs is bad public policy. Small Business Economics 33, 141-149.
Shaver, J.M., Flyer, F., 2000. Agglomeration economies, firm heterogeneity, and foreign direct investment in the United States. Strategic Management Journal 21, 1175-1193.
Steffensen, M., Rogers, E.M., 2000. Spin-Offs From Research Centers at a Research University. Journal of Business Venturing 15, 93.
Stephan, P., 2012. How economics shapes science. Harvard University Press.
Stimson, J.A., 1985. Regression in space and time: A statistical essay. American Journal of Political Science, 914-947.

Stuart, T.E., Sorenson, O., 2003a. The geography of opportunity: spatial heterogeneity in founding rates and the performance of biotechnology firms. Research Policy 32, 229.
Stuart, T.E., Sorenson, O., 2003b. Liquidity Events and the Geographic Distribution of Entrepreneurial Activity. Administrative Science Quarterly 48, 175-201.
Tijssen, R.J.W., 2002. Science dependence of technologies: evidence from inventions and their inventors. Research Policy 31, 509-526.
Toole, A.A., 2012. The impact of public basic research on industrial innovation: Evidence from the pharmaceutical industry. Research Policy 41, 1-12.
Van Praag, C.M., Versloot, P.H., 2007. What is the value of entrepreneurship? A review of recent research. Small Business Economics 29, 351-382.
Wennekers, S., Thurik, R., 1999. Linking entrepreneurship and economic growth. Small Business Economics 13, 27-56.
Wessner (ed.), W.C., 2009. An Assessment of the SBIR Program at the National Institutes of Health. National Research Council, Washington, D.C.
Whittington, K.B., Owen-Smith, J., Powell, W.W., 2009. Networks, propinquity, and innovation in knowledge-intensive industries. Administrative Science Quarterly 54, 90-122.
Wobbekind, R., Lewandowski, B., DiPersio, C., Ford, R., Streit, R., 2012. Economic Impacts of the University of Colorado on the State and Counties of Operations.
Woodward, D., Figueiredo, O., Guimaraes, P., 2006. Beyond the Silicon Valley: University R&D and high-technology location. Journal of Urban Economics 60, 15-32.
Wooldridge, J.M., 1999. Distribution-free estimation of some nonlinear panel data models. Journal of Econometrics 90, 77-97.
Wooldridge, J.M., 2002. Econometric analysis of cross section and panel data. The MIT press.
Wooldridge, J.M., 2009. Introductory econometrics: A modern approach. South Western Cengage Learning.
Woolley, J.L., Rottner, R.M., 2008. Innovation Policy and Nanotechnology Entrepreneurship. Entrepreneurship: Theory & Practice 32, 791-811.
Zhang, J., 2009. The performance of university spin-offs: an exploratory analysis using venture capital data. The Journal of Technology Transfer 34, 255-285.
Zorn, C., 2006. Comparing GEE and robust standard errors for conditionally dependent data. Political Research Quarterly 59, 329-341.
Zucker, L.G., Darby, M.R., Brewer, M.B., 1998. Intellectual Human Capital and the Birth of U.S. Biotechnology Enterprises. American Economic Review 88, 290-306.

Table 1

Table 1. Correlation Coefficients Between Award Amounts per MSA Year

	UN	IN	PR
UN	1.00	0.55	0.57
IN	0.55	1.00	0.52
PR	0.57	0.52	1.00

UN	Average NIH Funds from t-1 to t-5 towards universities per MSA Year
IN	Average NIH Funds from t-1 to t-5 towards institutes and hospitals per MSA Year
PR	Average NIH Funds from t-1 to t-5 towards private firms per MSA Year

Table 2

Table 2. Descriptive Statistics of Variables Used in the Empirical Analysis

Variable / Statistic	Mean	Median	Mode	Standard Deviation
Number of Biotechnology Firm Births for each MSA Year	0.184	0.000	0.000	1.019
Average Federal Funds Amount towards MSA universities in the 5 years proceeding firm birth (2007 M$)	3.695	0.000	0.000	13.795
Average Federal Funds Amount towards MSA private firms in the 5 years proceeding firm birth (2007 M$)	0.119	0.000	0.000	0.692
Average Federal Funds Amount towards MSA institutes in the 5 years proceeding firm birth (2007 M$)	0.996	0.000	0.000	7.460
Average total venture capital funds invested in the MSA in the 5 years proceeding firm birth (2007 M$)	4.881	0.000	0.000	36.817
MSA population at time t (Million)	0.654	0.225	0.110	1.512
Average MSA GDP in the 5 years proceeding firm birth (2007 M$)	18,955.818	4,653.830	2,473.650	55,877.052

Table 3

Table 3. Count Estimates of Poisson Model with Mean Equal Variance Assumption Relaxed. The Dependent Variable is the Number of Biotechnology Firm Births at Time t in MSA i.

	Model	Model 1: Poisson (without Variance Restriction) Full Model			Model 2: Poisson (without Variance Restriction) Excluding Temporal Lag		
		Estimate		S.E.	Estimate		S.E.
	Intercept	-4.2939	***	0.3264	-4.2626	***	0.3090
	Biotech Firm Births in MSA in t-1	0.0186		0.0235			
	Average Amount Awarded ($2007 M.) to MSA Universities from t-1 to t-5[a]	0.0612	***	0.0237	0.0612	***	0.0239
	Average Amount Awarded ($2007 M.) to MSA Inst./Hospitals from t-1 to t-5[a]	0.0508	***	0.0195	0.0538	***	0.0174
	Average Amount Awarded ($2007 M.) to MSA Private Firms from t-1 to t-5[a]	0.6127	***	0.1043	0.6245	***	0.1067
	(Average Amount Awarded ($2007 M.) to MSA Universities from t-1 to t-5)^2	-0.0001		0.0002	-0.0001		0.0002
	(Average Amount Awarded ($2007 M.) to MSA Inst./Hospitals from t-1 to t-5)^2	0.0002		0.0002	0.0002		0.0002
	(Average Amount Awarded ($2007 M.) to MSA Private Firms from t-1 to t-5)^2	-0.0014		0.0117	-0.0017		0.0119
	University Funds * Inst./Hospitals Funds	-0.0003		0.0004	-0.0004		0.0004
	University Funds * Private Firms Funds	-0.0065	***	0.0014	-0.0065	***	0.0014
	Private Firms Funds * Inst./Hospitals Funds	-0.0073	***	0.0019	-0.0076	***	0.0018
	Average Amount of Venture Capital Funds Invested to Biotechnology Firms from t-1 to t-5	-0.0009		0.0007	-0.0008		0.0007
	Population of the MSA at t	0.0267		0.1093	0.0288		0.1110
	Average GDP observed at the MSA from t-1 to t-5	0.0000		0.0000	0.0000		0.0000
Year Fixed Effects[b] Included		YES			YES		
MSA Fixed Effects Included		YES			YES		
Scale		0.5613			0.5615		
Fit Statistics (AIC and Log Likelihood from Maximum Likelihood Estimation)	Test of Joint Significance of Year Fixed Effects	3.660	**		4.180	**	
	Test of Joint Significance of MSA Fixed Effects	41.160	***		41.890	***	
	Log Likelihood	-1890.148			-1891.756		
	AIC	3504.438			3504.477		
	Multicollinearity Condition Number	39.673			38.395		
	Number of Observations	6480			6480		

[a] In order to include years 1992 to 1996 in the analysis, the averages are calculated as the average of available observations. For year 1996 for example, the average used in the model is the average NIH$ from 1992 to 1995, which is a 4 and not 5 year average.

[b] The omited year is 2007

*** .001 significance, ** .05 significance, * .10 significance

Notes: 1. The log link function was used for the Poisson model. 2. Standard errors reported are clustered at the MSA level

Table 4

Table 4. Semi-elasticities for the Variables that Measure the Rate at Which Federal Funds Towards Different Types of Institutions Associate with Biotechnology Firm Births at the MSA Level.

Model	Model 1: Poisson (without Variance Restriction) Full Model	Model 2: Poisson (without Variance Restriction) Excluding Temporal Lag
Percentage change in the expected number of firm births in the focal MSA at year t, given a 1 million increase in the average NIH funding level of universities located in the MSA from t-1 to t-5	5.9388	5.9288
Percentage change in the expected number of firm births in the focal MSA at year t, given a 1 million increase in the average NIH funding level of research institutes / hospitals located in the MSA from t-1 to t-5	4.9923	5.2518
Percentage change in the expected number of firm births in the focal MSA at year t, given a 1 million increase in the average NIH funding level of private firms located in the MSA from t-1 to t-5	58.1078	59.2508

Table 5a

Table 5. Estimates of Models Testing the Robustness of the Results. The Dependent Variable is the Number of Biotechnology Firm Births at Time t in MSA i.

	Model Number	1		2		3		4	
	Model Description	Model where the NIH funds towards private firms measures only funds towards firms that were at least 7 years old at the year in question. Standard errors are clustered at the MSA level		Generalized Poisson		Linear Probability Model with Heteroskedasticty - Robust Standard Errors		Arellano - Bond Estimator	
		Estimate	S.E.	Estimate	S.E.	Estimate	S.E.	Estimate	S.E.
	Intercept	-4.3297 ***	0.2960	-4.3212 ***	0.1975	0.0381	0.0934	-0.2554 ***	0.0732
	Biotech Firm Births in MSA in t-1	0.0525 **	0.0230	0.0084	0.0161	0.1876 ***	0.0629	0.0620 ***	0.0135
	Average Amount Awarded ($2007 M.) to MSA Universities from t-1 to t-5[a]	0.0496 ***	0.0181	0.0676 ***	0.0080	0.0138 *	0.0078	0.0129 ***	0.0043
	Average Amount Awarded ($2007 M.) to MSA Inst./Hospitals from t-1 to t-5[a]	0.0381	0.0423	0.0546 ***	0.0078	0.0881 ***	0.0211	0.0942 ***	0.0158
	Average Amount Awarded ($2007 M.) to MSA Private Firms from t-1 to t-5[a]	0.9593 ***	0.2990	0.5855 ***	0.0595	0.2635 *	0.1597	0.1638 ***	0.0603
	(Average Amount Awarded ($2007 M.) to MSA Universities from t-1 to t-5)^2	0.0000	0.0001	-0.0001 ***	0.0000	0.0001	0.0001	0.0000	0.0000
	(Average Amount Awarded ($2007 M.) to MSA Inst./Hospitals from t-1 to t-5)^2	0.0000	0.0002	0.0002 ***	0.0000	-0.0001	0.0002	-0.0011 **	0.0005
	(Average Amount Awarded ($2007 M.) to MSA Private Firms from t-1 to t-5)^2	-0.0292	0.0301	0.0050	0.0062	0.0152	0.0187	0.0083	0.0054
	University Funds * Inst./Hospitals Funds	-0.0005	0.0006	-0.0002	0.0002	-0.0002	0.0004	-0.0009 ***	0.0003
	University Funds * Private Firms Funds	-0.0095	0.0073	-0.0074 ***	0.0008	-0.0054 ***	0.0021	-0.0017	0.0011
	Private Firms Funds * Inst./Hospitals Funds	0.0081	0.0099	-0.0080 ***	0.0014	0.0014	0.0080	0.0039	0.0034
	Average Amount of Venture Capital Funds Invested to Biotechnology Firms from t-1 to t-5	-0.0016	0.0018	-0.0008	0.0008	-0.0023	0.0044	-0.0002	0.0007
	Population of the MSA at t	0.2593 ***	0.0787	0.0366	0.0494	0.1564 ***	0.0474	0.9392 ***	0.1660
	Average GDP observed at the MSA from t-1 to t-5	0.0000	0.0000	0.0000 ***	0.0000	0.0000 ***	0.0000	0.0000 ***	0.0000
Year Fixed Effects[b] Included		YES		YES		YES		YES	
MSA Fixed Effects Included		YES		YES		YES		YES	
Scale		0.5849							
	Test of Joint Significance of Year Fixed Effects	6.690 ***		5.190 **		32.850 **		37.612 **	
	Test of Joint Significance of MSA Fixed Effects	31.360 ***		171.030 ***		102.040 ***		115.347 ***	
Fit Statistics (for count models the Log Likelihood and the AIC are from models estimated with Maximum Likelihood)	Log Likelihood	-1992.011							
	AIC	3678.757		3379.300					
	Adjusted R^2					0.739			
	Wald χ^2							297.350 ***	
	Multicollinearity Condition Number	41.079		39.673		41.579		33.978	
	Number of Observations	6480		6480		6480		5831	

[a] In order to include years 1992 to 1996 in the analysis, the averages are calculated as the average of available observations. For year 1996 for example, the average used in the model is the average NIH$ from 1992 to 1995, which is a 4 and not 5 year average. In models 9 and 10 the estimates represent a one year lag and a three years average respectively. The square terms as well as the interaction effects are calculated accordingly.

[b] The omited year is 2007

*** .001 significance, ** .05 significance, * .10 significance

The log link function was used for the Poisson model

Table 5b

Table 5 continued. Estimates of Models Testing the Robustness of the Results. The Dependent Variable is the Number of Biotechnology Firm Births at Time t in MSA i.

	Model Number	5		6		7		8	
	Model Description	Model including only NIH funds towards universities. Standard errors are clustered at the MSA level		Model including only NIH funds towards institutes and hospitals. Standard errors are clustered at the MSA level		Model including only NIH funds towards firms. Standard errors are clustered at the MSA level		Model excluding interaction terms from the analysis. Standard errors are clustered at the MSA level	
		Estimate	S.E.	Estimate	S.E.	Estimate	S.E.	Estimate	S.E.
	Intercept	-4.4941 ***	0.6441	-3.3875 ***	0.3248	-3.5408 ***	0.4910	-4.3855 ***	0.3343
	Biotech Firm Births in MSA in t-1	0.1172 ***	0.0346	0.0824 **	0.0401	0.1137 ***	0.0169	0.0398	0.0250
	Average Amount Awarded ($2007 M.) to MSA Universities from t-1 to t-5[a]	0.0902 ***	0.0206					0.0692 ***	0.0225
	Average Amount Awarded ($2007 M.) to MSA Inst./Hospitals from t-1 to t-5[a]			0.0709 ***	0.0111			0.0244 *	0.0125
	Average Amount Awarded ($2007 M.) to MSA Private Firms from t-1 to t-5[a]					0.9261 ***	0.1343	0.5981 *	0.3125
	(Average Amount Awarded ($2007 M.) to MSA Universities from t-1 to t-5)^2	-0.0004 **	0.0002					-0.0003 **	0.0002
	(Average Amount Awarded ($2007 M.) to MSA Inst./Hospitals from t-1 to t-5)^2			-0.0003	0.0000			-0.0001	0.0001
	(Average Amount Awarded ($2007 M.) to MSA Private Firms from t-1 to t-5)^2					-0.0668 ***	0.0125	-0.0291	0.0184
	University Funds * Inst./Hospitals Funds								
	University Funds * Private Firms Funds								
	Private Firms Funds * Inst./Hospitals Funds								
	Average Amount of Venture Capital Funds Invested to Biotechnology Firms from t-1 to t-5	-0.0002	0.0009	-0.0006	0.0004	0.0018 **	0.0008	-0.0044 ***	0.0016
	Population of the MSA at t	-0.1028	0.1475	0.2478 ***	0.0522	0.3224 ***	0.0509	-0.0295	0.1134
	Average GDP observed at the MSA from t-1 to t-5	0.0000	0.0000	0.0000 ***	0.0000	0.0000 ***	0.0000	0.0000	0.0000
Year Fixed Effects[b] Included		YES		YES		YES		YES	
MSA Fixed Effects Included		YES		YES		YES		YES	
Scale		0.6101		0.6418		0.6396		0.5802	
	Test of Joint Significance of Year Fixed Effects	4.110 **		0.540		0.310		8.030 ***	
	Test of Joint Significance of MSA Fixed Effects	10.100 ***		11.240 ***		16.440 ***		33.710 ***	
Fit Statistics (for count models the Log Likelihood and the AIC are from models estimated with Maximum Likelihood)	Log Likelihood	-2091.908		-2197.114		-2190.437		-1974.693	
	AIC	3856.823		4109.498		4091.873		3637.283	
	Adjusted R^2								
	Wald χ^2								
	Multicollinearity Condition Number	14.822		12.412		12.768		18.177	
	Number of Observations	6480		6480		6480		6480	

[a] In order to include years 1992 to 1996 in the analysis, the averages are calculated as the average of available observations. For year 1996 for example, the average used in the model is the average NIH$ from 1992 to 1995, which is a 4 and not 5 year average. In models 9 and 10 the estimates represent a one year lag and a three years average respectively. The square terms as well as the interaction effects are calculated accordingly.

[b] The omited year is 2007

*** .001 significance, ** .05 significance, * .10 significance

The log link function was used for the Poisson model

Table 5c

Table 5 continued. Estimates of Models Testing the Robustness of the Results. The Dependent Variable is the Number of Biotechnology Firm Births at Time t in MSA i.

	Model Number	9		10		11	
	Model Description	Model where the 5 year lag average of the NIH funds is replaced with a one year lag. Standard errors are clustered at the MSA level		Model where the 5 year lag average of the NIH funds is replaced with a 3 year lag average. Standard errors are clustered at the MSA level		Model where all observations have a 5 year lag average. Standard errors are clustered at the MSA level	
		Estimate	S.E.	Estimate	S.E.	Estimate	S.E.
	Intercept	-4.3137 ***	0.2933	-4.3607 ***	0.2923	-4.2763 ***	0.2773
	Biotech Firm Births in MSA in t-1	0.0499	0.0323	0.0161	0.0277	-0.0002	0.0232
	Average Amount Awarded ($2007 M.) to MSA Universities from t-1 to t-5[a]	0.0598 ***	0.0141	0.0571 ***	0.0173	0.0596 ***	0.0181
	Average Amount Awarded ($2007 M.) to MSA Inst./Hospitals from t-1 to t-5[a]	0.0337 ***	0.0118	0.0488 ***	0.0159	0.0478 ***	0.0174
	Average Amount Awarded ($2007 M.) to MSA Private Firms from t-1 to t-5[a]	0.4764 ***	0.0399	0.6066 ***	0.0772	0.6731 ***	0.1212
	(Average Amount Awarded ($2007 M.) to MSA Universities from t-1 to t-5)^2	-0.0001	0.0001	-0.0001	0.0001	0.0000	0.0002
	(Average Amount Awarded ($2007 M.) to MSA Inst./Hospitals from t-1 to t-5)^2	0.0000	0.0001	0.0002	0.0001	0.0002	0.0002
	(Average Amount Awarded ($2007 M.) to MSA Private Firms from t-1 to t-5)^2	-0.0026	0.0017	-0.0062	0.0067	-0.0028	0.0119
	University Funds * Inst./Hospitals Funds	-0.0001	0.0002	-0.0003	0.0003	-0.0004	0.0003
	University Funds * Private Firms Funds	-0.0046 ***	0.0010	-0.0051 ***	0.0013	-0.0074 ***	0.0012
	Private Firms Funds * Inst./Hospitals Funds	-0.0037 ***	0.0013	-0.0071 ***	0.0015	-0.0069 ***	0.0021
	Average Amount of Venture Capital Funds Invested to Biotechnology Firms from t-1 to t-5	-0.0006 *	0.0004	-0.0008	0.0007	-0.0006	0.0009
	Population of the MSA at t	-0.0067	0.1164	0.0226	0.1140	-0.0282	0.1319
	Average GDP observed at the MSA from t-1 to t-5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Year Fixed Effects[b] Included		YES		YES		YES	
MSA Fixed Effects Included		YES		YES		YES	
Scale		0.5637		0.5613		0.5559	
Fit Statistics (for count models the Log Likelihood and the AIC are from models estimated with Maximum Likelihood)	Test of Joint Significance of Year Fixed Effects	4.370 **		5.110 **		3.100 *	
	Test of Joint Significance of MSA Fixed Effects	38.930 ***		41.340 ***		54.520 ***	
	Log Likelihood	-1901.148		-1890.202		-1160.255	
	AIC	3521.668		-1633.262		2760.192	
	Adjusted R^2						
	Wald χ^2						
	Multicollinearity Condition Number	34.609		37.300		39.569	
	Number of Observations	6480		6480		5040	

[a] In order to include years 1992 to 1996 in the analysis, the averages are calculated as the average of available observations. For year 1996 for example, the average used in the model is the average NIH$ from 1992 to 1995, which is a 4 and not 5 year average. In models 9 and 10 the estimates represent a one year lag and a three years average respectively. The square terms as well as the interaction effects are calculated

[b] The omited year is 2007

*** .001 significance, ** .05 significance, * .10 significance

The log link function was used for the Poisson model

Appendix Table

Appendix Table. Keywords used to identify biotechnology related grants

affinity chromatography	Chinese Hamster Ovary	gene silencing	oligonucleotide
agarose	cho cells	gene targeting	oligo-nucleotide
Agarose gel electrophoresis	chromatid	Gene therapy	oligonucleotide ligation assay
allele	chromatin	gene transfer	oligonucleotide microarray
amplified fragment length polymorphism	Chromatography	geneflow	oligonucleotide probes
anticodon	chromosomal fragmentation	genetic	PCR
Antigen	chromosomal mapping	genetic discoveries	pcr test
Antisense	chromosomal mutation	genetic disorders	peptide
Arabidopsis	Chromosome	genetic engineering	plasmid
ascites	chromosome walking	genetic map	Polyacrylamide gel electrophoresis
assay	chrondocyte differentiation	genetic marker	polyclonal antibodies
bacillus	Cistron	genetic modification	polymerase chain reaction
Bacillus thuringiensis	clone	genetic parameters	Polymerase chain reaction (PCR)
bacteriophage	coli	genomics	recombinant adenovirus technology
Beta-glucans	collagen	glycopeptides	recombinant allergens
beta-glucuronidase	combinatorial biocatalysis	glycoprotein	recombinant antigens
bioassay	Combinatorial chemistry	glycosaminoglycan	recombinant collagens
biocomputing	Cyclic AMP (cyclic adenosine monophosphate)	glycosidase	recombinant enzymes
Biofiltration	Cytogenetic	glycosylation	recombinant genes
biolistics	cytokines	glycosyltransferases	recombinant proteins
biomass	cytokinesis	hormone	Restriction-fragment-length polymorphism (RFLP
biomedicine	cytosine	immunoaffinity chromatography	Reverse transcriptase
biopharma	Directional cloning	immunoassay	Southern blot
Biopharming	dna	Interferon	Southern hybridization (Southern blotting)
bioplastics	dna biosensor	Introgression	stem cells
biopolymers	dna chips	kinase	tissue engineering
bioprocess	dna detection	knockout mice	transcription factors
Bioprocessing	dna inihibitors	ligase chain reaction	Transgenic plants
Bioreactor	dna modification	Microarray	Western blot
Bioremediation	dna polymerases	microbial biotechnology	
biosensor	dna-chip	mitosis	
biosynthesis	elisa	monoclonal antibodies	
Biotelemetry	embryoandgenetic	Mouse model	
Biotic stress	enzyme	Mutagenesis	
blastocyst	Enzyme-linked immunosorbent assay (ELISA):	mutagenic substance	
bovine somatotropin	fab	mutation	
Cdna	Field trial	nanobiotechnology	
cell culture	functional genomics	neuron	
cellular assays	gene	neuropithelial stem cells	
cellular signaling	Gene (DNA) sequencing	Northern blot	
centromere	gene amplification	nucleotide	
chimeraplasty	Gene mapping	o-glycolsylation	

Figure 1

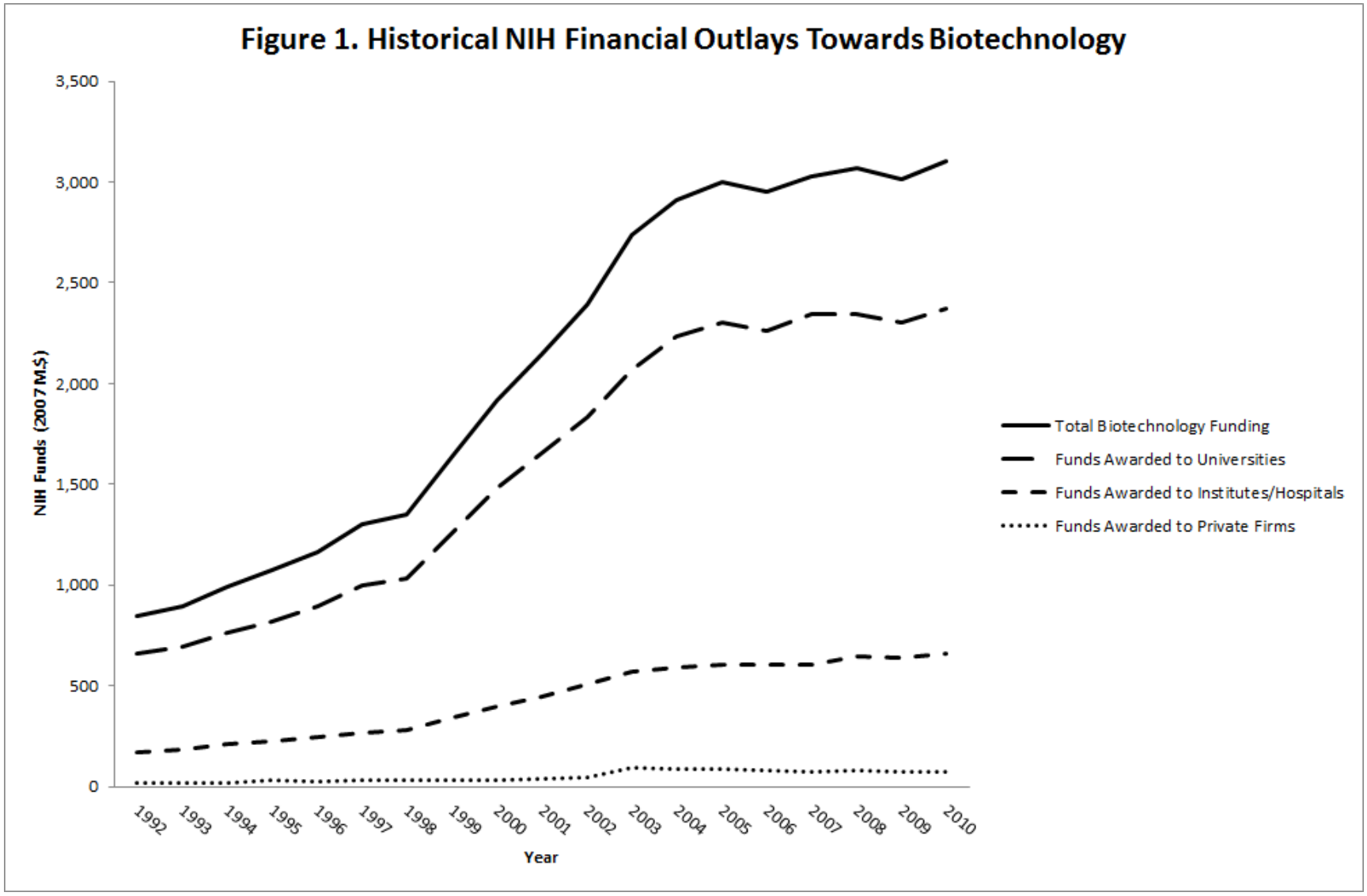
Figure 1. Historical NIH Financial Outlays Towards Biotechnology
NIH Funds (2007 M$)
3,500
3,000
2,500
2,000
1,500
1,000
500
0
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
Year
Total Biotechnology Funding
Funds Awarded to Universities
Funds Awarded to Institutes/Hospitals
Funds Awarded to Private Firms

Figure 2

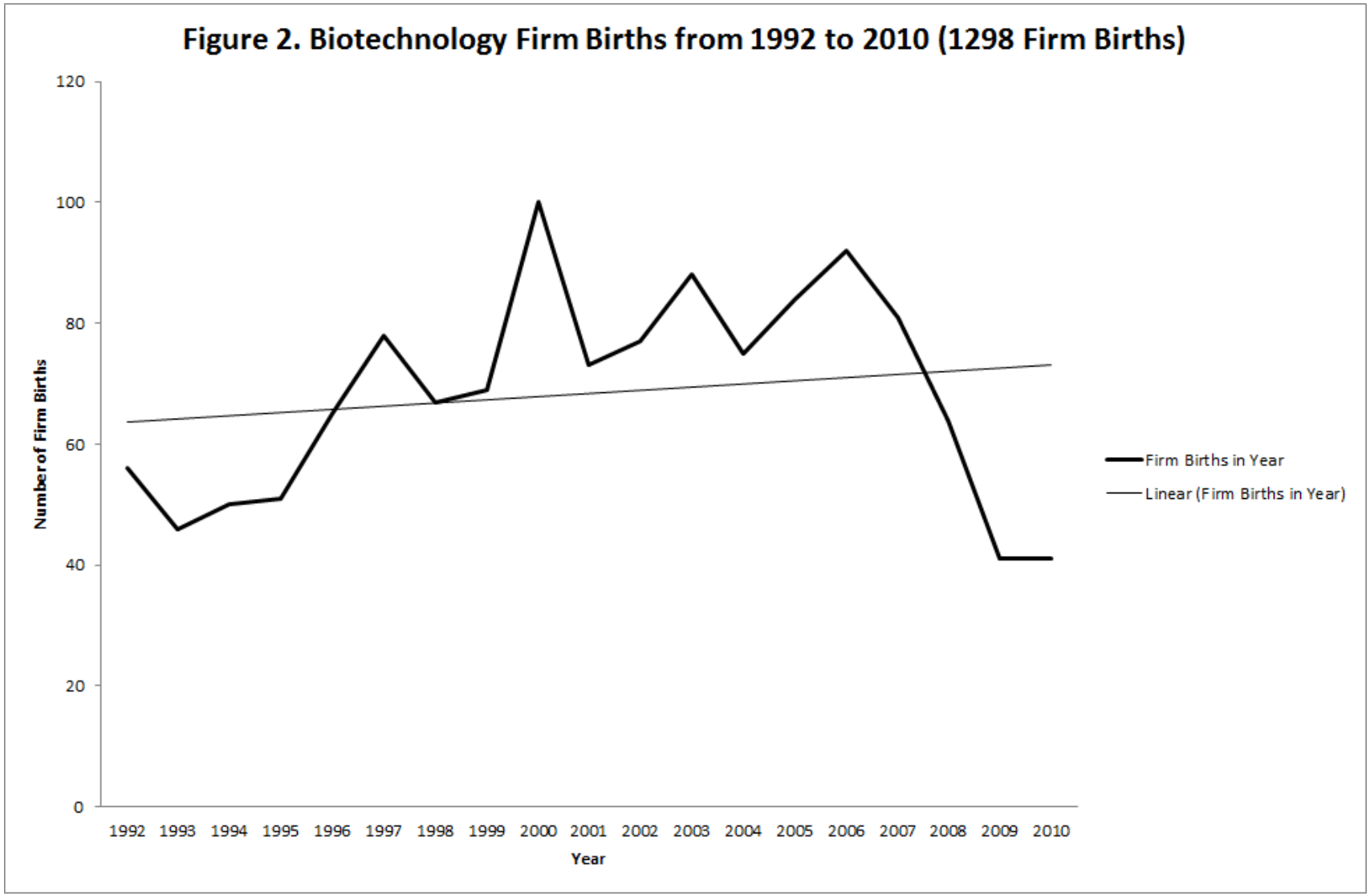
Figure 2. Biotechnology Firm Births from 1992 to 2010 (1298 Firm Births)
Number of Firm Births
120
100
80
60
40
20
0
1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010
Year
Firm Births in Year
Linear (Firm Births in Year)

Figure 3

Figure 3. MSA NIH Funds (2007$) and Firm Births from 1992 to 2010.